



European society for vascular surgery (ESVS) 2023 Clinical practice guidelines on the management of atherosclerotic carotid and vertebral artery disease

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FINAL DRAFT

EUROPEAN SOCIETY FOR VASCULAR SURGERY (ESVS) 2023 CLINICAL PRACTICE GUIDELINES ON THE MANAGEMENT OF ATHEROSCLEROTIC CAROTID AND VERTEBRAL ARTERY DISEASE

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A. Abbreviations and acronyms

ACAS	Asymptomatic Carotid Atherosclerosis Study	GA	General anaesthesia
ACE	Aspirin and Carotid Endarterectomy Trial	GC	Guidelines Committee
ACES	Asymptomatic Carotid Emboli Study	GWC	Guideline Writing Committee
ACS	Asymptomatic carotid stenosis	HDU	High Dependency Unit
ACSRs	Asymptomatic Carotid Stenosis and Risk of Stroke Study	HR	Hazard ratio
ACST	Asymptomatic Carotid Surgery Trial (1 & 2)	HRF	High risk feature
ACT-1	Asymptomatic Carotid Trial-1	HS	Hyperperfusion syndrome
AHA	American Heart Association	HTPR	High on treatment platelet reactivity
APRx	Antiplatelet therapy	ICA	Internal carotid artery
ARR	Absolute risk reduction	ICH	Intracerebral haemorrhage
ARWMC	Age related white matter change	ICSS	International Carotid Stenting Study
AF	Atrial fibrillation	IPH	Intraplaque haemorrhage
BA	Basilar artery	IA	Innominate artery
BD	<i>Bis die</i> (twice daily)	ISR	In stent re-stenosis
BES	Balloon expandable stent	ITU	Intensive therapy unit
BMS	Bare metal stent	iv	Intravenous
BMI	Body mass index	JBA	Juxtaluminal black area
BMT	Best medical therapy	LAA	Large artery atherosclerosis
BP	Blood pressure	LDL-C	Low density lipoprotein cholesterol
CA	Carotid angioplasty	LMWH	Low molecular weight heparin
CABG	Coronary artery bypass graft	LRA	Locoregional anaesthesia
CAD	Coronary artery disease	MCA	Middle cerebral artery
CAS	Carotid artery stenting	MDT	Multidisciplinary team
		MES	Micro-embolic signals
		MI	Myocardial infarction

CAVATAS	Carotid & Vertebral Artery Transluminal Angioplasty Study	MRA	Magnetic resonance angiography
		MRI	Magnetic resonance imaging
CaW	Carotid web	mRS	Modified Rankin Score
CCA	Common carotid artery	MT	Mechanical thrombectomy
CCF	Congestive cardiac failure	NASCET	North American Symptomatic Carotid Endarterectomy Trial
CEA	Carotid endarterectomy		
cCEA	Conventional carotid endarterectomy	NIBL	New ischaemic brain lesion
CEMRA	Contrast enhanced magnetic resonance angiography	NIHSS	National Institute of Health Stroke Score
		OR	Odds Ratio
CETC	Carotid Endarterectomy Trialists Collaboration	PAD	Peripheral arterial disease
		PCA	Posterior cerebral artery
CFA	Common femoral artery	PCSK9	Proprotein convertase subtilisin/kexin type 9
CI	Confidence Interval	PPI	Proton pump inhibitor
CNI	Cranial nerve injury	PSV	Peak systolic velocity
CNO	Carotid near occlusion	PTFE	Polytetrafluoroethylene
COMPASS	Cardiovascular Outcomes for People Using Anticoagulation Strategies	QC	Quality control
		QIP	Quality improvement programme
COPD	Chronic obstructive pulmonary disease	RCT	Randomised controlled trial
CoW	Circle of Willis	rTPA	Recombinant Tissue Plasminogen Activator
CPD	Cerebral protection device	RLN	Recurrent laryngeal nerve
CREST	Carotid Revascularisation vs. Stenting Trial	RR	Relative risk
CSTC	Carotid Stent Trialists Collaboration	RRI	Relative risk increase
CT	Computerised tomography	RRR	Relative risk reduction
CTA	Computerised tomography angiography	SAPPHIRE	Stenting & Angioplasty with Protection in Patients at High Risk for Endarterectomy
CVR	Cerebral vascular reserve		
DAPT	Dual antiplatelet therapy	SAMMPRIS	Stenting & Aggressive Medical Management for Preventing Recurrent Stroke & Intracranial Stenosis
DBP	Diastolic blood pressure		
DES	Drug eluting stent		
DLS	Dual layer stent	SBP	Systolic blood pressure
DM	Diabetes mellitus	SCS	Symptomatic carotid stenosis
DOAC	Direct oral anticoagulant	SVS	Society for Vascular Surgery (North America)
DSA	Digital subtraction angiography	SPACE	Stent Protected Angioplasty vs. Carotid Endarterectomy
DUS	Duplex ultrasound		
DWI	Diffusion weighted imaging	SSEP	Somatosensory evoked potentials

EAS	European Atherosclerosis Society	TCD	Transcranial Doppler
ECA	External carotid artery	TCAR	Transcarotid artery revascularisation
eCEA	Eversion carotid endarterectomy	TFCAS	Transfemoral carotid artery stenting
ECG	Electrocardiogram	TIA	Transient ischaemic attack
EC-IC	Extracranial intracranial	TOAST	Trial of ORG 10172 in Acute Stroke Treatment
ECST	European Carotid Surgery Trial	TRA	Transradial artery access
EEG	Electroencephalography	TT	Thrombolysis therapy
EJVES	European Journal of Vascular and Endovascular Surgery	UFH	Unfractionated heparin
ESC	European Society of Cardiology	USPSTF	US Preventive Services Taskforce
ESH	European Society of Hypertension	VACS	Veterans Affairs Co-operative Study
ESO	European Stroke Organisation	VA	Vertebral artery
ESVS	European Society for Vascular Surgery	VAST	Vertebral Artery Stenting Trial
EVA-3S	Endarterectomy vs. Stenting in patients with Symptomatic Severe carotid Stenosis	VB	Vertebrobasilar
FLAIR	Fluid attenuated inverse recovery	VISSIT	Vitesse Intracranial Stent Study for Ischaemic Stroke Therapy
FFT	Free floating thrombus	VAST	Vertebral Artery Ischaemia Stenting Trial
		VKA	Vitamin K antagonist
		VQI	Vascular Quality Initiative
		VSGNE	The Vascular Surgery Group of New England

B. What is 'new' in the 2023 guidelines?

Each section has been revised or rewritten and five new sections added; (i) management of free floating thrombus (**section 4.13**), (ii) management of carotid webs (**section 4.14**), (iii) management of symptomatic patients with an ipsilateral 50-99% carotid stenosis and atrial fibrillation (AF) (**section 4.16**), (iv) planning carotid interventions in anticoagulated patients (**section 4.2.6**) and (v) timing of carotid interventions in patients with acute ischaemic stroke undergoing thrombolysis (**section 4.8**). The 2023 European Society for Vascular Surgery (ESVS) carotid and vertebral guidelines also highlight similarities/discrepancies with the 2021 American Heart Association (AHA) guidelines on the management of stroke/transient ischaemic attack (TIA),¹ the 2021 European Stroke Organisation (ESO) guidelines on carotid

endarterectomy (CEA) and carotid artery stenting (CAS),² the 2021 German-Austrian guidelines on the management of carotid disease³ and the 2021 Society for Vascular Surgery (SVS) guidelines on the management of patients with carotid and vertebral artery disease.⁴ There are 133 recommendations, of which, 84 are unchanged, 11 have been 're-graded' since 2017 and 38 are new. The 2023 ESVS guidelines benefit from 289 new references (240 published between 2017-2022), including 39 primary or secondary analyses from randomised controlled trials (RCTs),⁵⁻⁴³ 71 systematic reviews and/or meta-analyses⁴⁴⁻¹¹⁴ and data from 50 vascular registries or quality initiative programmes (QIPs).¹¹⁵⁻¹⁶⁴

There is an expanded section on 'best medical therapy' (BMT) in asymptomatic (**section 3.1**) and symptomatic patients (**section 4.2**). There are new sections on the role of combination anti-platelet therapy (APRx) in recently symptomatic patients (**section 4.2.2.2**), including the peri-operative period (**sections 4.2.2.3 and 4.2.2.4**); thresholds for treating hypertension (**section 4.2.8**) and targets for lipid lowering therapy (**section 4.2.7.3**). There is a rewritten section on the relationship between asymptomatic carotid stenosis (ACS) and cognitive impairment (**section 3.10**). Since 2017, there is evidence that ACS patients with impaired cerebral vascular reserve (CVR) may be more likely to develop cognitive decline, but there remains no compelling evidence that CEA or CAS improves or prevents cognitive impairment. In the section on timing of CEA after thrombolysis (TT), meta-regression analyses suggest that a delay of six days after lysis completion should be considered before performing CEA, to maintain 30 day death/stroke rates within the 6% recommended threshold (**section 4.8**). The impetus towards treating symptomatic patients as soon as possible after transient ischaemic attack (TIA) or minor stroke is retained (**section 4.5**), with CEA being preferred over transfemoral CAS (TFCAS) when interventions are performed in the first 7-14 days after symptom onset (**section 4.5.4**). Whilst Transcarotid Artery Revascularisation (TCAR) has emerged as a promising new CAS technology since 2017, only one registry¹¹⁸ has reported outcomes stratified for delays from symptom

onset to TCAR (**section 4.5.5**). The recommendation that patients with 60 - 99% ACS in the presence of one or more clinical or imaging features that make them higher risk for stroke on best medical therapy (BMT), and who should be considered for CEA or CAS has been retained (**section 3.6**), but 80 - 99% ACS was not added to the 'high risk' criteria. The rationale underlying this decision is detailed in **section 3.6**. The section on CAS techniques has been expanded to reflect advances in technology since 2017 (**section 6**) and there is an updated section on carotid interventions after mechanical thrombectomy (MT) (**section 4.9**). The guidelines conclude with a list of 'unanswered questions' which highlight areas for future research (**Section 13**) and a new section on Information for the Patient (**Section 14**).

C. New Recommendations in the 2023 guidelines

No.	CLASS I
11	<i>For patients with asymptomatic carotid stenosis who are undergoing carotid endarterectomy, lower dose aspirin (75-325mg daily) rather than higher dose aspirin (>325mg daily) is recommended.</i>
23	<i>For symptomatic carotid stenosis patients who are not being considered for carotid endarterectomy or stenting following a transient ischaemic attack or minor ischaemic stroke, short term aspirin plus clopidogrel for 21 days followed by clopidogrel monotherapy, or long term aspirin plus dipyridamole modified release is recommended</i>
24	<i>For recently symptomatic carotid stenosis patients who are not being considered for carotid endarterectomy or stenting who are intolerant of, or allergic to, aspirin and clopidogrel, dipyridamole monotherapy or ticagrelor monotherapy is recommended</i>
25	<i>For recently symptomatic carotid stenosis patients in whom carotid endarterectomy is being considered, it is recommended that neurologists/stroke physicians and vascular surgeons develop local protocols to specify preferred antiplatelet regimens (combination therapy vs. monotherapy), so as not to delay urgent carotid surgery.</i>
29	<i>For symptomatic patients undergoing carotid endarterectomy on aspirin monotherapy, lower dose aspirin (75 – 325mg daily) rather than higher doses (> 325mg daily) is recommended.</i>
30	<i>In symptomatic carotid stenosis patients undergoing carotid endarterectomy who are intolerant of, or allergic to, aspirin and clopidogrel, dipyridamole modified release monotherapy is recommended.</i>

35	<i>For symptomatic carotid stenosis patients who do not reach their lipid targets on maximum doses or maximum tolerated doses of statins, ezetimibe (10mg daily) is recommended.</i>
58	<i>For patients presenting with recent carotid territory symptoms and evidence of free floating thrombus within the carotid artery, therapeutic anticoagulation is recommended.</i>
63	<i>For patients with a transient ischaemic attack or minor ischaemic stroke in the presence of newly diagnosed or known atrial fibrillation and an ipsilateral 50-99% carotid stenosis, comprehensive neurovascular work up with multidisciplinary team review is recommended to determine whether urgent carotid revascularisation or anticoagulation alone is indicated.</i>
64	<i>For a patient who has been started on anticoagulation (on the basis that cardiac embolism was considered the most likely cause of their transient ischaemic attack or stroke) but who then has recurrent event(s) in the territory ipsilateral to a 50-99% carotid stenosis whilst on therapeutic levels of anticoagulation, carotid endarterectomy or carotid artery stenting is recommended.</i>
66	<i>For patients undergoing carotid endarterectomy, it is recommended that the operation be performed by trained vascular surgeons, rather than by surgeons from other specialties.</i>
91	<i>For patients with a peri-operative stroke, it is recommended to differentiate between intra- and post-operative stroke.</i>
92	<i>For patients who develop an ipsilateral neurological deficit after flow is restored after carotid clamp release when carotid endarterectomy is performed under locoregional anaesthesia, immediate re-exploration of the carotid artery is recommended.</i>
93	<i>For patients who develop an ipsilateral or contralateral stroke at any time period following carotid endarterectomy, urgent diagnostic neurovascular imaging of both carotid arteries and the brain is recommended.</i>

CLASS IIa

10	<i>For patients with >50% asymptomatic carotid stenosis who are intolerant or allergic to aspirin, clopidogrel 75mg daily should be considered. If intolerant or allergic to both aspirin and clopidogrel, dipyridamole monotherapy (200mg twice daily) should be considered.</i>
14	<i>For patients with asymptomatic carotid stenosis with dyslipidaemia who are intolerant of statins, with or without ezetimibe, lipid lowering therapy with PCSK9 inhibitors should be considered.</i>
27	<i>For recently symptomatic patients with a 50-99% carotid stenosis who are undergoing carotid endarterectomy, peri-operative combination antiplatelet therapy should be considered, and should be started after imaging has excluded intracranial haemorrhage.</i>
28	<i>In recently symptomatic patients with a 50-99% carotid stenosis who are to undergo carotid endarterectomy where antiplatelet monotherapy is preferred to combination therapy, aspirin (300-325mg daily for 14 days, followed by 75-162mg daily) should be considered.</i>

36	<i>For symptomatic carotid stenosis patients who are intolerant of, or not achieving target LDL levels on statins, with or without ezetimibe, additional or alternative treatment with PCSK9 inhibitors should be considered</i>
49	<i>For patients with acute ischaemic stroke due to a symptomatic 50-99% carotid stenosis who have received intravenous thrombolysis, delaying carotid endarterectomy or carotid stenting by six days following completion of thrombolysis should be considered.</i>
54	<i>For recently symptomatic patients with 50-99% stenoses with contralateral carotid occlusion or previous cervical radiation therapy, the choice of carotid endarterectomy or carotid artery stenting should be considered on an individual basis.</i>
62	<i>For patients with confirmed ocular ischaemia syndrome and a 50-99% ipsilateral carotid stenosis, carotid endarterectomy or carotid stenting should be considered to prevent further ischaemia induced retinal neovascularisation.</i>
77	<i>For patients undergoing carotid endarterectomy, intra-operative completion imaging with angiography, duplex ultrasound or angioscopy should be considered in order to reduce the risk of peri-operative stroke.</i>
79	<i>For patients undergoing carotid endarterectomy, selective wound drainage should be considered</i>
82	<i>For patients selected to undergo carotid artery stenting, transradial or transcarotid artery revascularisation should be considered as an alternative to transfemoral carotid artery stenting, especially where transfemoral access may confer a higher risk of complications.</i>
83	<i>For patients undergoing carotid artery stenting, decisions regarding stent design (open cell, closed cell) should be considered at the discretion of the operator.</i>
85	<i>For patients undergoing carotid artery stenting, when pre-dilatation is planned, balloon diameters <5 mm should be considered in order to reduce peri-procedural stroke or transient ischaemic attack.</i>
88	<i>For patients undergoing carotid artery stenting, decisions regarding choice of cerebral protection (filter, proximal flow reversal) should be considered at the discretion of the operator performing the stenting procedure.</i>
CLASS IIb	
51	<i>For a patient with acute ischaemic stroke undergoing intracranial mechanical thrombectomy with a tandem 50-99% carotid stenosis and a small area of ipsilateral infarction, synchronous carotid stenting may be considered in the presence of poor antegrade internal carotid artery flow or poor collateralisation via the circle of Willis after mechanical thrombectomy.</i>
57	<i>For symptomatic patients with carotid near occlusion and distal vessel collapse with recurrent carotid territory symptoms (despite best medical therapy), carotid endarterectomy or carotid artery stenting may be considered after multidisciplinary team review.</i>
59	<i>For patients presenting with recent carotid territory symptoms and free floating thrombus who develop recurrent symptoms whilst receiving anticoagulation therapy, surgical or endovascular removal of the thrombus may be considered.</i>

61	<i>For recently symptomatic patients with a carotid web in whom no other cause for stroke can be identified after detailed neurovascular work up, carotid endarterectomy or carotid artery stenting may be considered to prevent recurrent stroke.</i>
84	<i>For patients undergoing elective carotid artery stenting, dual layer mesh covered stents may be considered.</i>
90	<i>For patients undergoing transfemoral carotid stenting, at least twelve carotid stent procedures per year (per operator) may be considered an appropriate operator volume threshold in order to maintain optimal outcomes.</i>
101	<i>In selected 'high risk of surgery' or emergency patients with suspected prosthetic patch infection, insertion of a covered stent may be considered, as part of the three stage EndoVAC technique</i>
CLASS III	
60	<i>For patients presenting with recent carotid territory symptoms and evidence of free floating thrombus, intravenous thrombolysis is not recommended.</i>
86	<i>For patients undergoing carotid artery stenting, post-dilation is not recommended when the residual stenosis is <30%, in order to reduce haemodynamic instability.</i>
128	<i>For patients presenting with a vertebrobasilar territory transient ischaemic attack or stroke and a 50-99% vertebral artery stenosis, routine stenting is not recommended.</i>

D. 'Unanswered questions' from the 2017 guidelines

In the 2017 guidelines, a series of 'unanswered questions' were identified as being priorities for future research.¹⁶⁵ These involved scenarios where there were either no data, or conflicting evidence that did not allow recommendations to be made. The current guidelines have addressed some of the questions (see below). 'Unanswered questions' arising from the 2023 guidelines are detailed in **section 13**.

Is there a validated algorithm for identifying 'higher risk for stroke' ACS patients?

*The six 'higher risk of stroke on BMT' criteria in the 2017 ESVS guidelines have been corroborated by a 2020 meta-analysis of 64 observational studies,⁶⁷ with the new data summarised in **section 3.6**.*

Does ACS cause cognitive decline and can this be reversed or prevented by CEA or CAS?

*A 2021 systematic review identified significant associations between ACS and cognitive impairment (**section 3.7**), but without clear evidence of a causal relationship, apart from in patients with impaired CVR.⁸⁷ Impaired CVR is an*

ESVS criterion for being 'higher risk for stroke on BMT' in whom CEA (should) or CAS (may) be considered. A second systematic review found no evidence that CEA/CAS significantly improved cognitive function in ACS patients.⁴⁶

Should symptomatic patients start combination antiplatelet therapy once parenchymal haemorrhage is excluded on computed tomography (CT) or magnetic resonance imaging (MRI)?

Addressed in **sections 4.2.2.2 and 4.2.2.4**. A meta-analysis of three randomised controlled trials (RCTs)⁵⁹ showed that early institution of combination APRx significantly reduced non-fatal ischaemic and haemorrhagic stroke, fatal ischaemic stroke, moderate to severe functional disability, and poor quality of life at 90 days vs. aspirin alone in patients with a high risk TIA or minor ischaemic stroke. The 2023 guidelines include a new algorithm detailing various peri-operative combination APRx strategies.

What is the relevance of new DW-MRI lesions after CEA and CAS, and do they contribute towards higher rates of recurrent stroke or cognitive decline?

Since 2017, a large study involving patients undergoing non-cardiac surgery reported that post-operative new ischaemic brain lesions (NIBLs) were associated with cognitive impairment, and increased rates of recurrent stroke/TIA.¹⁶⁶ The International Carotid Stenting Study (ICSS) also showed that NIBLs were associated with higher rates of recurrent stroke/TIA¹⁶⁷ (**section 7.1.6**).

Which recently symptomatic patients with < 50% stenoses might benefit from urgent CEA or CAS?

Addressed in **section 4.10**. In selected patients experiencing recurrent TIAs or minor ischaemic stroke, despite BMT and who have a < 50% stenosis, CEA or CAS may be considered, but only after multidisciplinary team (MDT) review.

What is the optimal timing for CEA or CAS after intravenous TT after acute ischaemic stroke?

Addressed in **section 4.8**. Meta-regression analyses of non-randomised studies showed that performing CEA early after TT was associated with significantly higher risks, with the absolute risk of stroke/death being reduced to within the current 6% accepted risk threshold after six days had elapsed after TT.⁶⁶ There remains debate as to whether CEA should be deferred for six days in all TT patients, or only in those with CT/MRI evidence of acute infarction.

Which symptomatic patients are ‘high risk for CEA’ in whom one should preferentially perform CAS?

*Addressed in **section 4.11**. Vascular registries have proposed several clinical and imaging criteria that were considered to make a patient higher risk for CEA. However, many have now been shown to be incorrect.*

Which symptomatic patients are ‘high risk for CAS’ in whom one should preferentially perform CEA?

*Addressed in **section 7.1.2.1** and includes anatomical variables associated with increases in peri-operative stroke;¹⁶; age > 70;¹⁶; performing transfemoral CAS < 7 days after TIA/stroke,¹⁷⁰ long or sequential carotid stenoses,¹⁷¹ heavy calcification¹⁷² and a high age related white matter change (ARWMC) score.¹⁷³*

What is the optimal brain protection method during transfemoral CAS; none, distal filter, proximal protection?

*The role of cerebral protection and evidence for varying types of protection systems are addressed in **section 6.5**. There are no RCT data, but expert consensus remains that some form of protection should be used during CAS.*

Is there a role for stenting in symptomatic patients with extracranial vertebral artery (VA) stenoses?

*Addressed in **section 12.6.2.1**, which includes a 2019 meta-analysis of three RCTs.⁷⁷ Recommendations remain unchanged; VA stenting should only be considered in patients with recurrent symptoms despite BMT.*

What is the optimal way to treat a recently symptomatic patient with an intracranial VA stenosis?

*Addressed in **section 12.6.2.1**, which includes a 2019 meta-analysis of three RCTs.⁷⁷ The 2023 guidelines recommend BMT, rather than stenting.*

Should symptomatic patients with vertebrobasilar TIA/stroke be started on combination APRx once parenchymal haemorrhage is excluded on CT/MRI?

*No RCTs have addressed this question in patients with vertebrobasilar (VB) symptoms. However, a meta-analysis of three RCTs⁵⁹ in patients with minor ischaemic stroke or TIA (which included VB patients) showed that early institution of combination APRx significantly reduced non-fatal ischaemic and haemorrhagic stroke, fatal ischaemic stroke, moderate to severe functional disability and poor quality of life at 90 days vs. aspirin alone (**section 4.2.2.2**). Recommendations regarding APRx in VB patients are the same as for carotid territory stroke/TIA.*

What is the optimal method for detecting VA re-stenoses after stenting?

Duplex ultrasound (DUS) may be performed after stenting of ostial or proximal VA lesions (section 12.7). Suspected re-stenoses should be corroborated by CT angiography (CTA) or MR angiography (MRA). Distal VA interventions require surveillance with CTA/MRA.

How should > 70% asymptomatic re-stenoses after VA stenting be managed?

Only one registry (n = 72) has addressed this question¹⁷⁴ (section 12.6.5.2). Re-intervention did not significantly reduce stroke/TIA at one year (vs. BMT patients), but 33% of treated patients developed recurrent re-stenoses. Recurrent re-stenoses were significantly more likely to occur after balloon angioplasty than redo stenting.

Section 1: Methodology**1.1 Purpose of the Guidelines**

ESVS has prepared guidelines for treating patients with atherosclerotic carotid and VA disease, in succession to the 2009 and 2017 versions.^{165,175} Non-atherosclerotic pathologies (arteritis, fibromuscular dysplasia, dissection, aneurysm) are not included as they will be the subject of a separate guideline. Potential users include vascular surgeons, neurologists, angiologists, stroke physicians, primary care doctors, cardiologists, and interventional radiologists. A key aim is to optimise 'shared decision making', where the patient has choice and control over how they prefer to be treated and how their care is delivered. This requires the doctor to provide as much evidence based information as possible regarding all available treatment options (ie. not just those preferred by the treating doctor), together with a balanced discussion of risks, benefits, and potential consequences in a manner the patient understands, and which takes account of his/her preferences. Guidelines promote standards of care but are not a legal standard of care. They are a 'guiding principle' and care delivered depends on patient presentation, choice,

comorbidities and setting (techniques available, local expertise). The 2023 guidelines are published in the European Journal of Vascular and Endovascular Surgery (EJVES), as an online open access publication, as well as being free to access via the ESVS website. They will also be available on a dedicated ESVS App.

1.2 Compliance with AGREE II standards

AGREE II reporting standards for assessing the quality and reporting of practice guidelines were adopted during preparation of the 2023 guidelines¹⁷⁶ and a checklist is available (**Appendix A**). There was no formal evaluation of *Facilitators and Barriers* and the guidelines did not have scope to go into detail regarding health economics, largely because individual countries have different processes for determining cost acceptability.

1.3 Guideline Writing Committee (GWC)

GWC members were selected by the GWC chairs and ESVS Guidelines Committee (GC) chair to represent clinicians involved in decision making in patients with atherosclerotic carotid and VA disease. The GWC was comprised of vascular surgeons, stroke physicians/neurologists, interventional radiologists and interventional cardiologists (see **Appendix B** for specialty and institution). Views and preferences for the target population were not sought directly, but Mr Chris Macey of the Irish Heart Foundation and the Stroke Alliance for Europe collaborated in preparing **section 14** (Information for Patients). GWC members provided disclosure statements regarding relationships that could be perceived as conflicts of interest (these are filed and available at ESVS headquarters via info@esvs.org). GWC members received no financial support from any pharmaceutical, device, or industry body, to develop the guidelines.

1.4 Evidence Collection

A video conference was held on 6th July 2020, where topics and tasks were allocated. The GWC met monthly (by video conference) to review progress. Search strategies were undertaken for each of the 46 sub-sections, using Medline, Embase and the Cardiosource Clinical Trials and Cochrane databases to December 31st 2020, plus reference checking of cited papers. Hand searches were undertaken of 11 journals between 2017-2020 including: *EJVES*, the *Journal of Vascular Surgery*, *Annals of Vascular Surgery*, *Stroke*, *The Journal of Stroke and Cerebrovascular Disease*, *Neurology*, *Lancet Neurology*, *Cerebrovascular Diseases*, the *International Journal of Stroke*, *Stroke and Vascular Neurology* and the *European Stroke Journal*. At the request of the GC, selected articles published between January to December 2021 were included if they added important information that influenced decision making and recommendations. Only peer reviewed publications were included, following the *Pyramid of Evidence* principle (**Tables 1 and 2**). Multiple RCTs or meta-analyses of multiple RCTs were at the top, then single RCTs or large non-randomised studies (including meta-analyses of large non-RCTs), meta-analyses of small non-RCTs, observational studies, case series and large prospective audits. Expert opinion was at the bottom of the pyramid, while case reports and abstracts were excluded. The evidence used in each of the 38 new recommendations is detailed in the Tables of Evidence (**Appendix C**).

1.5 Studies commissioned for the guidelines

Four systematic reviews/meta-analyses were commissioned including; (i) the association between ACS and cognitive impairment;⁸⁷ (ii) the effect of carotid interventions on cognitive function in ACS patients;⁴⁶ (iii) the effect of timing of carotid interventions on outcomes in the early time period after symptom onset⁵² and (iv) the effect of timing of carotid interventions on outcomes in patients with acute ischaemic stroke undergoing TT.⁶⁶

1.6 Recommendations

The European Society of Cardiology (ESC) system was used to develop classes of recommendation and levels of evidence.¹⁷⁷ The strength (class) is graded from I to III, with 'I' being the strongest (Table 1).

Table 1: Class of Recommendation

Classes of recommendations	Definition	Suggested wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended/is indicated
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
<i>Class IIa</i>	<i>Weight of evidence/opinion is in favour of usefulness/efficacy.</i>	Should be considered
<i>Class IIb</i>	<i>Usefulness/efficacy is less well established by evidence/opinion.</i>	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended

The letters A, B, C denote evidence levels (Table 2), with 'A' being the highest.

Table 2. Levels of evidence.

Level of Evidence A	Data derived from multiple randomised clinical trials or meta-analyses of randomised trials
Level of Evidence B	Data derived from a single randomised clinical trial or large non-randomised studies
Level of Evidence C	Consensus opinion of experts and/or small studies, retrospective studies, registries

Recommendations were developed by GWC members assigned to each section and all GWC members then reviewed each completed section and approved the final wording and grading

of the recommendation. During preparation of the first (and subsequent) drafts, GWC members participated in video conferences where the wording and grading of all recommendations were checked before being submitted for external review. If there was not unanimous agreement to begin with, regarding the grading/wording of recommendations, discussions were held to decide how this might be achieved. Ultimately, the wording and grading of all published recommendations secured unanimous agreement amongst the GWC, although a majority vote (11:3) was taken on the decision not to include 80 - 99% ACS as a 'high risk of stroke on medical therapy' criterion in ACS patients (**section 3.6**).

Since 2017, the GC undertook a review of the criteria for grading the class and level of evidence, to ensure these were standardised for future ESVS guidelines, especially regarding subgroup analyses from RCTs. A modified ESC system was used to classify the level of evidence and to determine the strength of recommendation. In this modified system, RCT meta-analyses are level A; larger non-RCT meta-analyses are level B, while meta-analyses of small non-randomised studies are level C. Furthermore, pre-defined subgroup analyses of RCTs or large RCT subgroup analyses can be level A, while other subgroup analyses of RCTs should be considered level B. As a consequence, while the wording of 11 recommendations remain essentially unchanged (compared with 2017), grades of evidence have been revised and the relevant recommendation box is highlighted as having been 're-graded'.

1.7 Review process

There were three rounds of external review, involving 25 reviewers (16 GC members plus 9 external reviewers). Review comments were assessed by the co-chairs, who co-ordinated a response to each comment via a formal revision process and GWC video conferences. The final version was approved by GWC members before submission to EJVES Editors on 6th April 2022.

1.8 Audit and Update plan

This guideline will be updated every four years. Vascular centres are encouraged to audit implementations made as a result of the guideline. Audit cycles should be repeated and changes implemented. There are many ways to perform clinical audit and most centres now require they are registered with local audit committees.

Section 2: Introduction

Primary prevention aims to reduce the clinical impact of ACS and VA stenoses (to prevent TIA or stroke). The goal of **secondary prevention** is to prevent recurrent TIA, stroke or vascular events in patients presenting with TIA or ischaemic stroke, secondary to carotid or VA stenoses.

2.1 Definition of stroke and transient ischaemic attack

The term '*cerebrovascular accident*' has been replaced with TIA or stroke. Because many studies in carotid stenosis patients pre-dated debates about whether to classify TIA/stroke as time based or tissue based,¹⁷⁸ this guideline has retained time based definitions. TIA is an episode of focal brain, retinal or spinal cord dysfunction lasting < 24 hrs which is of a non-traumatic, vascular origin.¹⁷⁹ Crescendo TIAs refer to multiple TIAs in a short time period, defined by some as > 2 TIAs in 24 hours,¹⁸⁰ or ≥ 3 events in seven days,¹⁸¹ with full recovery between. Stroke is a sudden onset focal (rather than global) neurological dysfunction, with symptoms lasting > 24 hrs (or causing death < 24 hrs), which is of non-traumatic, vascular origin.¹⁷⁹ Stroke in evolution refers to a fluctuating neurological deficit (without full recovery), or a progressively worsening neurological deficit over 24 hours.¹⁸⁰

2.2 Burden of stroke

1.4 million strokes occur annually in a European population of 715 million.¹²⁷ Stroke accounts for 1.1 million deaths annually in Europe and is the second commonest cause of death after coronary artery disease (CAD).¹²⁷ Europeans living with stroke as a chronic condition may increase by 25% from 3.7 million (2015) to 4.6 million (2035), due to an ageing population.¹⁵⁵ Including indirect costs, European health systems spent € 45 billion annually on stroke care in 2015.¹⁵⁵ In the United States of America, total stroke costs were \$ 49.5 billion (€ 43.9 billion) in 2015 - 2016¹⁸² and expected to increase to \$ 129 billion (€ 114 billion) by 2035.¹⁸³

2.3 Aetiology of stroke

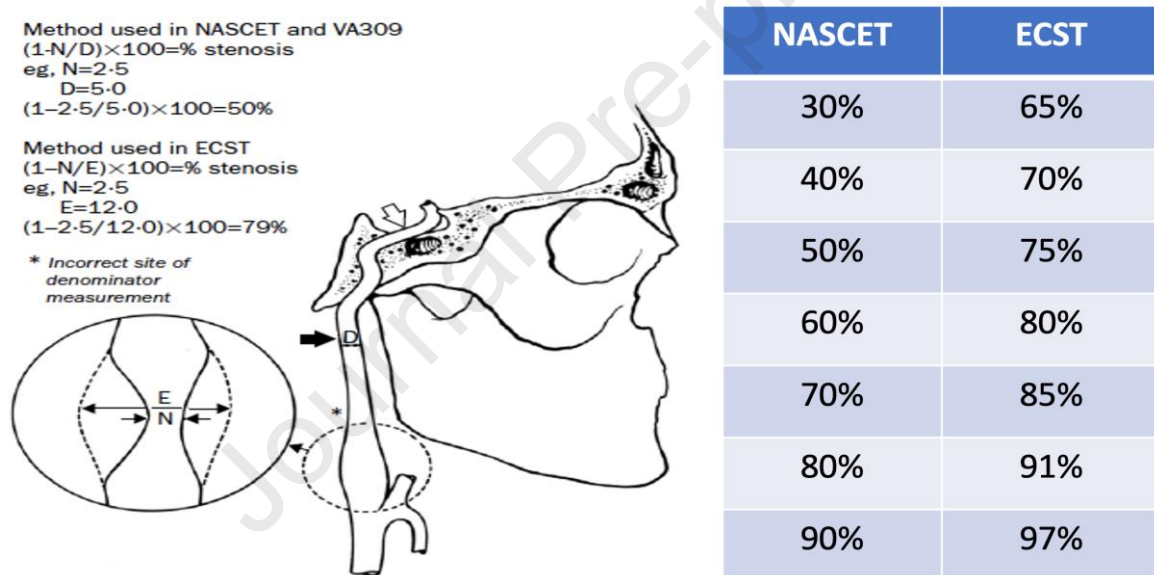
15-20% of strokes are haemorrhagic (intracranial (ICH), subarachnoid), while 20% of ischaemic strokes are vertebrobasilar (VB). The Trial of ORG 10172 in Acute Stroke Treatment (TOAST) classification for TIA/ischaemic stroke includes five categories: (1) large artery atherosclerosis (LAA): defined as $\geq 50\%$ stenosis or occlusion of an extra- or intracranial artery); (2) cardio-embolic; (3) small vessel occlusion; (4) other aetiologies (arteritis, dissection) and (5) undetermined aetiology (two potential causes, no cause identified, incomplete investigations).¹⁸⁴ In 2 204 ischaemic stroke patients, LAA was responsible for 16.6% of strokes. An ipsilateral 50 - 99% carotid stenosis was identified in 8%, while carotid occlusion or intracranial disease accounted for 3.5% each.¹⁸⁵ In another prospective study (883 patients with carotid territory symptoms), 4% had 50 - 69% ipsilateral carotid stenoses, while 8% had a 70 - 99% stenosis. Overall, 12.5% had an ipsilateral 50 - 99% stenosis, while another 5.2% had ipsilateral occlusion.¹²¹ The proportion of LAA strokes may be declining, in association with proportional increases in cardio-embolic stroke,¹⁸⁶ attributed to declines in total cholesterol, low density lipoprotein cholesterol (LDL-C), blood pressure (BP), increases in high density lipoprotein cholesterol¹⁸⁷ and significant increases in antiplatelet (APRx), anti-hypertensive, and statin prescriptions.¹⁸⁶ Between 2002 - 2014, there was a 30% decline in the prevalence of 60 -

99% carotid stenoses and a 36% decline in 80 - 99% stenoses in patients referred to a TIA/stroke service.¹⁸⁷

2.4 Methods for measuring carotid artery stenosis severity

The European Carotid Surgery Trial (ECST)¹⁸⁸ and the North American Symptomatic Carotid Endarterectomy Trial (NASCET)¹⁸⁹ adopted different methods for measuring stenosis (**Figure 1**).

Figure 1: NASCET and ECST methods for measuring carotid stenosis severity



NASCET = North American Symptomatic Carotid Endarterectomy Trial; ECST = European Carotid Surgery Trial.

Reproduced with permission from Rothwell et al. Analysis of pooled data from randomised controlled trials of endarterectomy for symptomatic carotid stenosis. *Lancet* 2003;361:107-16. Table comparing ECST and NASCET stenosis measurements was derived from Donnan GA, Davis SM, Chambers BR, Gates PC. Surgery for prevention of stroke. *Lancet* 1998;351:1372-3

Both methods used residual lumen diameter as numerator. In ECST, the denominator was the estimated vessel diameter where the residual lumen was measured (usually the carotid bulb). In NASCET, the denominator was the diameter of disease free internal carotid artery (ICA) above the stenosis, where vessel walls were parallel. A 50% NASCET stenosis equates to a 75% ECST, while a 70% NASCET stenosis equates to an 85% ECST (**Figure 1**).¹⁹⁰ Uncertainty about methods

used can lead to inappropriate patient selection (exclusion) for interventions.¹⁹¹ The NASCET method has been adopted in the current guidelines, unless stated otherwise. The NASCET method does not permit measurement of stenosis severity in large volume plaques in dilated carotid bulbs. Here, the lumen may be slightly less than that of the distal ICA, so NASCET records a < 50% stenosis, while ECST measures > 70%. Symptomatic patients with large volume plaques consistent with an ECST > 70% stenosis should, therefore, be considered for revascularisation.

The NASCET method has limitations regarding chronic near occlusion (CNO) with distal vessel collapse (**section 4.12**) unless the contralateral ICA is used as denominator. In the RCTs, angiographic criteria for differentiating between CNO and a severe stenosis without distal collapse included at least two of (i) delayed contrast filling above ipsilateral stenosis; (ii) recruitment of circle of Willis (CoW) or distal ICA collaterals; (iii) diameter of distal ipsilateral ICA less than contralateral ICA and (iv) distal ICA diameter equal to or less than diameter of the ipsilateral external carotid artery (ECA).¹⁷ CNO with complete vessel collapse and a 'threadlike' distal lumen (previously known as string sign, slim sign, or subocclusion) and CNO with partial vessel collapse have a prevalence < 10% in patients with significant carotid disease.¹⁹² Because angiograms are not routinely performed, CTA criteria have been developed to differentiate CNO from a 90 - 95% stenosis with no distal vessel collapse, including (i) residual lumen ≤ 1.3 mm; (ii) ipsilateral distal ICA diameter ≤ 3.5 mm; (iii) ratio of ipsilateral distal ICA diameter to contralateral ICA ≤ 0.87 ; and (iv) ratio of ipsilateral distal ICA diameter to ipsilateral ECA diameter ≤ 1.27 ¹⁹³. It has also been proposed that the combination of distal ICA diameter ≤ 2 mm and an ICA diameter ratio ≤ 0.42 offers better prognostic discrimination.¹⁹⁴

2.5 Imaging strategies in carotid artery disease

During ECST and NASCET, all participants underwent intra-arterial angiography. This policy has now been abandoned because of angiogram related stroke. In the Asymptomatic Carotid

Atherosclerosis Study (ACAS), 30 day death/stroke after CEA was 2.3%, but half of the peri-operative strokes were angiogram related.¹⁹⁵ Colour DUS is the first line imaging modality due to low cost and accessibility and there are consensus criteria for diagnosing stenosis severity.¹⁹⁶⁻¹⁹⁸ Alternatives include CTA or MRA which can simultaneously image the aortic arch, supra-aortic trunks, carotid bifurcation, distal ICA and intracranial circulation, which is important if CAS is being considered. Contrast enhanced MRA (CEMRA) has higher accuracy than non-contrast MRA (time of flight) but requires paramagnetic contrast agents (gadolinium). In a Health Technology Assessment meta-analysis of 41 non-randomised studies, DUS, MRA and CTA were equivalent in detecting significant stenoses,¹⁹⁹ but it was advised that centres relying on DUS before CEA should perform a second DUS, preferably by a second operator.¹⁹⁹ A combination of two imaging modalities (DUS + CTA or DUS + MRA) improves accuracy and is routine practice in many centres.²⁰⁰ **Table 3** summarises the sensitivity and specificity of DUS, CTA and CEMRA, compared with the gold standard of digital subtraction angiography (DSA). Patients with ACS or SCS also benefit from functional CT/MRI imaging. In ACS patients, the presence of silent infarction confers a higher risk of stroke (**section 3.6**). In symptomatic patients, increasing acute infarction size predicts higher risks of stroke or intracranial haemorrhage after carotid revascularisation (**section 4.7**).

Table 3: sensitivity and specificity of DUS, CTA and CEMRA, compared with DSA*

		DUS	CTA	CEMRA
Sensitivity	Occlusion	97%	97%	99%
	Stenosis	89%	75-85%	94-95%
Specificity	Occlusion	99%	99%	99.6%
	Stenosis	84%	93-96%	92-93%

* Data derived from Rojoa⁹¹ and Wardlaw¹⁹⁹. DUS = Duplex ultrasound; CTA = computed tomographic angiography; CEMRA = contrast enhanced magnetic resonance angiography; DSA = digital subtraction angiography.

Recommendation 1 (Regraded)	Class	Level	References
For patients undergoing evaluation of the extent and severity of extracranial carotid stenoses, duplex ultrasound, computed tomographic angiography and/or magnetic resonance angiography are recommended.	I	B	199,200

Recommendation 2 (Regraded)	Class	Level	References
For patients where carotid endarterectomy is being considered, it is recommended that duplex ultrasound stenosis estimation be corroborated by computed tomographic angiography or magnetic resonance angiography, or by a repeat duplex ultrasound performed by a second operator.	I	B	199

Recommendation 3 (Regraded)	Class	Level	References
For a patient where carotid artery stenting is being considered, it is recommended that any duplex ultrasound study be followed by computed tomographic angiography or magnetic resonance angiography, which will provide additional information on the aortic arch, as well as the extra- and intracranial circulation	I	B	199

Recommendation 4 (Unchanged)	Class	Level	References
In units which base management decisions in patients with atherosclerotic carotid disease on duplex ultrasound measurement, it is recommended that reports should state which measurement method is used.	I	C	191

Recommendation 5 (Regraded)	Class	Level	References
For patients with atherosclerotic disease being considered for revascularisation, intra-arterial digital subtraction angiography is not	III	B	199

recommended, unless there are significant discrepancies on non-invasive imaging.

2.6 Role of the Multidisciplinary Team (MDT)

Where possible, decisions about carotid interventions should involve an MDT, which might include neurologists or stroke physicians, vascular surgeons and interventional cardiologists or radiologists. This advice is supported by the 2021 ESO and German-Austrian guidelines.^{2,3} MDTs increase the proportion undergoing urgent CEA (22% vs. 4%, $p < .0001$).²⁰¹ Waiting for MDT meetings should not introduce unnecessary delay and urgent decisions can be made by at least two members. Procedural risks vary according to who assesses the patient. In a systematic review of 50 studies ($n = 15\,956$), 30 day death/stroke was 7.7% (CI 95%; 5.0 - 10.2) if the assessor was a neurologist vs. 2.3% (95% CI 1.8 - 2.7) where the surgeon adjudicated outcomes.²⁰² The German ProCAS Stent registry observed that neurologist assessment reported higher rates of transient (8.2% vs. 5.1%) or permanent neurological deficits (3.3% vs. 0.9%), vs. when assessments were undertaken by the operator performing CAS.²⁰³

Recommendation 6 (Unchanged)	Class	Level	References
Multidisciplinary team review is recommended to reach consensus decisions regarding the indications for, and treatment of, patients with carotid stenosis regarding carotid endarterectomy, carotid stenting or optimal medical therapy.	I	C	201

Recommendation 7 (Unchanged)	Class	Level	References
Independent neurological assessment before and after carotid interventions is recommended to audit peri-procedural risks	I	C	202,203

Section 3: Management of asymptomatic carotid disease

An asymptomatic carotid artery stenosis (ACS) refers to a stenosis which is detected in patients without any clinical history of ischaemic stroke, TIA, or other neurological symptoms which might be referable to the carotid arteries. These were the inclusion criteria adopted by ACAS,¹⁹⁵ whilst patients randomised within ACST-1 should not have reported any symptoms referable to the ipsilateral ACS within the preceding six months.²⁰⁴

3.1 Optimal Medical Therapy

Most primary prevention RCTs did not specifically recruit ACS patients, focussing primarily on stroke prevention in general. Some did include ACS patients or published subgroup analyses in ACS patients, and these have been highlighted where appropriate.

3.1.1 Lifestyle measures

Patients with ACS or symptomatic carotid stenoses (SCS) require lifestyle advice about diet, exercise, smoking cessation, and weight loss. Diets should be high in fruits, vegetables, whole grains, nuts, and legumes; moderate in low fat dairy and seafood and low in processed meats, sugar sweetened drinks, refined grains and sodium.²⁰⁵ In a meta-analysis of four ACS screening cohorts, smoking increased the prevalence of > 70% ACS (Odds Ratio [OR] 3.0; 95% CI 2.1 - 4.4),²⁰ plaque progression²⁰⁷ and ischaemic stroke (Relative Risk Increase [RRI] 1.9; 95% CI 1.7 - 2.2).²⁰ Moderate to high exercise conferred a 25% relative risk reduction (RRR) in stroke,²⁰⁹ while obesity was associated with significant increases in stroke (RRI 1.64; 95% CI 1.36-1.99).²¹⁰ The AHA recommended exercise intensity to prevent cardiovascular disease is 30 minutes, five times a week to reach at least 150 minutes per week of moderate exercise, or 25 minutes, three

times a week to reach at least 75 minutes per week of vigorous activity.²¹¹ A US Preventive Services Task Force (USPSTF) meta-analysis of 9 RCTs ($n = 12\,551$) evaluated behavioural counselling to promote healthy diets and physical activity. There was a significantly reduced risk of cardiovascular events at 24 months (RRR 0.80; 95% CI 0.73 - 0.87) attributed to significant reductions in BP, LDL-C, fasting glucose, and obesity.⁸⁵

Recommendation 8 (Regraded)	Class	Level	References
For patients with asymptomatic and symptomatic carotid disease, behavioural counselling to promote healthy diet, smoking cessation and physical activity is recommended.	I	B	85,207-210

3.1.2 Antiplatelet therapy

3.1.2.1 Monotherapy

Only one RCT (did not show benefit) and one observational study (did show benefit) evaluated APRx in patients with > 50% ACS on BMT (**Table 4**).

Table 4: Studies evaluating antiplatelet therapy in ACS patients

Study name	Study Method	Principle findings
Stenosis severity	Follow up	
Asymptomatic Cervical Bruit Study ²¹² 50-100% ACS	RCT: 325mg enteric coated aspirin daily ($n = 188$) vs. placebo ($n = 188$) Median of 2.3 years	No difference in composite endpoint of 'TIA, ischaemic stroke, unstable angina, MI and any cause death between groups (HR 0.99; 95% CI 0.67 - 1.46, $p = .61$)

Asymptomatic Carotid Emboli Study ²¹³	Observational: APRx (<i>n</i> = 419) vs. no APRx (<i>n</i> = 58) at baseline Mean of two years	APRx significantly reduced risk of 'ipsilateral stroke or TIA (HR 0.45; 95% CI 0.31-0.66) and 'any stroke or cardiovascular death' (HR 0.13; 95% CI 0.06-0.27) vs. no APRx.
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ACS = asymptomatic carotid stenosis; RCT = randomised controlled trial; APRx = antiplatelet therapy; TIA = transient ischaemic attack; MI = myocardial infarction; HR = Hazard ratio; CI = confidence intervals.

Two-thirds of ACS patients have subclinical CAD.²¹⁴ In a systematic review of 17 observational studies in 11 391 patients with > 50% ACS, 63% of deaths were cardiac (average annual cardiac mortality 2.9%).²¹⁵ A meta-analysis of primary prevention trials reported that aspirin conferred a 12% reduction in serious vascular events, mainly through reduced non-fatal myocardial infarction (MI), 0.18% vs. 0.23% per year (HR 0.77; 95% CI 0.67-0.89, $p < .0001$).²¹⁶ There are no large scale RCT data on the efficacy of clopidogrel, dipyridamole, ticagrelor or prasugrel in ACS patients. If intolerant of aspirin, clopidogrel is a reasonable alternative, based on data extrapolation from ischaemic stroke patients.^{81,217} If intolerant of, or allergic to, aspirin and clopidogrel, 200mg dipyridamole twice daily (bd) is an alternative,⁸¹ also based on data extrapolation from TIA/stroke patients.²¹⁸

3.1.2.2 Combination

No RCT data support long term aspirin + clopidogrel or aspirin + dipyridamole in ACS patients, unless for other clinical indications.

3.1.2.3 Antiplatelet therapy in ACS patients undergoing CEA

In the Aspirin and Carotid Endarterectomy Trial (ACE), 2 849 ACS/SCS patients undergoing CEA were randomised to four doses of aspirin (81 mg, 325 mg, 650 mg, 1 300 mg). In an efficacy analysis, which excluded patients on ≥ 650 mg aspirin before randomisation, the composite risk of 30 day stroke/MI/death was significantly lower in patients randomised to 81 - 325 mg aspirin

(3.7%) vs. 650 - 1300 mg (8.2%; $p = .0002$).²¹⁹ No RCTs have evaluated clopidogrel monotherapy or combination APRx in ACS patients undergoing CEA. If aspirin intolerant, it is reasonable to prescribe clopidogrel.⁸¹ If intolerant or allergic to aspirin and clopidogrel, 200mg dipyridamole monotherapy bd is an alternative.⁸¹

3.1.2.5 Antiplatelet therapy in ACS patients undergoing CAS

Table 5 summarises two RCTs evaluating APRx (and i.v. heparin) in patients undergoing CAS.

Table 5: RCTs evaluating antiplatelet and i.v. heparin therapy in CAS patients

Study	Method (Stenosis)	Antithrombotic therapy	Main findings
Dalainas ²²⁰	RCT ($n=100$; 88 with ACS) (70-99%)	325 mg aspirin daily for seven days pre-CAS + 24 h i.v. heparin post-op, then 325 mg aspirin daily vs. 325 mg aspirin daily + 250 mg ticlopidine bd for seven days pre-CAS and 30 days post-CAS, then 325 mg aspirin daily	Aspirin + heparin associated with significant increase in ipsilateral; ischaemic stroke/TIA (16%) vs. 2% ($p < .05$). No difference in bleeding complications (4% vs. 2%; $p > .05$)
McKevitt ²²¹	RCT ($n=47$; 9 with ACS) (70-99%)	75 mg aspirin daily + 24 hours i.v. heparin (APTT ratio 1.5-2.5) vs. 75 mg aspirin daily + clopidogrel (300 mg stat 6-12 hours pre-op, 75 mg two hours pre-op + 75 mg daily for days 1-28)	Aspirin + heparin associated with significant increase in 30 day ipsilateral amaurosis fugax, TIA, any stroke (25% vs. 0%, $p = .02$). No difference in incidence of groin haematoma (17% vs. 9%; $p = .35$)

CAS = carotid artery stenting; ACS = asymptomatic carotid stenosis; RCT = randomised controlled trial; APRx = antiplatelet therapy; TIA = transient ischaemic attack; MI = myocardial infarction; HR = Hazard ratio; CI = confidence intervals; APTT = activated partial thromboplastin clotting time.

In RCTs comparing CEA *with* CAS in ACS patients, aspirin + clopidogrel was recommended for > 24 hours^{222,223} to three days pre-operatively^{224,225} and for 2 - 4 weeks^{223,224} or ≥ 6 weeks^{222,225} post-procedurally in CAS patients. The choice of three days pre-treatment with clopidogrel 75 mg daily (without a loading dose) is based on evidence that clopidogrel's maximum antiplatelet effect occurs after 3-5 days of therapy.²²⁶ In CREST, aspirin 325 mg bd and clopidogrel 75 mg bd was recommended for ≥ 48 hours before CAS, followed by aspirin 325 mg daily for 30 days, combined with either clopidogrel 75 mg daily or ticlopidine 250 mg BD for ≥ 4 weeks.²²⁷ Patients were not randomised to different APRx regimens in the larger RCTs and ticlopidine is no longer used, due to unfavourable side ef effects.

3.1.3 Combination of Antiplatelet & Direct Oral Anticoagulants (DOACs)

The Cardiovascular Outcomes for People Using Anticoagulation Strategies (COMPASS) trial randomised 27 395 patients with stable atherosclerotic disease, defined as CAD, peripheral arterial disease (PAD), or carotid disease (prior CEA/CAS or $\geq 50\%$ ACS) to 100 mg enteric coated aspirin daily ($n = 9\ 126$), combination low dose rivaroxaban (2.5 mg bd) plus 100 mg aspirin daily ($n = 9\ 152$) or 5 mg bd rivaroxaban ($n = 9\ 117$).¹⁵ After a mean follow up of 23 months, the composite endpoint of stroke, MI or cardiovascular death was significantly reduced from 5.4% in aspirin patients to 4.1% with low dose rivaroxaban + aspirin (HR 0.76; 95% CI 0.66 - 0.86, $p < .001$). There was, however, a significantly higher rate of major bleeding complications with combination therapy (3.1% vs. 1.9%: HR 1.7, 95% CI 1.4-2.05, $p < .001$).¹⁵

Within COMPASS, 1 919 had carotid disease,⁹ but patients were excluded if they had a 'non-lacunar' ischaemic stroke within one month of randomisation or had a history of lacunar or haemorrhagic stroke.^{9,11} After a median follow up of 21 months, there was a non-significant reduction in the composite endpoint from 6.1% (aspirin) to 3.9% with low dose rivaroxaban +

aspirin (HR 0.63; 95% CI 0.38-1.05, $p = .07$).⁹ The upper limit of the 95% CI was close to 1.0, suggesting the subgroup analysis was underpowered due to insufficient carotid patients being recruited. There was no significant increase in major bleeding risks with low dose rivaroxaban + aspirin vs. aspirin alone (HR 1.18; 95% CI 0.55-2.51, $p = .6$).⁹ Higher dose rivaroxaban did not reduce major vascular events in carotid patients (HR 1.01; 95% CI 0.65 - 1.56) but increased major bleeding risks (HR 2.34; 95% CI 1.21 - 4.52, $p = .009$). Despite forest plots showing similarly beneficial results in carotid patients and those with PAD and CAD, further trials are required before low dose rivaroxaban + aspirin can be recommended as routine antithrombotic treatment in well phenotyped ACS patients. No other guideline currently recommends low dose rivaroxaban + aspirin in ACS patients.¹⁻⁴

Recommendation 9 (Regraded)	Class	Level	References
For patients with >50% asymptomatic carotid stenosis, lower dose aspirin (75-325mg daily) should be considered, mainly for the prevention of late myocardial infarction and other cardiovascular events.	Ila	C	213,216

Recommendation 10 (New)	Class	Level	References
			ToE
For patients with >50% asymptomatic carotid stenosis who are intolerant or allergic to aspirin, clopidogrel 75mg daily should be considered. If intolerant or allergic to both aspirin and clopidogrel, dipyridamole monotherapy (200mg twice daily) should be considered.	Ila	C	81

Recommendation 11 (New)	Class	Level	References
			ToE

For patients with asymptomatic carotid stenosis who are undergoing carotid endarterectomy, lower dose aspirin (75-325mg daily) rather than higher dose aspirin (>325mg daily) is recommended.	I	B	219
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Recommendation 12 (Unchanged)	Class	Level	References
For patients with asymptomatic carotid stenosis undergoing carotid stenting, combination antiplatelet therapy with aspirin (75-325mg daily) and clopidogrel (75mg daily) is recommended. Clopidogrel (75mg daily) should be started at least three days before stenting or as a single 300mg loading dose given in urgent cases. Aspirin and clopidogrel should be continued for at least four weeks after stenting and then antiplatelet monotherapy should be continued indefinitely.	I	B	81,221-226

3.1.4 Lipid lowering therapy

No RCTs have evaluated lipid lowering therapy in ACS patients. A *post hoc* analysis from the Asymptomatic Carotid Surgery Trial-1 (ACST-1) reported that patients taking statins had lower 10 year rates of non-peri-operative stroke, vs. no statins (13.4% vs. 24.1%).²²⁸ In a meta-analysis of 27 RCTs ($n = 174\ 149$), statins were associated with significant reductions in stroke in people with a $\leq 10\%$ five year predicted risk of major vascular events (RR 0.76, 95% CI 0.61 - 0.95, $p = .0012$) per 1 mmol/L reduction in LDL-C.²²⁹ Because of higher rates of cardiovascular events in ACS patients and low rates of serious adverse effects with treatment, statins (with or without ezetimibe¹¹¹) are recommended as for SCS patients (**section 4.2.7**), independent of age and presence of hyperlipidaemia. At present, evidence is lacking to support specific LDL-C targets in ACS patients. Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors may stabilise plaques,²³⁰ but no RCTs included large numbers of ACS patients.⁹⁵ However, in ACS patients with

hyperlipidaemia who are intolerant of statins or ezetimibe, it is reasonable to consider PCSK9 inhibitors.¹⁸

Recommendation 13 (Regraded)	Class	Level	References
For patients with asymptomatic carotid stenosis, lipid lowering therapy with statins (with or without ezetimibe) is recommended for the long-term prevention of stroke, myocardial infarction, and other cardiovascular events.	I	B	111,228,229

Recommendation 14 (New)	Class	Level	References
			ToE
For patients with asymptomatic carotid stenosis with dyslipidaemia who are intolerant of statins, with or without ezetimibe, lipid lowering therapy with PCSK9 inhibitors should be considered.	Ila	C	18,95

3.1.5 Management of hypertension

Hypertension increases the likelihood of developing ACS²³¹ and treatment in adults with ICA stenosis (vs. placebo) reduces stenosis progression (14% vs. 31%; $p = .02$).²³² No RCT has evaluated anti-hypertensive therapy for stroke prevention in ACS patients, but in a meta-analysis of 61 observational studies (1 million adults), there was a significant relationship between BP and stroke or death. Between 40 - 69 years of age, every 20 mmHg increase in systolic blood pressure (SBP), or 10 mmHg increase in diastolic blood pressure (DBP), was associated with a two fold increase in stroke/death. Differences in vascular morbidity/mortality were half as pronounced in patients aged 80 - 89 years. The influence of age was similar in men vs. women and for cerebral ischaemia vs. haemorrhage.²³³ In another meta-analysis of 25 RCTs in patients with no vascular disease (standardised for 10 mmHg SBP and 5 mmHg DBP reduction), there was a significant reduction in late stroke (RR 0.54; 95% CI 0.45 - 0.65).²³⁴ In

another RCT, hypertensive patients ($n = 20\,702$) with no prior stroke/MI, enalapril + folic acid (vs. enalapril alone) reduced first ever stroke (HR 0.79; 95% CI 0.68 - 0.93).²³⁵ The GWC advise the adoption of ESC-European Society for Hypertension (ESC-ESH) recommendations, which the GWC consider reasonable for treating ACS and SCS patients.²³⁶ The ESC-ESH guidelines recommend a target BP < 130 mmHg/< 80 mmHg in non-diabetic patients < 65 years of age and < 140mmHg/< 80mmHg in non-diabetic patients ≥ 65 years old.²³⁶ In diabetic patients, ESC-ESH advise a target SBP of 120 - 129 mmHg and a DBP of 70 - 79 mmHg in patients < 65 years of age and a target SBP of 130 - 139 mmHg and a DBP of 70 - 79 mmHg in patients > 65 years.²³⁶

Recommendation 15 (Unchanged)	Class	Level	References
For patients with asymptomatic or symptomatic carotid stenoses and hypertension, antihypertensive treatment is recommended.	I	A	236

3.1.6 Management of Diabetes Mellitus (DM)

DM patients are more likely to develop stroke (vs. the general population without DM) and 20% of DM patients will die after a stroke.²³⁷ DM is associated with a higher prevalence of ACS,²⁰⁶ hypertension and abnormal lipid profiles, but neither plaque burden nor plaque instability are increased in DM patients.²³⁸ No RCTs have been performed in ACS patients, but in type II DM patients randomised to intensive vs. conventional therapy, intensive intervention with multiple drug combinations and behaviour modification was associated with a 60% RRR in cardiovascular events (HR 0.41; 95% CI 0.25 - 0.69, $p < .001$) and cardiovascular death (HR 0.43; 95% CI 0.19 - 0.94, $p = .04$).²³⁹ In the Collaborative Atorvastatin Diabetes Study (2 838 type II DM patients without increased cholesterol levels), there was a significant reduction in stroke in patients treated (vs. not treated) with atorvastatin 10 mg / day (RRR 48%; 95% CI 11 - 69%).²⁴⁰ Meta-analyses found no evidence that optimal glycaemic control reduced stroke risk,²⁴¹ but it did

reduce other DM related complications. The Prospective Pioglitazone Clinical Trial in macro-Vascular Events (PROACTIVE) trial ($n = 5\,238$) reported that 45mg pioglitazone (+ existing glucose lowering and cardiovascular medications), lowered stroke risks in type II DM patients.²⁴² Accordingly, it is important to aim for optimal glycaemic control in ACS patients, as per DM guidelines.²⁴³⁻²⁴⁶

Recommendation 16 (Unchanged)	Class	Level	References
For diabetic patients with asymptomatic carotid stenoses, optimal glycaemic control is recommended	I	B	243-246

3.1.7 Adherence to medications

In ACS patients, full adherence to medications is reduced with cognitive impairment, a patient's lack of insight regarding their illness, a lack of belief in the benefits of prescribed treatments, mental health issues, inadequate follow up or discharge planning, poor doctor patient relationships, barriers to accessing medications, missed appointments, treatment complexity and drug costs.^{247,48} In a simulation model in ACS patients, survival was significantly higher in patients who remained compliant, vs. non-compliant with BMT.²⁴⁹

3.2 Screening for Asymptomatic Carotid Stenoses

The rationale for screening is that: (i) the condition being prevented is important, has a latent phase and its natural history is fully understood; (ii) there is a reliable screening test, acceptable

to the population in question; (iii) an accepted treatment for screen positive patients and an agreed policy for who to treat and (iv) interventions should be cost effective.²⁵⁰

3.2.1 Is stroke prevention important?

Section 2.1.1 summarises the burden and costs associated with stroke, which is also an important cause of long term disability.

3.2.2 Unheralded stroke and asymptomatic carotid stenoses

About 15% of ischaemic strokes are due to an ipsilateral 50 - 99% carotid stenosis or occlusion.¹⁸⁵

Stroke in ACS patients has decreased over the last decade (**section 2.3**), attributed to better BMT and risk factor control.^{186,251}

3.2.3 Is Duplex ultrasound reliable for diagnosing stenosis severity?

The USPSTF noted that DUS was accessible and non-invasive, with 94% sensitivity and 92% specificity for diagnosing 60 - 99% ACS.²⁵² Accuracy varied (especially in inexperienced hands) and indiscriminate use in low prevalence populations resulted in low positive predictive values, due to high numbers of false positives. USPSTF reported that screening 100 000 adults for 60 - 99% ACS with a predicted prevalence of 1% yielded 893 true positives plus 7 920 false positives. Even if all false positive tests underwent CEMRA, 792 with false positive scans might undergo CEA or CAS (almost as many as the 893 true positives).²⁵² If, however, the preferred therapy in screened patients was BMT, diagnosing stenosis severity becomes less important.²⁵³

3.2.4 Prevalence of asymptomatic carotid stenoses

The prevalence of > 50% and > 70% ACS in 23 706 people recruited from four general population based cohorts was 2% and 0.5%, respectively.²⁰⁶ **Table 6** details prevalences of > 50% and > 70%

ACS, stratified for age and sex. The yield for finding > 70% ACS through unselected screening of patients aged < 80 years would be < 2%,²⁰⁶ ie. neither cost nor clinically effective. In a 2020 global meta-analysis, the prevalence of > 50% ACS in patients aged 30 - 79 years was 1.5% (95% CI 1.1 - 2.1), but this represented a 59% increase since 2000.⁹⁶

Table 6: DUS prevalence of > 50% and > 70% ACS in the general population*

Age	Stenosis	Men	Women
<50 years	>50%	0.2%	0.0%
	>70%	0.1%	0.0%
50-59 years	>50%	0.7%	0.5%
	>70%	0.2%	0.1%
60-69 years	>50%	2.3%	2.0%
	>70%	0.8%	0.2%
70-79 years	>50%	6.0%	3.6%
	>70%	2.1%	1.0%
≥80 years	>50%	7.5%	5.0%
	>70%	3.1%	0.9%

* Based on data from de Weerd et al²⁰⁶. DUS = duplex ultrasound; ACS = asymptomatic carotid stenosis.

3.2.5 Can a high risk of stenosis cohort be identified?

Poorthuis validated a model to identify > 50% and > 70% ACS, involving 596 000 people attending screening clinics.^{254,255} Significant predictors included increasing age, male sex, smoking, DM, prior stroke/TIA, CAD, PAD, high BP and raised lipids. Using the highest risk decile

in this model, one patient with > 50% ACS was detected for every 13 patients screened (while one patient with > 70% stenosis was found for every 58 patients screened). Screening of the highest decile might therefore identify 41% of people with > 50% stenosis and 51% with >70% ACS.

3.2.6 Potential benefits of selective screening

Screening permits risk factor modification and BMT optimisation in screen detected patients, irrespective of stenosis severity. 'Higher risk of stroke on BMT' patients may be candidates for CEA or CAS (**section 3.6**). In a study on compliance, 3 532 participants prescribed primary prevention therapy were randomised to undergo (or not undergo) DUS. Patients randomised to DUS and who had a carotid stenosis were shown their carotid lesions to reinforce the importance of compliance. In the DUS group, the Framingham Risk Score reduced significantly at one year but increased in those not shown their atherosclerotic lesions.³⁴

3.2.7 Potential harms with screening

Patients may undergo unnecessary interventions following a false positive screen, and some may suffer peri-operative stroke/death. Meta-analyses of RCTs comparing CEA with CAS report a 30 day death/stroke of 3.17% after CAS and 2.24% after CEA⁹⁴ (**section 3.3.2**). There may also be patient anxiety associated with screening.

3.2.8 Does screening prevent stroke in the general population?

There is no evidence that screening the general population reduces stroke and no RCTs have evaluated the benefits of screening vs. non-screening for ACS.

3.2.9 Who advocates routine or selective screening?

All published guidelines advise against routine screening. The 14-Society, ESC, SVS and German-Austrian guidelines recommend screening patients with multiple risk factors, provided they are willing to consider CEA or CAS if a significant stenosis is found.^{3,4,256,-258} SVS risk factors include PAD, age > 65 years with CAD, smoking or hypercholesterolaemia⁴, while '14-Society' advice is to include those with no clinical evidence of atherosclerosis but with ≥ 2 of: hypertension, hyperlipidaemia, smoking, family history of stroke, or patients with early onset atherosclerosis.²⁵⁶ The 2021 USPSTF guidelines advise against any form of ACS screening.¹⁰⁵ ESO made no recommendation.²

Recommendation 17 (Unchanged)	Class	Level	References
Routine population screening for asymptomatic carotid stenosis is not recommended	III	C	Expert Opinion

Recommendation 18 (Unchanged)	Class	Level	References
For patients with two or more vascular risk factors, selective screening for asymptomatic carotid stenosis may be considered in order to optimise risk factor control and medical therapy. The main purpose is to reduce late cardiovascular morbidity and mortality, rather than identifying candidates for carotid interventions.	IIb	B	4,254-258

3.3 Randomised Trials: Endarterectomy vs. Best Medical Therapy

The Veteran's Affairs Co-operative Study (VACS), ACAS and ACST-1 compared CEA plus BMT vs. BMT alone in 5 526 ACS patients.^{195,204,259} Angiogram related stroke in patients randomised to CEA were included in intention to treat analyses.¹⁹⁵

3.3.1. BMT in the RCTs

In VACS, 650 mg aspirin (daily) was taken by 55% of patients, while 27% took lower doses. Anti-hypertensive therapy was less commonly prescribed in VACS, and no-one received statins. In ACAS and ACST-1, BP, APRx and lipid lowering therapy increased (13% of ACAS patients were on lipid lowering therapy at entry vs. 32% in ACST-1).^{195,204,259}

3.3.2 RCT Outcomes

Table 7 details early and late outcomes in the three RCTs. In VACS and ACAS, half of all peri-operative strokes in CEA patients occurred after angiography.^{195,259} VACS reported no difference in any or ipsilateral stroke at four years.²⁵⁹ ACST found that CEA conferred significant reductions in any stroke at five and 10 years,²²⁸ while ACAS reported that CEA conferred significant reductions in ipsilateral and any stroke at five years.¹⁹⁵

Table 7: Five and ten year outcomes in VACS, ACAS, and ACST-1

RCT	30 day D/S after CEA	Ipsilateral stroke (including peri-operative stroke/death) *					Any stroke including peri-operative stroke/death) *				
		CEA %	BMT %	ARR %	NNT	stroke/1 000	CEA %	BMT %	ARR %	NNT	stroke/1 000
VACS 4y ²⁵⁹	4.6%	7.0	9.4	2.4	42	24@5y	10.4	12.0	1.6	63	16@4y
ACAS 5y ¹⁹⁵	2.3%	5.1	11.0	5.9	17	59@5y	12.4	17.8	5.4	19	53@5y
ACST 5y ²⁰⁴	2.8%	no published data					6.4	11.8	5.4	19	53@5y
ACST 10y ²²⁸	2.8%	no published data					13.4	17.9	4.5	22	45@10y

* Includes strokes occurring after diagnostic angiography; y = years; CEA = carotid endarterectomy; BMT = best medical therapy; 30 day D/S = 30 day death/stroke after CEA; ARR = absolute risk reduction; NNT = number needed to treat to prevent one stroke; stroke/1000 = number of

3.4 Important subgroup analyses from the RCTs

3.4.1 Effect of age

ACST-1 published outcomes stratified for age (< 65yrs [$n = 912$]; 65 - 74yrs [$n = 1\,558$], and > 75yrs [$n = 650$]). Excluding peri-operative risks, CEA patients aged < 65 years had a five year risk of any stroke of 1.8% vs. 9.6% after BMT (ARR 7.8%; 95% CI 4.3 - 11.3). CEA patients aged 65 - 74 years had a five year risk of any stroke of 2.2% vs. 9.7% after BMT (ARR 7.5%; 95% CI 4.7 - 10.3), while CEA patients aged > 75 years had a 5.5% risk of any stroke at five years vs. 8.8% after BMT (ARR 3.3%; 95% CI 1.9 - 8.4).²²⁸ Half of those aged > 75 who were randomised to CEA died in < 5 years and once peri-operative risks (3.7%) were included, there was no evidence that CEA conferred benefit in patients aged > 75 years.²⁰⁴ However, selected patients aged > 75 years with a predicted life expectancy > 5 years and ≥ 1 clinical/imaging feature that may make them higher risk of stroke on BMT might benefit from intervention (**section 3.6**).

3.4.2 Sex

A meta-analysis of ACAS and ACST-1 data at five years reported that men randomised to BMT were twice as likely to have a stroke vs. CEA (HR 2.04; 95% CI 1.5 - 2.8), while CEA did not appear to benefit women (OR 0.96; 95% CI 0.63 - 1.45).²⁶⁰ At 10 years, however, ACST-1 reported that women gained significant benefit from CEA (ARR 5.8%; 95% CI 1.1 - 11.4), as did men (ARR 5.5%; 95% CI 0.9 - 10).²²⁸ Reasons for the lack of early benefit in women may be that whilst procedural risks after CEA were similar to men, long term stroke risks on BMT were lower in women, so benefit took longer to accrue.

3.4.3 Stenosis severity

ACST-1 and ACAS reported that increasing stenosis severity was not associated with higher rates of stroke in BMT patients.^{195,228} Meta-analyses of ACAS and ACST data showed that patients with 80 - 99% ACS were not more likely to suffer late stroke than < 80% ACS patients (OR 0.9; 95% CI 0.6 - 1.2).⁶² The lack of a relationship between stenosis severity and stroke risk was also reported in a meta-analysis of six RCTS and 35 observational studies, which observed that ipsilateral stroke rates were 1.9/100 person years (50 - 69% ACS,) vs. 2.1/100 person years for 70 - 99% ACS ($p = .427$).²⁵¹ The 2017 ESVS guidelines concluded that increasing stenosis severity was not associated with increased stroke risk.¹⁶⁵

Since 2017, two meta-analyses have informed the debate. The first (five RCTs, 36 prospective observational cohort studies and 15 retrospective cohort studies ($n = 13\ 717$)) reported that ipsilateral stroke in cohort studies (but not in RCTs) were highly correlated with increasing stenosis severity.⁶² It was hypothesised that the absence of increased stroke in 80 - 99% vs. < 80% ACS in the RCTs may have been due to selection bias because trial investigators might have randomly assigned patients with severe stenosis whom they considered to be relatively low risk and enrolled patients with moderate ACS, who they thought to be high risk.⁶² If ACAS and ACST-1 data are excluded, patients in cohort studies with 80 - 99% ACS were significantly more likely to experience late ipsilateral stroke vs. patients with < 80% ACS (OR 2.5; 95% CI 1.8 - 3.5).⁶² However, six of the 11 cohort studies included ACS patients with a history of contralateral stroke/TIA, which is known to increase stroke risk.⁶² Contralateral TIA/stroke was included in the 2017 ESVS guidelines as a higher risk of stroke on BMT criterion¹⁶⁵ when considering performing CEA or CAS in ACS patients (**section 3.6**).

In OXVASC, where contralateral ACS was diagnosed in patients presenting with stroke/TIA, all strokes ipsilateral to the ACS occurred in the first two years after the contralateral stroke/TIA⁶²

(rather than spread evenly over a five year period), suggesting a systemic vulnerability in this type of patient. When meta-analyses were restricted to the five cohort studies with no history of prior TIA/stroke, 80 - 99% ACS was still associated with significantly higher rates of ipsilateral stroke compared with < 80% ACS (11.5% vs. 4.5%; OR 3.1, 95% CI 1.8 - 5.5).⁶² However, four of the five cohort studies completed recruitment in the 1980s/early 1990s, when BMT was not comparable to the modern era and there were only 218 patients with 80 - 99% ACS in the five cohort studies.⁶²

In the second meta-analysis (64 non-randomised cohort studies ($n = 20\,751$)), nine high risk features (HRFs) were defined in ACS patients.⁶⁷ These included AHA plaque type IV-V (MRI diagnosed lipid or necrotic core surrounded by fibrous tissue with possible calcification²⁶²), plaque type VI (MRI diagnosed complex plaque with surface defect, haemorrhage, or thrombus²⁶²); plaque echolucency; large lipid rich necrotic core; silent brain infarction; thin/ruptured fibrous cap; plaque ulceration; intraplaque haemorrhage (IPH); impaired CVR and spontaneous micro-embolisation (MES) on TCD.⁶⁷ Six of the 9 HRFs were already high risk of stroke on BMT criteria in the 2017 guidelines.¹⁶⁵ The incidence of ipsilateral stroke was significantly higher with ACS plus ≥ 1 HRF vs. no HRFs (OR 2.0; 95% CI 1.5 - 2.7).⁶⁷ HRFs significantly increased late stroke/TIA as stenosis severity increased. In patients with 50 - 99% ACS, stroke/TIA was 4.3/100 patient years in patients with ≥ 1 HRF vs. 0.9/100 patient years with no HRFs (OR 4.5; 95% CI 1.8 - 10.9). In patients with 70 - 99% ACS, the risk of stroke/TIA increased to 7.3/100 patient years in patients with ≥ 1 HRF vs. 1.7/100 patient years in patients with no HRFs (OR 3.2; 95% CI 1.7 - 5.9).⁶⁷

The second meta-analysis suggests that increasing stenosis severity was an important predictor for late ipsilateral stroke/TIA, but only with concurrent HRFs.⁶⁷ The impact of HRFs on late ipsilateral stroke was reported in more detail by the Asymptomatic Carotid Stenosis and Risk of

Stroke (ACSRS) study, where annual stroke rates varied from 0.2 - 8.7% with 50 - 79% ACS and from 0.5 - 10% in patients with 80 - 99% ACS, depending upon whether patients did (or did not) have a history of contralateral TIA/stroke or had low vs. high carotid plaque area or had low vs. high gray scale median plaque scores on computerised plaque analysis.^{263,264}

3.5 Controversy regarding modern medical therapy

ACAS, ACST-1 and VACS recruited between 1983 - 2003 when fewer patients took statins and a greater proportion smoked. Some now question whether the data remain relevant in the modern era.²⁶⁵ A meta-analysis (six RCTs, 35 prospective cohort studies ($n = 16\ 178$)) reported ipsilateral stroke rates of 2.3/100 person years in studies completing recruitment before 2000 vs. 1.0/100 person years for 2000 - 2010 ($p < .001$).²⁵¹ The decline in stroke was attributed to BMT improvements and smoking cessation. In studies where $> 25\%$ took statins, ipsilateral stroke was 1.2/100 person years vs. 2.3/100 person years where $< 25\%$ took statins ($p = .009$).²⁵¹ Another systematic review (3 RCTs, 17 cohort studies) reported declining annual stroke rates in BMT patients occurring across all grades of ACS severity (50 - 99%, 60 - 99% and 70 - 99%), which was also apparent in ACAS and ACST, where annual rates of stroke may have declined by 60% between 1995 and 2010.²⁶⁶

3.6 Who is at high risk of stroke on best medical therapy?

The 2021 SVS guidelines recommend CEA in 'low surgical risk' patients with 70 - 99% ACS,⁴ while AHA guidelines advise that only highly selected patients should undergo CEA,²⁶⁷ without defining what 'highly selected' meant. In the 2021 ESC guidelines, coronary calcium score or carotid plaque/stenosis were recognised as being important "risk modifiers. ESC considered that the presence of ACS in people without clinical signs of cardiovascular disease, placed the patient in the same very high risk group as patients with CAD or PAD.²⁶⁸ The 2021 ESO guidelines advise

that CEA is recommended in patients with $\geq 60\%$ ACS considered to be at increased risk of stroke on BMT alone, citing the higher risk criteria published in the 2017 ESVS guidelines to inform this aspect of the ESO guideline.² The 2017 ESVS guidelines and the 2017 ESC/ESVS PAD guidelines were the first to propose clinical/imaging criteria for identifying a higher risk of stroke on BMT cohort in whom CEA or CAS might be targeted.^{165,269} **Table 8** summarises these criteria, which were based on meta-analyses, multicentre studies and RCT subgroup analyses (but not single centre data). Criteria include silent infarction on CT/MRI, $\geq 20\%$ stenosis progression, large plaque area or large juxtaluminal black area (JBA) on computerised ultrasound plaque analysis (defined as an area of pixels with a grayscale value < 25 adjacent to the lumen without a visible echogenic cap after image normalisation²⁶⁴), plaque echolucency, IPH on MRI, impaired CVR (defined in **section 3.10.1**) and ≥ 1 spontaneous MES during ≥ 1 hour of transcranial Doppler (TCD) monitoring.

Table 8: Clinical/Imaging features associated with an increased risk of late stroke in patients with asymptomatic 50 - 99% stenoses treated medically.

Imaging/Clinical Parameter and stenosis severity Type of study	Annual rate of ipsilateral stroke	OR/HR of increased stroke (95%CI) P value
Silent ipsilateral infarction on CT²⁷⁰ 60-99% stenoses multicentre observational	Yes = 3.6% No = 1.0%	Yes vs. No 3.0 (1.46-6.29) $p = .002$
Stenosis progression $>20\%$²⁷¹ 50-99% stenoses multicentre observational	regression = 0.0% unchanged = 1.1% progression = 2.0%	Progression vs. unchanged 1.92 (1.14-3.25) $p = .05$

Stenosis progression ²⁷² 70-99% stenoses multicentre RCT		Regression 0.7 (0.4-1.3) No change comparator Prog 1 sten grade 1.6 (1.1-2.4) Prog 2 sten grades 4.7 (2.3-9.6)
Plaque area on computerised ultrasound plaque analysis ²⁷³ 70-99% multicentre observational	<40 mm ² = 1.0% 40-80 mm ² = 1.4% >80 mm ² = 4.6%	comparator 2.08 (95% CI 1.05-4.12) 5.81 (95% CI 2.67-12.67)
Juxtaluminal black area on computerised ultrasound plaque analysis ²⁶⁴ 50-99% stenoses multicentre observational	<4 mm ² = 0.4% 4-8 mm ² = 1.4% 8-10 mm ² = 3.2% >10 mm ² = 5.0%	trend $p < .001$
Intraplaque haemorrhage on MRI ²⁷⁴ 50-99% stenoses meta-analysis		Yes vs. No OR 3.66 (2.77-4.95) $p < .01$
Impaired CVR ²⁷⁵ 70-99% stenoses meta-analysis		Yes vs. No OR 6.14 (95% CI 1.27-29.5) $p = .02$
Plaque lucency on DUS ²⁷⁶ 50-99% stenoses meta-analysis	predominantly echolucent 4.2% predominantly echogenic 1.6%	echolucent vs. echogenic OR 2.61 (95%CI 1.47-4.63) $p = .0$
≥1 spontaneous MES during ≥1 hour TCD monitoring ²⁷⁷ 50-99% stenoses meta-analysis		Yes vs. No OR 7.46 (95%CI 2.24-24.89) $P = .001$
Spontaneous embolisation plus uniformly or predominantly	Yes = 8.9% No = 0.8%	Yes vs. No OR 10.61 (95%CI 2.98-37.82)

echolucent plaque ²⁷⁸ 70-99% stenoses multicentre, observational		$P = .0003$
Contralateral TIA/stroke ²⁶¹ 50-99% stenoses multicentre, observational	Yes = 3.4% No = 1.2%	Yes vs. No OR 3.0 (95% CI 1.9-4.73) $P = .0001$

OR/HR = odds ratio/hazard ratio; 95%CI = 95% confidence intervals; CT = computed tomography; RCT = randomised controlled trial; JBA = juxtaluminal black area; MRI = magnetic resonance imaging; CVR = cerebral vascular reserve; DUS = duplex ultrasound; MES = microembolic signals; TCD = transcranial Doppler; TIA = transient ischaemic attack.

Corroboration of the ESVS criteria come from a 2020 meta-analysis of 64 cohort studies ($n = 20\,751$), which evaluated stroke/TIA rates in ACS patients, stratified for whether they had HRFs or not.⁶⁷ Six of the 9 HRFs were already adopted in the 2017 ESVS higher risk of stroke on BMT criteria (**table 8**). The pooled prevalence of HRFs was 26.5% (ie. a minority of ACS patients). The evidence for including plaque morphology features (within the ESVS criteria) is detailed in **Table 8** and is supported by a recent study comparing computer based analyses of plaque morphology using CT with plaque biological processes, including transcriptomic analyses. Symptomatic and asymptomatic patients with a large lipid rich necrotic core, IPH, plaque matrix and increased plaque burden had molecular signatures associated with inflammation and extracellular matrix degradation (usually associated with plaque instability and a higher risk of symptoms). By contrast, highly calcified plaques exhibited a molecular signature indicative of plaque stability with increased profibrotic pathways and reduced inflammation.²⁷⁹

The GWC considered the evidence from the two new meta-analyses (**section 3.4.3**) regarding whether 80 - 99% ACS should now be included as a higher risk of stroke on BMT criterion in the 2023 guidelines. After reviewing the evidence, the GWC decided (by a vote of 11:3) against including 80 - 99% ACS for four reasons. First, most patients in the cohort studies had a prior

history of contralateral TIA/stroke, which increases stroke rates in ACS patients, and which would already make them candidates for CEA/CAS.¹⁶⁵ Second, even though there was statistical significance, 4/5 cohort studies which included ACS patients without a history of stroke/TIA were published 25 - 35 years ago, raising questions about generalisability in the modern era of better BMT. In addition, there were only 218 patients with 80 - 99% ACS in these five cohort studies with no prior stroke/TIA. Third, the GWC felt it counterintuitive to simply dismiss RCT data (normally considered the highest level of evidence) on the basis there might have been selection biases 20 - 30 years ago (a hypothesis never raised before). There are many examples in carotid practice where RCT data appear discordant with observational studies (eg. locoregional vs. general anaesthesia⁶⁰ and eversion vs. conventional CEA⁸⁶). Finally, the Kamtchum-Tatuene meta-analysis and ACSRS demonstrated that increasing stenosis severity was an important predictor for late ipsilateral stroke, but only in the presence of concurrent HRFs.⁶⁷ The decision not to include 80 - 99% ACS as a high risk of stroke on BMT criterion in the 2023 guidelines will be reconsidered following publication of CREST-2, which will provide contemporaneous data on whether > 80% ACS is associated with higher stroke risks in the context of modern BMT.

The 2021 German-Austrian guidelines have adopted the ESVS high risk of stroke on BMT criteria, with the addition of males aged < 75 years, based on five year ACST-1 data which showed no significant benefit for CEA in women.³ However, because the ARR in 10 year stroke conferred by CEA in males < 75 years in ACST-1 (5.5%; 95% CI 0.9 - 10) was very similar to females (ARR 5.8%; 95% CI 1.1 - 11.4),²²⁸ the ESVS GWC decided against including males aged < 75 years as a high risk of stroke on BMT criterion.

3.7 DUS surveillance in ACS patients

In patients with a 50 - 60% ACS who would consider a future CEA or CAS (if indicated), it is reasonable to offer annual DUS surveillance (plus assessment of plaque lucency, MES etc) as this allows monitoring of risk factors and BMT. Patients progressing to a 60 - 99% stenosis and who have ≥ 1 clinical or imaging feature making them higher risk of stroke on BMT, might then be considered for CEA or CAS. The 2021 German-Austrian guidelines give similar advice.³ There is no consensus about how long surveillance should continue, but the patient's wishes should be considered. If a patient would not consent to any future carotid intervention, surveillance is not indicated, but the patient should be advised to seek urgent medical advice if symptoms occur.

3.8 Randomised trials: endarterectomy vs. stenting

3.8.1 30 day outcomes in average risk patients

Table 9 details 30 day outcomes in meta-analyses of six RCTs comparing CEA vs. CAS in 7 030 ACS patients (excluding carotid angioplasty [CA]).⁹⁴ CAS (mostly TFCAS) incurred significantly higher rates of 30 day any stroke and death/any stroke. Compared with CEA, CAS had significantly lower 30 day MI.⁹⁴ There was no significant difference in any other endpoint.

Table 9: 30 day outcomes in six RCTs comparing CAS with CEA in ACS patients*.

	Death	Stroke	Death/ Stroke	Disabling Stroke	Death/ Disabling stroke	MI	Death/ Stroke/MI
No RCTs	3 RCTs	6 RCTs	6 RCTs	3 RCTs	2 RCTs	3 RCTs	4 RCTs
n =	n = 5 313	n = 7 030	n = 7 030	n = 6 257	n = 5 076	n = 6 257	n = 6 393

RCTs included	ACT-1 SAPPHIRE, ACST-2	CREST-1, ACT-1	CREST-1, ACT-1	CREST-1 ACT-1 ACST-2	ACT-1 ACST-2	CREST-1 ACT-1, ACST-2	CREST-1 ACT-1 Mannheim ACST-2
		Mannheim SPACE-2, SAPPHIRE ACST-2	Mannheim SPACE-2 SAPPHIRE ACST-2				
CAS	5/3 017 0.16%	119/3 876 3.07%	123/3 876 3.17%	21/3 494 0.60%	21/2 900 0.72%	17/3 494 0.49%	125/3 562 3.5%
CEA	8/2 298 0.35%	63/3 156 2.00%	71/3 156 2.24%	15/2 765 0.54%	20/2 178 0.92%	28/2 765 1.01%	86/2 833 3.03%
OR (95%CI) p =	0.53 (0.17- 1.65) 0.27	1.61 (1.18-2.21) 0.003	1.47 (1.09-1.99) 0.011	1.19 (0.61-2.35) 0.61	0.86 (0.46-1.61) 0.63	0.49 (0.26- 0.90) 0.024	1.19 (0.89-1.59)

Yellow Box: No significant difference; **Red Box:** Significant benefit favouring CEA; **Green box:** significant benefit favouring CAS

RCTs = randomised controlled trials; MI = myocardial infarction; CEA = carotid endarterectomy; CAS = carotid artery stenting; OR (95% CI) = odds ratio (95% confidence intervals); p = p value. * Reproduced with permission from Saratzis⁹⁴.

Table 10 details 30 day outcomes for 6 659 patients in four RCTs randomising > 500 patients, including the Carotid Revascularisation Endarterectomy vs. Stenting Trial (CREST-1), the Stent Protected percutaneous Angioplasty of the Carotid artery vs. Endarterectomy trial-2 (SPACE-2), the Asymptomatic Carotid Trial-1 (ACT-1) and ACST-220,^{224,225,280}. 30 day any stroke and death/any stroke was significantly higher after CAS, while 30 day MI was significantly higher after CEA.⁹⁴ There was no significant difference in other endpoints.

Table 10: 30 day outcomes in four RCTs (comparing CAS with CEA) which randomised > 500 ACS patients *.

	Death	Stroke	Death/ Stroke	Disabling Stroke	Death/ Disabling stroke	MI	Death/ Stroke/MI
No RCTs	2 RCTs	4 RCTs	4 RCTs	3 RCTs	2 RCTs	3 RCTs	3 RCTs
N =	n = 5 078	n = 6 659	n = 6 659	n = 6 259	n = 5 078	n = 6 259	n = 6 259
RCTs included	ACT-1 ACST-2	CREST-1 ACT-1 SPACE-2 ACST-2	CREST-1 ACT-1 SPACE-2 ACST-2	CREST-1 ACT-1 ACST-2	ACT-1 ACST-2	CREST-1, ACT-1, ACST-2	CREST-1 ACT-1 ACST-2
CAS	3/2 900 0.10%	111/3 691 3.00%	114/3 691 3.08%	21/3 494 0.60%	21/2 900 0.72%	17/3494 0.49%	123/3 494 3.52%
CEA	7/2 178 0.32%	58/2 968 1.95%	65/2 968 2.19%	15/2 765 0.54%	20/2 178 0.92%	28/2 765 1.01%	85/2 765 3.07%
OR (95%CI) p =	0.33 (0.08-1.34) 0.12	1.61 (1.16-2.23) 0.0046	1.47 (1.07-2.01) 0.017	1.19 (0.61-2.36) 0.60	0.86 (0.42-1.66) 0.63	0.49 (0.26-0.91) 0.023	1.18 (0.89-1.58) 0.25

Yellow Box: No significant difference; **Red Box:** Significant benefit favouring CEA; **Green box:** significant benefit favouring CAS

*Reproduced with permission from Saratzis.⁹⁴ RCTs = randomised controlled trials; MI = myocardial infarction; CEA = carotid endarterectomy;

CAS = carotid artery stenting; OR (95%CI) = odds ratio (95% confidence intervals); p = p value.

ACST-2 have commented that contemporary procedural risks may be better evaluated in large representative registries (rather than from meta-analyses of RCT data), on the basis that this may better reflect routine clinical practice.²⁰ This is despite the fact that registry outcome data are often 'self reported' rather than independently assessed (as occurs in RCTs). In this respect, the German mandatory registry of in hospital procedural risks after CEA ($n = 86\,000$) and CAS ($n = 18\,000$) in asymptomatic patients, reported no significant difference in the risks of disabling stroke or death (0.7% CAS; 0.7% CEA) and any stroke or death (1.8% CAS; 1.4% CEA). About half of the German

registry patients had pre- and post-operative independent neurological assessment. Outcome data were also unaffected by gender or age.¹⁴³

3.8.2 Long term outcomes in average risk of surgery patients

Table 11 details rates of late ipsilateral and any stroke (excluding 30 day stroke/death), showing that late stroke rates after CAS were similar to CEA, ie, CAS was as durable as CEA.

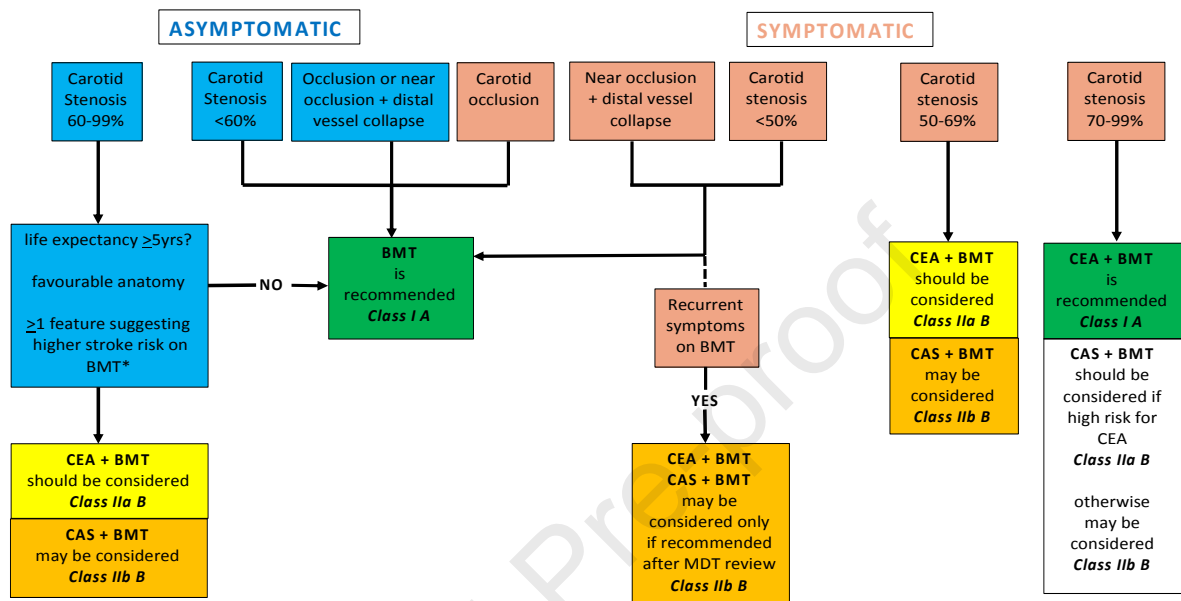
Table 11: Late ipsilateral and any stroke after CEA and CAS (excluding 30 day)

Trial	FU	ipsilateral stroke		any stroke	
		CAS	CEA	CAS	CEA
Lexington ²⁸¹	4yrs	0% (avg 0% pa)	0% (avg 0% pa)	0% (avg 0% pa)	0% (avg 0% pa)
Mannheim ²²²	26mths	0% (avg 0% pa)	0% (avg 0% pa)	0% (avg 0% pa)	0% (avg 0% pa)
ACT-1 ²²⁴	5yrs	2.2% (avg 0.44% pa)	2.7% (avg 0.54% pa)	6.9% (avg 1.38% pa)	5.3% (avg 1.01% pa)
CREST-1 ^{227,280}	5yrs	2.5% (avg 0.50% pa)	2.7% (avg 0.54% pa)	7.1% (avg 1.42% pa)	6.8% (avg 1.36% pa)
CREST-1 ^{227,280}	10yrs	6.9% (avg 0.69% pa)	5.6% (avg 0.56% pa)	13.4% (avg 1.34% pa)	12.5% (avg 1.25% pa)
ACST-2 ²⁰	5yrs	2.1% (avg 0.42% pa)	1.0% (avg 0.20% pa)	5.2% (avg 1.04% pa)	4.5% (avg 0.90% pa)

FU = follow up; CAS = carotid artery stenting; CEA = carotid endarterectomy; avg = average; pa = per annum; yrs = years; mths = months.

An algorithm for managing 'average risk' ACS and SCS patients is presented in **Figure 2**.

Figure 2: Management of average risk patients with asymptomatic and symptomatic carotid stenoses.



Green boxes denote Level I recommendations; yellow boxes denote level IIa and IIb recommendations

*see **table 8** for Imaging/clinical criteria that confer an increased risk of stroke on BMT. CEA = carotid endarterectomy; CAS = carotid artery stenting; BMT = best medical therapy

3.8.3 High risk for CEA patients

SAPPHIRE (Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy) randomised 334 *high risk for CEA* patients to CEA vs. CAS²⁸². High risk criteria were 70 - 99% ACS plus ≥ 1 of: significant cardiac disease (congestive cardiac failure [CCF], abnormal stress test, awaiting cardiac surgery); severe pulmonary disease; contralateral occlusion; contralateral recurrent laryngeal nerve (RLN) palsy; prior radical neck surgery, cervical irradiation; re-stenosis after CEA and age > 80 years.²⁸² The majority (70%) were asymptomatic, in whom 30 day

death/stroke was 5.8% (CAS) vs. 6.1% (CEA).²⁸² At these levels of risk, most would gain no benefit (regarding late stroke prevention), suggesting they would be better treated medically.

3.9 Should the 3% risk threshold for carotid interventions be modified?

Guidelines since 1998 advise that CEA should be performed with a 30 day stroke/death rate \leq 3%²⁸³ and that this should be independently audited (**section 2.6**). However, there is debate about whether the 3% threshold should be reduced. The 2021 German-Austrian and ESO guidelines advise that *in hospital* death/stroke should be \leq 2%^{2,3}. However, this does not mean that the 30 day 3% threshold is being reduced. It is more an attempt to define acceptable risk thresholds while the patient remains in hospital (ie. easier to audit). RCTs suggest that 19 - 24% of peri-operative strokes and deaths occur after the eighth post-operative day,²⁸⁴ which effectively means that the 3% 30 day death/stroke threshold continues to be retained by these two guidelines.

Given the apparent reduction in stroke on modern BMT,²⁵¹ plus a meta-analysis of six RCTs and 47 community registries ($n = 259\,053$) reporting that by 2013, 30 day death/stroke after CEA in ACS patients had fallen to 1.2%,⁸⁰ the GWC debated whether the 30 day 3% threshold should be reduced. After reviewing the evidence, the GWC concluded that it would not be appropriate to do so at present. This was based on recognition that some authors do not accept that the risk of stroke on BMT has decreased,^{285,286} while meta-analyses of four large RCTs comparing CEA with CAS ($n = 6\,659$) showed that the 30 day death/stroke rate was 2.19% (CEA) vs. 3.08% (CAS) (**section 3.8.1**), which differs from meta-analyses suggesting a decline in risks to $< 2\%$.⁸⁰ CREST-2 is currently randomising ACS patients to CEA or CAS vs. BMT, and this debate will not be resolved until it reports whether there has been a decline in stroke rates on modern BMT, compared with when ACAS/ACST were recruiting.

Recommendation 19 (Unchanged)	Class	Level	References
For average surgical risk patients with an asymptomatic 60-99% stenosis, carotid endarterectomy should be considered in the presence of one or more imaging or clinical characteristics that may be associated with an increased risk of late stroke*, provided 30 day stroke/death rates are $\leq 3\%$ and patient life expectancy exceeds five years.	IIa	B	195,204,228, 261,264,270-278

Recommendation 20 (Unchanged)	Class	Level	References
For average surgical risk patients with an asymptomatic 60-99% stenosis in the presence of one or more imaging or clinical characteristics that may be associated with an increased risk of late stroke*, carotid stenting may be an alternative to carotid endarterectomy, provided 30 day stroke/death rates are $\leq 3\%$ and patient life expectancy exceeds five years	IIb	B	222,224,225,261, 264,270-278,280

Recommendation 21 (Unchanged)	Class	Level	References
For asymptomatic patients deemed by the multidisciplinary team to be 'high risk for surgery' and who have an asymptomatic 60-99% stenosis in the presence of one or more imaging/clinical characteristics that may be associated with an increased risk of late stroke on best medical therapy, carotid stenting may be considered provided anatomy is favourable, 30 day death/stroke rates are $\leq 3\%$ and patient life expectancy exceeds five years*.	IIb	B	223,261,264,270-278,282

* See **Table 8** for imaging/clinical criteria conferring an increased risk of stroke on BMT in ACS patients.

3.10 Carotid revascularisation and cognitive impairment

Five percent of patients aged > 60 have dementia. Globally, the annual cost of treating dementia exceeds \$US 1 trillion (€ 816 billion) and may reach \$US 2 trillion (€ 1.6 trillion) by 2030²⁸⁷. In

20% of dementia patients, atherosclerosis or other occlusive diseases affecting cerebral vessels is responsible (vascular dementia), while 20 - 30% have vascular dementia and Alzheimer's.

3.10.1 Do asymptomatic carotid stenoses cause cognitive impairment?

There is speculation that ACS may be responsible for cognitive decline. A 2013 systematic review reported that 9 of 10 observational studies reported an association between ACS and cognitive impairment⁵⁰, but there was no further scrutiny as to whether this translated into a causal association. In a larger systematic review (35 observational studies; 3 626 ACS patients, 10 936 controls), 33/35 studies (94%) reported an association between ACS and cognitive impairment.⁸⁷ However, a significant association does not necessarily mean ACS has an aetiological role, vs. being a marker for something else. The systematic review examined the evidence and was unable to unequivocally demonstrate that ACS was causally associated with cognitive dysfunction via involvement in the pathophysiology of white matter hyperintensities on MRI, lacunar infarction or via an embolic mechanism.⁸⁷ Surprisingly few studies have evaluated the relationship between ACS, ipsilateral cortical infarction, and cognitive impairment. An alternative mechanism whereby ACS might cause cognitive impairment is haemodynamic. As the ACS becomes more severe, patients with a non-functioning CoW and poor collateralisation compensate by vasodilation of ipsilateral intracranial arterioles. This maintains cerebral blood flow, but a point arises where arterioles cannot dilate further. The patient then enters a state of impaired then exhausted cerebral vascular reserve (CVR) with limited (or no) capacity to vasodilate further and blood flow then starts to decline. CVR can be measured using Single Photon Emission Tomography, Positron Emission Tomography, or TCD monitoring of ipsilateral mean middle cerebral artery (MCA) velocities during CO₂ inhalation or breath holding (which raises blood CO₂ levels) which causes vasodilatation and increased MCA velocities, but only if CVR is not exhausted.

Ten studies have evaluated the relationship between impaired CVR and cognitive impairment, with 90% reporting ≥ 1 test of impaired cognition.⁸⁷ There was a stepwise increase in severity of cognitive impairment from normal in patients with severe ACS plus normal CVR (bilaterally), through unilateral impaired CVR (increased cognitive impairment), with maximum cognitive dysfunction in patients with bilateral impaired CVR.²⁸⁸ Patients with severe ACS (unilateral or bilateral) and normal CVR had cognitive scores similar to controls.^{289,290} Finally, patients with severe ACS and impaired CVR were more likely to suffer further cognitive decline over time vs. patients with severe ACS and normal CVR.^{288,291-293}

3.10.2 Do carotid interventions improve cognition in ACS patients?

A second systematic review (31 observational studies) evaluated the effect of carotid interventions on early and late post-operative cognition in ACS patients.⁴⁶ Assessment of early cognitive function was defined as re-assessment ≤ 3 months after CEA or CAS (vs. baseline). Assessment of late cognitive function involved assessment ≥ 5 months after CEA or CAS. In 13/21 cohorts, late reassessment was ≥ 1 year after baseline.⁴⁶ **Table 12** details the effect of carotid interventions on early post-operative cognition in 24 patient cohorts (11 CEA; 10 CAS; 3 CEA + CAS), and late cognitive function in 21 patient cohorts (12 CEA; 7 CAS; 2 CEA + CAS).⁴⁶

At late follow up (**Table 12**), 69% reported no significant change in cognitive function, while in 25%, cognitive scores were mostly unchanged, but 1-2 individual tests were significantly improved. Few patients had significant improvement in late cognitive function (1 cohort; 1.5% of study population) and only one cohort (1.8% of the overall study population) had significant late cognitive impairment.

Table 12: Effect of carotid interventions on cognitive function*

	EARLY (Baseline vs. <3mths)		LATE (Baseline vs. >5mths)	
	number of cohorts	number of patients	number of cohorts**	number of patients
All domains/tests significantly improved	2/24	91/2 059 (4.4%)	1/21	24/1 554 (1.5%)
Most domains unchanged, 1-2 tests significantly improved	7/24	250/2 059 (12.1%)	11/21	386/1 554 (24.8%)
Mixed findings (some tests improved; similar proportion worse)	3/24	257/2 059 (12.5%)	1/21	19/1 554 (1.2%)
No change in cognitive function	9/24	1 086/2 059 (52.7%)	6/21	1 073/1 554 (69.0%)
Most domains unchanged 1-2 significantly few worse	2/24	347/2 059 (16.8%)	1/21	24/1 554 (1.5%)
All domains/tests significantly worse	1/14	28/2 059 (1.4%)	1/21	28/1 554 (1.8%)

* Reproduced with permission from Ancetti⁴⁶

Only one study has evaluated whether haemodynamic status influenced post-operative cognitive function in three groups of ACS patients.²⁹⁴ Patients with 80 - 99% ACS plus normal CVR undergoing CAS had no change in post-operative cognition. Controls with 80 - 99% ACS plus impaired CVR who did not undergo CAS had no change in cognition at follow up assessment. However, patients with 80 - 99% ACS plus impaired CVR who underwent CAS had significant improvements across all cognitive domains after CAS.²⁹⁴

Not included in the systematic review was a *post hoc* analysis of 1 601 UK and Swedish patients, randomised within ACST-1. Using trial data, electronic health records and (in the UK) telephone and postal review, there was no difference in 10 year rates of recorded dementia between CEA

and BMT patients (6.7% vs. 6.6%) or in 20 year rates (14.3% vs. 15.5%), ie. CEA was not associated with reductions in late dementia vs. BMT (HR 0.98; 95% CI 0.75-1.28, $p = .89$).²¹

Until new research clearly identifies at risk ACS subgroups for developing cognitive impairment which is then improved by carotid interventions or provides direct evidence that silent embolisation from ACS causes cognitive impairment, indications for CEA and CAS in ACS patients (to prevent or reverse cognitive decline) are lacking. Impaired CVR is a criterion for being higher risk of stroke on BMT, in whom CEA or CAS may be considered in ACS patients (**section 3.6**). No other guideline has made any recommendations regarding a role for CEA/CAS in preventing or reversing cognitive impairment in ACS patients.¹⁻⁴

Recommendation 22 (Unchanged)	Class	Level	References
For patients with a 70-99% asymptomatic carotid stenosis, carotid interventions are not recommended for the prevention of cognitive impairment until a causal association between severe asymptomatic carotid stenoses and cognitive decline has been established.	III	B	21,87

Section 4: Management of symptomatic carotid disease

4.1 Symptoms attributable to carotid and VA disease

Being classed as recently symptomatic includes patients with symptoms in the past six months, which was the inclusion criterion in ECST/NASCET (**Table 13**). Most TIA/stroke symptoms are negative (eg. loss/impairment of power, sensation, coordination) vs. positive (eg. paraesthesia). Occasional patients with carotid embolism can develop ischaemia or infarction in the posterior cerebral artery (PCA) territory, due to a persisting foetal PCA origin from the ICA via the

posterior communicating artery. The severity of symptoms can be scored using the modified Rankin Score (mRS) or National Institute for Health Stroke Scale (NIHSS).^{295,296}

Table 13: carotid and vertebrobasilar territory symptoms

Carotid territory symptoms	Vertebrobasilar territory symptoms
Higher cortical dysfunction (<i>aphasia, dysgraphia, apraxia, visuospatial problems, visual field deficits</i>)	Complete visual loss or blurring, hemianopia
Amaurosis fugax / transient monocular blindness or blurring	Diplopia, ptosis
Chronic ocular ischaemia syndrome	Vertigo; usually with other brain stem symptoms
Weakness and/or sensory impairment of face/arm/leg (<i>one or all areas may be affected</i>)	Acute sensorineural hearing loss
Upper/lower limb clumsiness	Dysarthria (also occurs with carotid territory ischaemia)
'Limb shaking TIAs' (<i>haemodynamic events in patients with severe SCS and exhausted CVR</i>)	Dysphagia (also occurs with carotid territory ischaemia)
	Dysphonia
	Bilateral facial or limb weakness/numbness

The term 'non-hemispheric symptoms' is applied to patients with isolated syncope (blackout, drop attack), pre-syncope (faintness), isolated dizziness, isolated double vision (diplopia), tinnitus and isolated vertigo. There is no evidence that patients with non-hemispheric symptoms benefit from carotid (or vertebral) interventions, unless they co-exist with the more focal symptoms listed in **table 13**.

4.2. Optimal medical therapy

Most secondary prevention RCTs (APRx, hypertension, lipid lowering, DM) did not specifically recruit SCS patients, focussing primarily on the prevention of stroke in general. Some did publish subgroup analyses in SCS patients, and these have been highlighted.

4.2.1 Lifestyle measures

Management of risk factors and lifestyle is the same as for ACS (**section 3.1.1**).

4.2.2 Antiplatelet therapy

4.2.2.1 Aspirin monotherapy

No adequately powered RCTs have evaluated monotherapy vs. combination APRx in SCS patients. However, older RCTs suggest aspirin monotherapy should be started urgently in APRx

naive TIA/ischaemic stroke patients, to reduce recurrent ischaemic stroke, death, or dependency.^{297,298} If monotherapy is adopted, 300mg aspirin may be prescribed for days 1-14 to maximally inhibit thromboxane biosynthesis,^{299,300} followed by 75 - 325mg daily.

4.2.2.2 Combination antiplatelet therapy

There is increasing interest in the role of combination or dual antiplatelet therapy (DAPT), over monotherapy, to optimise protection against recurrent vascular events in patients with TIA or ischaemic stroke, including those with SCS. **Table 14** summarises data from three RCTs evaluating aspirin + dipyridamole, which randomised patients < 24 hours to six months after TIA/ischaemic stroke to aspirin + dipyridamole vs. aspirin monotherapy or placebo.³⁰¹⁻³⁰³ Aspirin + dipyridamole was more effective than aspirin monotherapy in preventing recurrent stroke,³⁰¹ or recurrent ischaemic vascular events in patients with TIA or ischaemic stroke³⁰² and can be safely started < 24 hours after symptom onset.³⁰³ Long term aspirin + dipyridamole has not been shown to be superior to clopidogrel monotherapy in patients with ischaemic stroke or neuro-imaging confirmed TIAs, although 28.3 - 28.8% of patients had symptoms attributed to 'large artery atherosclerosis', the precise proportion with symptomatic extracranial ICA stenosis was not specified, and those scheduled for urgent CEA were excluded.³⁰⁴

Table 14: Main findings of three RCTs comparing aspirin + dipyridamole antiplatelet therapy with aspirin monotherapy after TIA/ischaemic stroke.

RCT <i>n</i> = cohort	Combination antiplatelet strategy	Main findings
ESPS-2 ³⁰¹	Dipyridamole 200mg bd	<u>RRR in stroke at two years</u>

= 6 602 TIA/ischaemic stroke <3mth % with SCS not clear	vs. Aspirin 25mg bd Vs. Aspirin 25mg bd + Dipyridamole 200mg bd Vs. Placebo	Dipyridamole vs. placebo: 16%; $p < .05$ Aspirin vs. placebo: 18%; $p < .05$ Aspirin + dipyridamole vs. placebo: 37%; $p < .05$ Aspirin + dipyridamole vs. dipyridamole: 25%; $p < .05$ Aspirin + dipyridamole vs. aspirin: 23%; $p < .05$
ESPRIT ^{*302} $n = 2\ 739$ TIA/ischaemic stroke <6mth 9-11% with >50% SCS	Aspirin 30-325mg daily Vs. Aspirin 30-325mg daily + Dipyridamole 200mg bd	<u>Non-fatal stroke/MI/ major bleed/ vascular death at 3yrs</u> aspirin + dipyridamole vs. aspirin (HR 0.80; 95% CI 0.66-0.98) <u>Non-fatal stroke or MI/ vascular death at 3yrs</u> Aspirin + dipyridamole vs. aspirin (HR 0.78; 95% CI 0.63-0.97)
EARLY ³⁰³ $n = 543$ ischaemic stroke <24 hrs: (NIHSS ≤ 20 + not for thrombolysis) % with SCS not clear	Aspirin 25mg bd + Dipyridamole 200mg MR bd days 1-90 ('Early') Vs. Aspirin 100mg/d x 7d; then Aspirin 25mg bd + Dipyridamole 200mg MR bd days 8-90 ('Late')	<u>Good Functional Outcome (MRS 0 – 1) at 90d:</u> <u>Early vs. Late treatment (56.4% vs. 52.4%, $p = .45$)</u> <u>Non-fatal stroke / TIA / Non-fatal MI / Non-fatal major bleeding complication / Vascular death:</u> <u>Early vs. Late treatment: 10% vs. 15% (HR 0.73; 95% CI 0.44- 1.19, $p = .2$)</u>

RCT = randomised controlled trial; TIA = transient ischaemic attack; bd = twice daily; MR= modified release; RRR = relative risk reduction; MI = myocardial infarction; mth = months; SCS = symptomatic carotid stenosis

Table 15 details studies evaluating aspirin + clopidogrel on rates of spontaneous MES in SCS patients, which is an important predictor of increased stroke risk.³⁰⁹ The CARESS RCT reported significant reductions in ongoing micro-embolisation in patients with > 50% SCS who were MES positive at baseline who were randomised to seven days of aspirin + clopidogrel vs. aspirin alone.³⁰⁶ However, it was not powered to show differences in clinical outcome. The AMBDAP study revealed similar reductions in embolisation on aspirin + dipyridamole vs. aspirin + clopidogrel in patients with > 50% SCS.³⁰⁷ In a prospective audit, starting aspirin + clopidogrel in

a rapid access TIA clinic after ICH was excluded on CT/MRI was associated with a significant reduction in recurrent TIA/stroke before expedited CEA, plus significant reductions in MES.³⁰⁸ Sustained embolisation in the early time period after CEA is a predictor of post-operative thrombo-embolic stroke.³⁰⁹ One study randomised 100 CEA patients established on 150mg aspirin daily (84% SCS), to a single dose of 75mg clopidogrel ($n = 46$) or placebo ($n = 54$) 12 hours before CEA.³¹⁰ In comparison with placebo, clopidogrel significantly reduced the odds of having > 20 emboli on TCD in the first three post-operative hours ($p = .01$).

Table 15: Effect of combination aspirin plus clopidogrel in reducing spontaneous embolisation in recently symptomatic patients and in patients undergoing carotid endarterectomy.

Author/Trial Method n= cohort	Combination antiplatelet strategy	Principle findings
Payne³¹⁰ RCT $n = 100$ SCS patients with $\geq 50\%$ stenosis or $\geq 70\%$ ACS	Aspirin 150mg daily for 4wks pre-op + placebo vs. Aspirin 150mg daily for four wks pre-op + single 75mg dose of clopidogrel 12 hours pre-op	During three hours of post-operative TCD monitoring, aspirin + clopidogrel was associated with a tenfold reduction in the proportion of patients with ≥ 20 emboli detected: (OR 0.1; 95% CI 0.01-0.80, $p = .01$)
CARESS³⁰⁶ RCT $n = 107$	Aspirin 75mg daily + clopidogrel 300mg on day 1, followed by 75mg Clopidogrel daily until day 7 vs. Aspirin 75mg daily	At seven days; aspirin + clopidogrel was associated with a significant reduction in the proportion of patients with persistent embolisation on TCD: (43.8% vs. 72.7%, [RRR 39.8%; 95% CI 13.8-58, $p =$.0046])

>50% SCS + ≥ 1 MES on TCD at baseline		
AMBDAP ³⁰⁷ RCT <i>n</i> = 60 SCS >50%	Aspirin 300mg, then 75mg daily + Dipyridamole 200mg bd for 30 days Vs. Aspirin 300mg, then 75mg daily + Clopidogrel 300mg, then 75mg daily for 30 days	At 48 hours, there was a similar reduction in the frequency of micro-embolisation for: Aspirin + Dipyridamole (75.5%) Aspirin + Clopidogrel (77.5%, <i>p</i> = .77)
Batchelder ³⁰⁸ observational <i>n</i> = 100 SCS patients undergoing CEA <8 days of symptom onset	Aspirin 300mg, then 75mg daily + 75mg Clopidogrel 12 hours pre-op vs. Aspirin 300mg, then 75mg daily + 75mg Clopidogrel daily for 48-72 hours pre-op	Starting aspirin + clopidogrel 48-72 hrs pre-op was associated with significant reductions in: Recurrent TIA/stroke prior to CEA (3% vs. 13%) (OR 0.20; 95% CI 0.06-0.66, <i>p</i> = .01) and Spontaneous embolisation pre-operatively (5% vs. 21%) (OR 0.2; 95% CI 0.09-0.66, <i>p</i> = .0047)

RCT = randomised controlled trial; TIA = transient ischaemic attack; SCS = symptomatic carotid stenosis; ACS = asymptomatic carotid stenosis;

CEA = carotid endarterectomy; bd = twice daily; RRR = relative risk reduction; wks = weeks; yrs = years.

It is now accepted that the highest risk period for recurrent stroke is the first 7 - 14 days after symptom onset (**section 4.5.1**). Three RCTs have evaluated whether very early institution of aspirin + clopidogrel (within 24 hours of symptom onset) reduces the risk of early recurrent stroke vs. aspirin alone.^{25,311,312} A fourth RCT undertook a similar evaluation of aspirin + ticagrelor vs. aspirin.²⁴ The methodology and results are summarised in **Table 16**. CHANCE, POINT and THALES excluded SCS patients in whom urgent CEA/CAS was planned.

Table 16: RCTs evaluating the effect of aspirin + clopidogrel or aspirin + ticagrelor vs. aspirin monotherapy, in preventing early recurrent stroke.

RCT n=; cohort	Combination antiplatelet strategy	Main Findings
FASTER^{# 311} n = 392 acute minor ischaemic stroke or TIA with initiation of APRx <24 hrs of symptom onset*	All patients received aspirin 81mg/d (162mg x 1 dose if aspirin naive) and were randomised to additional clopidogrel (300mg x 1 dose and then 75mg/d; clopidogrel + simvastatin 40mg/d; simvastatin 40mg/d; or placebo	Aspirin+clopidogrel did not significantly reduce 90d risk of stroke vs. aspirin monotherapy (5.1% vs. 9.5%, $p > .05$) Symptomatic bleeding higher in the 'clopidogrel' vs. 'no clopidogrel' groups (3 vs. 0%; $p = .03$)
CHANCE³¹² n = 5 170 acute minor ischaemic stroke or 'high risk' TIA patients in China, with initiation of APRx <24 hrs of symptom onset **	75-300mg aspirin x 1d, 75mg aspirin x 21d, + clopidogrel 300mg stat + clopidogrel 75mg/d days 2-90 vs. 75-300mg aspirin x 1d + aspirin 75 mg/d days 2-90	Compared with aspirin, aspirin+clopidogrel was associated with significant reductions in 90 day: Stroke (8.2% vs. 11.7%) HR 0.68; 95% CI 0.57-0.81, $p < .001$) Fatal/disabling stroke (5.2% vs. 6.8%) HR 0.75; 95% CI 0.6- 0.94, $p = .01$) Ischaemic stroke (7.9% vs. 11.4%) HR 0.67; 95% CI 0.56- 0.81, $p < .001$) Compared with aspirin, aspirin+clopidogrel was associated with no significant difference in 90 day: Moderate or severe bleeding (0.3% vs. 0.3%; $p = .73$)
POINT^{## 25} n = 4 881 acute minor ischaemic stroke or 'high risk' TIA, with initiation of APRx <12 hrs of symptom onset **	Aspirin 50-325mg/d + clopidogrel 600mg stat + clopidogrel 75mg/d days 2-90 Vs. Aspirin 50-325 mg/d x 90d (162mg aspirin/d for 5d and then 81mg/d recommended)	Compared with aspirin, aspirin+clopidogrel was associated with significant reductions in 90 day: Stroke/MI/Ischaemic vascular death (5% vs. 6.5%) HR 0.75; 95% CI 0.59-0.95, $p = .02$) Ischaemic stroke (4.6% vs. 6.3%) HR 0.72; 95% CI 0.56- 0.92, $p = .01$) Compared with aspirin, aspirin+clopidogrel was associated with significant increase in 90 day: Major bleeding (0.9% vs. 0.4%) HR 2.32; 95% CI 1.10-4.87, $p = .02$)

THALES ^{24,27} <i>n</i> = 11 016 acute minor ischaemic stroke or ‘high risk’ TIA, with initiation of APRx <24 hrs of symptom onset ***	Aspirin 300-325mg stat and then 75-100mg aspirin days 2-30 + ticagrelor 180mg stat + ticagrelor 90mg BD days 2-30 vs. Aspirin 300-325mg stat and 75- 100mg aspirin daily days 2-30	Compared with aspirin, aspirin+ticagrelor was associated with significant reductions in 30 day: Stroke/death (5.5% vs. 6.6%) HR 0.83; 95% CI 0.71-0.96, <i>p</i> = .02) Ischaemic stroke (5.0% vs. 6.3%) HR 0.79; 95% CI 0.68-0.93, <i>p</i> = .004) Compared with aspirin, aspirin+ticagrelor was associated with significant increase in 30 day: Severe bleeding: (0.5% vs. 0.1%) HR 3.9; 95% CI 1.74-9.14, <i>p</i> = .001)
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trial stopped early due to slow enrolment; ## trial stopped early because data and safety monitoring board determined that the combination of clopidogrel and aspirin was associated with both a lower risk of major ischaemic events and a higher risk of major haemorrhage at 90 days; * acute minor ischaemic stroke (NIHSS score ≤ 3) or TIA; ** acute minor ischaemic stroke (NIHSS score ≤ 3) or TIA with ABCD² score ≥ 4 ; *** acute minor ischaemic stroke (NIHSS score ≤ 5) or TIA with ABCD² score ≥ 6 , or symptomatic intracranial or extracranial stenosis $\geq 50\%$. RCT = randomised controlled trial; TIA = transient ischaemic attack; APRx = antiplatelet therapy; RR = Relative Risk; HR = Hazard ratio; 95% CI = 95% confidence intervals; d=day.

A meta-analysis of the three RCTs comparing aspirin + clopidogrel vs. aspirin alone showed that starting aspirin + clopidogrel within 24 hours of the onset of a high risk TIA or minor stroke significantly reduced (i) non-fatal recurrent ischaemic or haemorrhagic stroke at 90 days (ARR = 1.9%; RR 0.70, 95% CI 0.61-0.80); (ii) non-fatal ischaemic stroke (ARR = 2%; RR 0.69, 95% CI 0.60-0.79); (iii) moderate to severe functional disability (ARR 1.4%) and (iv) poor quality of life (ARR 1.3%). Combination APRx had no impact on all cause mortality or MI, but there was a small, but important increase in moderate to major extracranial bleeding (ARI 0.2%; RR 1.71, 95% CI 0.92-3.2).⁵⁹ Whilst the risk of bleeding complications increased slowly over the first 90 days of combination APRx treatment, early recurrent stroke was highest in the first 10 - 21 days.^{25,59} Accordingly, limiting combination APRx to 21 days after symptom onset would significantly reduce early recurrent stroke, whilst minimising major bleeding complications.⁵⁹

4.2.2.3: Antiplatelet therapy before carotid stenting

Patients with 50 - 99% SCS undergoing CAS are routinely prescribed combination APRx, based on two small RCTs (**section 3.1.2.4**). In most RCTs involving SCS patients, aspirin + clopidogrel³¹³⁻³¹⁷ or aspirin + ticlopidine^{314,316} were prescribed for 48 hours³¹⁶ to 72 hours^{314,317} before CAS and for ≥ 4 - 6 weeks thereafter.^{314,316,317} Ticlopidine is no longer prescribed, so aspirin + clopidogrel is preferred. It is reasonable to prescribe 300 – 325 mg aspirin daily for 14 days, followed by 75 – 81 mg daily (if aspirin naive), in combination with clopidogrel in CAS patients. Clopidogrel (75 mg daily) should start three days before CAS, to inhibit ADP induced platelet aggregation, or as a 300 mg loading dose in urgent cases. Aspirin + clopidogrel should continue for at least four weeks, after which patients should revert to monotherapy (usually clopidogrel 75 mg daily³¹⁸), to protect against late cardiovascular events.^{81,217} Long term aspirin + clopidogrel is not recommended, unless for other clinical indications, as the increased bleeding risk is not justified over the benefits conferred by APRx monotherapy in TIA/stroke patients.^{59,319,10,320} There are no large RCTs on aspirin + ticagrelor vs. aspirin monotherapy in CAS patients with a $\geq 50\%$ SCS.

4.2.2.4 Antiplatelet therapy prior to carotid endarterectomy

No RCT has compared APRx monotherapy with combination therapy in CEA patients. However, international guidelines increasingly recommend a 21 day course of aspirin + clopidogrel in patients with minor ischaemic stroke or high risk TIA, starting as soon as possible after symptom onset once ICH has been excluded on CT/MRI, in order to prevent early recurrent stroke.^{1,321-324} Although CHANCE, POINT and THALES excluded SCS patients in whom CEA was planned, any patients with a TIA or minor ischaemic stroke and a 50 - 99% stenosis who are deemed to require CEA by the MDT should otherwise also be considered high risk.

Monotherapy

Aspirin: Only one RCT has evaluated aspirin vs. placebo in CEA patients. 232 patients (215 SCS) were randomised to placebo or aspirin 75mg daily, starting the night before CEA and continuing for six months.³²⁵ Aspirin reduced disabling stroke at seven days vs. placebo (1.7% vs. 9.6%; $p = .01$), but there was no difference in recurrent TIA/stroke/death at six months. The ACE trial (**section 3.1.2.3**) showed that lower dose aspirin (81 – 325 mg) was preferable to higher dose (> 650 mg) in CEA patients.²¹⁹ Historically, surgeons have almost exclusively used aspirin monotherapy prior to CEA, although benefits may not be as good as combination APRx for preventing early recurrent stroke after symptom onset and before CEA (**section 3.1.2.2**).

Clopidogrel: No RCTs have compared clopidogrel with placebo or aspirin in SCS patients undergoing CEA. CAPRIE showed that 75 mg clopidogrel daily reduced the relative risk of ischaemic stroke, MI, or vascular death by 8.7% vs. 325 mg aspirin daily in a vascular disease population ($p = .043$). However, the 7.3% RR in the ischaemic stroke subgroup did not reach statistical significance.²¹⁷ Moreover, no patients were included within one week of stroke onset and patients undergoing CEA were excluded. However, in a SCS patient who has had a TIA/stroke whilst on aspirin (or who is aspirin or dipyridamole intolerant), clopidogrel monotherapy (75 mg daily) is an alternative in the peri-operative period, if APRx monotherapy is preferred. In this situation, it is reasonable to prescribe a 300 mg loading dose followed by 75 mg clopidogrel daily to produce a more rapid and stable inhibitory effect than seen with 75 mg daily.³²⁶ Clopidogrel monotherapy was equally effective as aspirin + dipyridamole at preventing recurrent stroke at 2.5 years.³⁰⁴

Dipyridamole: If intolerant of, or allergic to both aspirin and clopidogrel, 200 mg of dipyridamole MR monotherapy BD is an alternative peri-operative regimen.^{81,218}

Ticagrelor: Ticagrelor reversibly inhibits the platelet P2Y₁₂ ADP receptor.²⁴ A secondary analysis of the SOCRATES trial compared outcomes on ticagrelor ($n = 1\,542$) vs. aspirin ($n = 1\,539$) in patients randomised within 24 hours of a high risk TIA (ABCD² ≥ 4) or ischaemic stroke (NIHSS ≤ 5) and who had $\geq 50\%$ ipsilateral stenosis of an extracranial or intracranial artery, mobile thrombus in the aortic arch or aortic arch plaques $\geq 4\text{mm}$ thick.⁵ The risk of stroke, MI or death at 90 days was significantly lower in TIA/ischaemic stroke patients of atherosclerotic origin on ticagrelor vs. aspirin (6.7% vs. 9.6%; HR 0.68, 95% CI 0.53–0.88, $p = .003$).²⁴ The number with extracranial $\geq 50\%$ SCS was not specified and there were too few events in CEA patients to draw conclusions regarding the benefits of ticagrelor over aspirin. However, in SCS patients intolerant or allergic to aspirin, clopidogrel and dipyridamole (in whom CEA is **not** planned) or ticagrelor monotherapy is an option (180 mg loading dose, then 90 mg bd).²⁴

Combination therapy

Historically, surgeons have been reluctant to perform CEA in patients on aspirin + clopidogrel, due to concerns about peri-operative bleeding complications. However, evidence suggests that attitudes may be changing. In 2007, an audit of UK vascular surgeons reported that if patients were taking aspirin + clopidogrel, 52% would discontinue clopidogrel before CEA.³²⁷ By 2012, only 24% would discontinue clopidogrel¹⁵⁸. In a SVS vascular quality initiative (VQI) between 2003 - 2014 ($n = 28\,683$), 25% of CEA patients were on aspirin + clopidogrel,¹³⁷ increasing to 31% between 2010 - 2018 ($n = 100\,432$).¹⁵⁰ In a recent Danish multicentre audit ($n = 1\,125$), the proportion of SCS patients undergoing CEA on aspirin + clopidogrel was 50%.¹⁴⁴

The increase in the proportion of CEA patients prescribed aspirin + clopidogrel in the peri-operative period occurred before publication of CHANCE, POINT and THALES. However, international guidelines have now changed clinical practice in high risk patients with TIA/minor ischaemic stroke without carotid stenosis, with aspirin + clopidogrel increasingly being

recommended in the early time period after onset of symptoms (**section 4.2.2.2**). In THALES, a subgroup analysis of 2 351 patients with $\geq 30\%$ stenosis of an ipsilateral extracranial or intracranial brain supplying artery which might have accounted for their TIA/stroke (excluding those scheduled for urgent CEA with more severe stenoses) revealed that patients randomised to aspirin + ticagrelor had significantly lower risks of stroke/death at 30 days (8.1% vs. 10.9%) with aspirin alone (HR 0.73; 95% CI 0.56 - 0.96, $p = .023$).⁶ In the other 8 665 THALES patients without atherosclerotic stenosis, the 90 day risk of stroke/death was similar with aspirin + ticagrelor vs. aspirin alone (4.8% vs. 5.4%; HR 0.89; 95% CI 0.74 - 1.08, $p = .23$).⁶ In addition, the risk of stroke/death was not significantly different between those randomised to aspirin + ticagrelor vs. aspirin in the subgroup with $\geq 30\%$ extracranial arterial stenosis (7.6% vs. 8.9%; HR 0.84, 95% CI 0.6 - 1.17, $p = .306$) but was significantly lower in patients with intracranial stenosis on aspirin + ticagrelor (HR 0.66; 95% CI 0.47 - 0.93, $p = .016$). Exploratory analyses showed that the risk of stroke/death in patients undergoing post-randomisation CEA or CAS was 8.7% (4/46) with aspirin + ticagrelor vs. 23.7% (9/38) on aspirin ($p = .0692$), with severe bleeding in one patient in each group. However, the small number of subjects undergoing revascularisation precludes any definitive comment. THALES has not yet published outcomes on aspirin + ticagrelor therapy vs. aspirin alone in patients with recent TIA/ stroke and a 50 - 99% extracranial SCS.

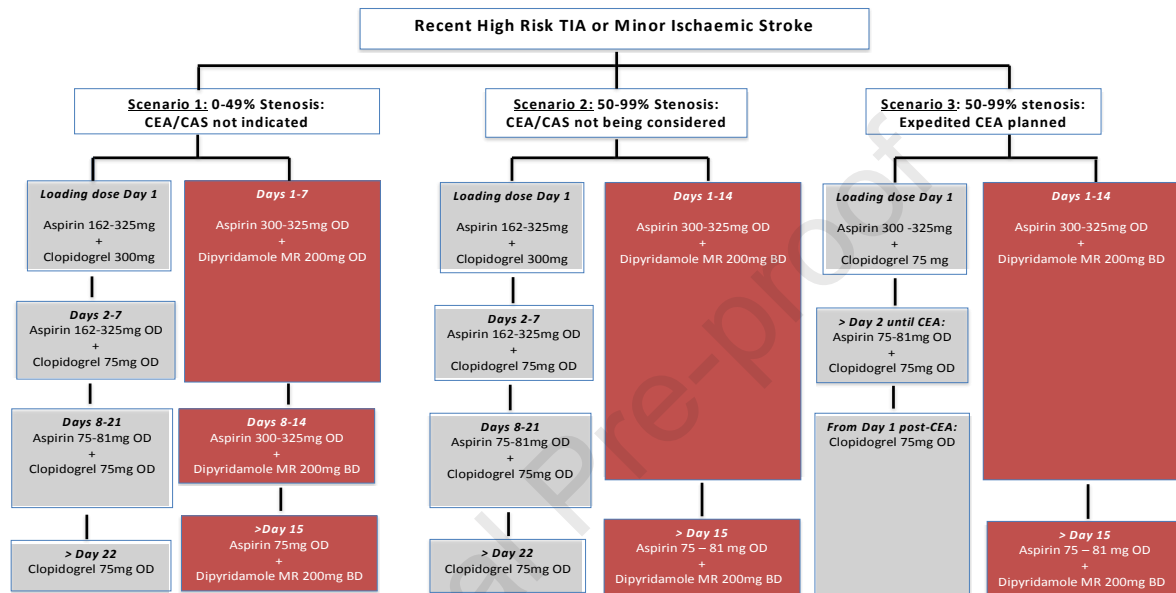
The debate regarding peri-operative monotherapy vs. combination APRx must take account of all potential benefits and not just focus on peri-operative bleeding risks. In addition to RCT evidence that aspirin + clopidogrel significantly reduces early recurrent stroke,^{25,311,312} evidence suggests it also reduces recurrent stroke in the 48 - 72 hour time period between SCS patients being seen in a TIA clinic and undergoing CEA,^{308,328} as well as evidence from national registries that aspirin + clopidogrel reduces peri-operative stroke,¹³⁷ especially early post-operative thrombo-embolic stroke.³⁰⁹ The most important bleeding complication after CEA is neck

haematoma, which is associated with increased morbidity and mortality.¹³⁷ In a 2011 audit of practice between 2003 - 2009 ($n = 5\,264$), the Vascular Study Group of New England (VSGNE) registry found no evidence that aspirin + clopidogrel was associated with higher rates of re-exploration for neck haematoma (1.5%: no APRx; 1.2%: aspirin monotherapy; 0.7%: clopidogrel monotherapy and 1.4%: aspirin + clopidogrel).³²⁹ However, in a meta-analysis of one RCT and seven observational studies ($n = 36\,881$), CEA patients on aspirin + clopidogrel ($n = 8\,536$) had a small but significantly higher rate of major bleeding complications (1.27%) vs. 0.83% than patients on APRx monotherapy (Risk Difference 0.005; 95% CI 0.00 - 0.01, $p = .003$).⁴⁷ Two prospective, observational studies which did not report increased risks of post-operative bleeding on aspirin + clopidogrel^{308,330} were not included in this meta-analysis.

For the increasing proportion of physicians/surgeons prescribing combination APRx in the peri-operative period, there are three scenarios (each with different durations and dosages), making it essential that neurologists and stroke physicians liaise with vascular surgical colleagues to develop protocols specifying preferred APRx regimens (combination vs. monotherapy) before commencing treatment, so as not to delay CEA. This is important as the antiplatelet effects of aspirin, clopidogrel and dipyridamole last the lifetime of the platelet (up to 10 days). The three scenarios include patients with: (1) 0 - 49% carotid stenosis with no other apparent cause for TIA/stroke on neurovascular work up in whom CEA/CAS is not indicated; (2) recent TIA/stroke with a 50 - 99% stenosis where CEA/CAS is not being considered (patient choice, co-morbidities) and (3) recent TIA/stroke with a 50 - 99% stenosis where urgent CEA or CAS is planned. **Figure 3** details choices of combination APRx for each scenario, including dosages and alternative antiplatelet strategies after neuro-imaging has excluded ICH. CEA should be performed with careful control of post-operative BP, as uncontrolled post-CEA hypertension increases the risk of hyperperfusion syndrome, ICH and neck haematoma formation (**section 7.1.4**). If one opts

for peri-operative aspirin + clopidogrel combination therapy, aspirin can be stopped on day one after CEA and clopidogrel 75mg daily continued indefinitely, unless contraindicated (**Figure 3**).

Figure 3: Timing, dose and duration of combination antiplatelet therapy in the early phase after onset of TIA or minor ischaemic stroke *.



CEA = carotid endarterectomy; CAS = carotid artery stenting; MR = modified release; od = once daily; bd = twice daily.

* Reproduced with permission from: Naylor AR, McCabe DJH. *Cerebrovascular Disease: Decision making including optimal medical therapy*. In: Eds: Sidawy A & Perler B. *Rutherford's Vascular Surgery and Endovascular Therapy*, 10th Edition. Philadelphia, Elsevier. 2021 (In press)³³¹.

The 2021 AHA guidelines made no recommendation regarding combination AP Rx prior to CEA.¹ The German-Austrian guidelines recommend combination AP Rx between symptom onset and CEA (to prevent early recurrent stroke) and that aspirin + clopidogrel may be considered to prevent peri-operative stroke after CEA.³ The SVS guidelines advise that in patients with a TIA or minor stroke within 24 hours of onset, aspirin + clopidogrel is recommended over aspirin alone, or as an alternative to aspirin + dipyridamole. However, it was unclear what policy SVS applied to CEA patients, as they advised that decisions regarding DAPT should be individualised.⁴

4.2.3 When to prescribe gastric protection medications?

Prescribing proton pump inhibitors (PPI) may prevent gastrointestinal bleeding, but some (omeprazole, esomeprazole, lansoprazole) may interfere with clopidogrel's antiplatelet effects.³³² In the absence of risk factors, DAPT can be prescribed without a PPI. However, if the patient to be started on DAPT has a higher than average risk of gastrointestinal (GI) bleeding (prior GI ulcer or GI haemorrhage, anticoagulation or corticosteroid prescription) or more than two of: age > 65 years, dyspepsia, gastro-oesophageal reflux, *helicobacter pylori* infection, chronic alcohol use), gastric protection should be considered.³³³ If a PPI is indicated, it is recommended to select a PPI which doesn't interact with clopidogrel (eg. pantoprazole).^{40,334} If the patient is PPI intolerant or they are ineffective, an H₂ receptor antagonist (eg. famotidine) is an alternative.³³⁵

Recommendation 23 (New)	Class	Level	References ToE
For symptomatic carotid stenosis patients who are not being considered for carotid endarterectomy or stenting following a transient ischaemic attack or minor ischaemic stroke, short term aspirin plus clopidogrel for 21 days followed by clopidogrel monotherapy, or long term aspirin plus modified release dipyridamole is recommended*	I	A	59,301,302, 304,307,

Recommendation 24 (New)	Class	Level	References ToE
For recently symptomatic carotid stenosis patients who are not being considered for carotid endarterectomy or stenting who are intolerant of, or allergic to, aspirin and clopidogrel, dipyridamole monotherapy or ticagrelor monotherapy is recommended*	I	B	5,218

Recommendation 25 (New)	Class	Level	References
			ToE
For recently symptomatic carotid stenosis patients in whom carotid endarterectomy is being considered, it is recommended that neurologists/stroke physicians and vascular surgeons develop local protocols to specify preferred antiplatelet regimens (combination therapy vs. monotherapy), so as not to delay urgent carotid surgery.	I	C	Expert Opinion

Recommendation 26 (UNCHANGED)	Class	Level	References
For recently symptomatic carotid stenosis patients scheduled to undergo carotid endarterectomy, it is recommended that all be prescribed antiplatelet therapy throughout the peri-operative period and in the long term.	I	A	81,325,219

Recommendation 27 (New)	Class	Level	References
			ToE
For recently symptomatic patients with a 50-99% carotid stenosis who are to undergo carotid endarterectomy, peri-operative combination antiplatelet therapy should be considered, and should be started after imaging has excluded intracranial haemorrhage*.	Ila	C	59,306, 308,310,

Recommendation 28 (New)	Class	Level	References
			ToE
In recently symptomatic patients with a 50-99% carotid stenosis who are to undergo carotid endarterectomy where antiplatelet monotherapy is preferred to combination therapy, aspirin (300-325mg daily for 14 days, followed by 75-162mg daily) should be considered.	Ila	B	219

Recommendation 29 (New)	Class	Level	References
			ToE
For recently symptomatic patients undergoing carotid endarterectomy on aspirin monotherapy, lower dose aspirin (75-325mg daily) rather than higher dose (>325mg daily) is recommended.	I	B	219

Recommendation 30 (New)	Class	Level	References
			ToE
For recently symptomatic carotid stenosis patients undergoing carotid endarterectomy who are intolerant of, or allergic to, aspirin and clopidogrel, dipyridamole modified release monotherapy (200mg twice daily) is recommended.	I	C	218

Recommendation 31 (Regraded)	Class	Level	References
For recently symptomatic patients undergoing carotid stenting, combination antiplatelet therapy with aspirin (75-325mg daily) and clopidogrel is recommended. Clopidogrel (75mg daily) should be started at least three days prior to stenting or as a single 300mg loading dose in urgent cases. Aspirin and clopidogrel should be continued for at least four weeks after stenting and then long term antiplatelet monotherapy (preferably clopidogrel 75mg daily) should be continued indefinitely.	I	C	81,221, 226,318

Recommendation 32 (Unchanged)	Class	Level	References
For patients who have undergone carotid endarterectomy or carotid stenting, long term aspirin + clopidogrel therapy is not recommended unless required for cardiac or other vascular disease indications.	III	A	59,320

Recommendation 33 (Unchanged)	Class	Level	References
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For patients on antiplatelet therapy with a higher than average risk of gastrointestinal bleeding**, gastroprotective treatment or proton pump inhibition should be considered. If a proton pump inhibitor is indicated, it is recommended to select one which does not significantly influence the antiplatelet effects of clopidogrel (e.g. pantoprazole).	Ila	B	40,332,
			333,334,335

* Alternative antiplatelet strategies and dosages in the event of allergy or intolerance to aspirin or clopidogrel are detailed in **section 4.2.2.4**.

** Criteria for being considered higher risk of gastrointestinal bleeding are detailed in **section 4.2.3**.

4.2.4 Combination Antiplatelet and direct oral anticoagulants

COMPASS provided no data on SCS patients,¹⁵ and patients were excluded if they reported a 'non-lacunar' ischaemic stroke within one month of randomisation.^{9,11} The 2021 AHA guidelines highlighted the absence of evidence regarding the effectiveness of DOACs plus low dose aspirin for secondary stroke prevention as being a knowledge gap to be addressed.¹ No guideline currently recommends low dose rivaroxaban + aspirin in SCS patients.¹⁻⁴

4.2.5 Antiplatelet High On Treatment Platelet Reactivity (HTPR)

In patients with > 50% SCS, the prevalence of antiplatelet HTPR (previously termed antiplatelet resistance) can vary between 9 - 64% for aspirin and 0 - 83% for clopidogrel.⁹⁹ In ACS patients, aspirin HTPR has been reported in 23 - 57% of patients, with clopidogrel HTPR in 25 - 100%.^{99,336,337} Reasons for the wide variability are that prescribed doses and timing of assessment of antiplatelet HTPR status after starting treatment varied between studies,⁹⁹ while the prevalence of antiplatelet HTPR is heavily influenced by shear stress levels to which platelets are exposed in the platelet function/reactivity testing platforms.^{20,338} Because of the wide prevalence ranges observed both within and between studies, it is not clear which (if any) of the currently available platelet function/reactivity assays are likely to inform treatment

decisions in ACS/SCS patients who may have 'antiplatelet HTPR' on their prescribed APRx regimen.⁹⁹ This is clinically important because a meta-analysis of 20 observational studies ($n = 4\ 989$) evaluating platelet function/reactivity testing showed a higher risk of recurrent TIA/stroke, MI, or vascular death in TIA/ischaemic stroke patients with vs. without antiplatelet HTPR on any antiplatelet regimen (OR 2.93; 95% CI 1.90 - 4.51).⁷⁶ However, no studies were adequately powered to determine if *ex vivo* antiplatelet HTPR status can predict risks of ischaemic or haemorrhagic events in SCS or ACS patients in the peri-operative or non-peri-operative periods.^{99,336}

The available evidence does not currently support the routine use of *ex vivo* HTPR testing to tailor APRx in individual patients with carotid stenosis unless they are included within research studies or clinical trials. These studies are vitally important and should include more than one type of testing platform to assess HTPR status, because no single device has been shown to be superior at predicting outcomes in patients with carotid stenosis.⁹⁹ No guidelines currently recommend routine antiplatelet HTPR testing to tailor APRx in individual patients. The SVS noted that routine testing for platelet reactivity is not yet supported by evidence.⁴

4.2.6: Carotid interventions in patients on anticoagulants

No guideline has specifically addressed how to manage patients undergoing carotid interventions who are taking anticoagulants pre-operatively. The aim is to minimise peri-operative thromboembolic and bleeding complications. The decision about whether CEA or CAS is preferred should be based on which is considered the best intervention for each individual patient. This section offers pragmatic advice on the management of patients awaiting a carotid intervention who are currently prescribed anticoagulants, based on a consensus of the GWC. Other guidelines have advised on when to stop and restart anticoagulation in patients requiring

a surgical or endovascular intervention,³³⁹ but not when to prescribe adjunctive antiplatelet therapy during the peri-operative period.

Planning appropriate antithrombotic strategies requires careful assessment of thrombotic and bleeding risks in individual patients, as well as the bleeding risk associated with the procedure. Conditions associated with high thrombotic risk include mechanical heart valves (aortic tilting disc, any mitral prosthesis), thrombophilias, and a venous thromboembolic event within three months or which occurred on therapeutic anticoagulation.^{339,340,341} Conditions associated with high bleeding risks include a HAS-BLED score > 3,³⁴² bleeding episode < 3 months, thrombocytopenia (< 50 x 10⁹/L) and previous bleeding after a similar procedure or with bridging therapy. Peri-operative antithrombotic management should be discussed within an MDT whenever thrombotic and/or bleeding risks are deemed high (ideally including specialists in coagulation), and an agreed strategy should be documented in the case notes. Whichever anticoagulation strategies are selected, careful control of post-operative BP after CEA and CAS is essential to reduce the risk of neck haematoma and ICH (**section 7.1.3.3**).

4.2.6.1 Assessing peri-operative bleeding risks: CEA

In an SVS-VQI audit ($n = 28\,683$), CEA patients undergoing re-exploration for neck haematoma incurred significantly higher in hospital risks vs. patients not re-explored stroke: 3.7% vs. 0.8%, ($p < .001$); MI: 6.2% vs. 0.8%, ($p < .001$); death: 2.5% vs. 0.2%, ($p < .001$); stroke/death: 5.0% vs. 0.9%, ($p < .001$).¹³⁷ Accordingly, CEA is classified as a 'high risk of bleeding' operation³⁴³.

4.2.6.2 Assessing peri-operative bleeding risks: CAS

Bleeding complications after CAS are mostly access related and the incidence of re-intervening for bleeding complications in RCTs was $\leq 1\%$.⁴⁸ Care should be taken to minimise access complications in patients on anticoagulants, including using smaller sheaths (≤ 6 Fr) and

ultrasound guided CFA puncture, which reduces bleeding complications by 50 - 60%.⁹⁷ CAS is classified as a low risk of bleeding intervention.^{343,344}

4.2.6.3 Peri-operative anticoagulation and antiplatelet strategies.

This depends on the procedure (CEA, CAS), thromboembolic risk, bleeding risk, type of anticoagulant (vitamin K antagonist (VKA) or Direct Oral Anticoagulant (DOAC)), renal function and whether bridging anticoagulation is required.

CEA

Because CEA is a high risk of bleeding procedure, the anticoagulants need to be stopped routinely and for longer durations than for low risk of bleeding procedures. **Figure 4** details suggested timings for stopping and re-starting VKAs and DOACs. Decisions regarding re-starting VKAs/DOACs must take account of post-operative bleeding complications, as well as the patient's ability to swallow. Aspirin 300mg daily should be prescribed as indicated in **Figure 4**.

Figure 4: Stopping and restarting anticoagulation prior to CEA

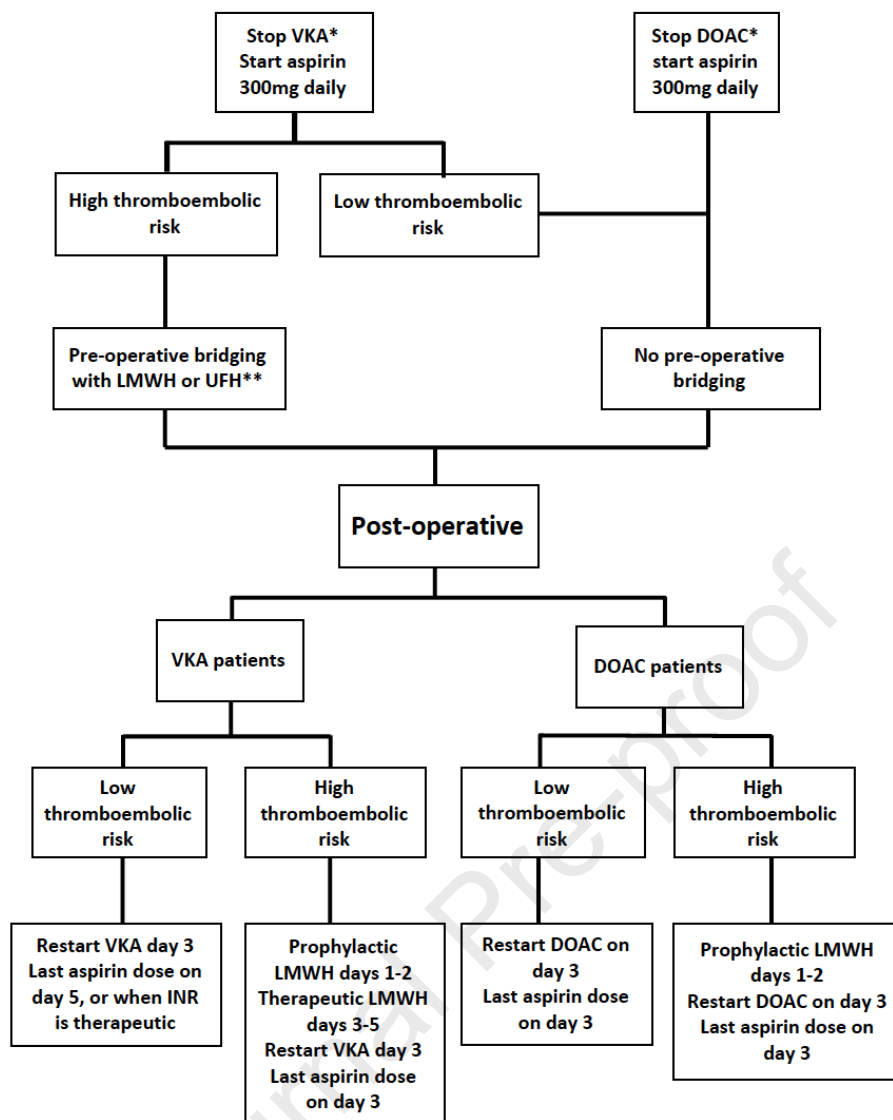
	eGFR	Days before and after surgery											
		-6	-5	-4	-3	-2	-1	0	+1	+2	+3	+4	+5
Warfarin or Acenocoumarol											*	*	*
Phenprocoumon											*	*	*
Dabigatran	>80												
Dabigatran	50-79												
Dabigatran	30-49												
Apixaban, Rivaroxaban, Edoxaban	>30												
Apixaban, Rivaroxaban, Edoxaban	15-29												

Blue boxes = days for taking anticoagulant; Yellow boxes = days to take 300mg aspirin. If intolerant of, or allergic to aspirin, 75mg of clopidogrel daily or 200mg of dipyridamole modified release monotherapy twice daily are alternatives; eGFR= estimated glomerular filtration rate, measured as mL/min/1.73m.²

** In VKA patients, post-operative aspirin is continued until the International Normalised Ratio is therapeutic (after VKA re-started) or until the patient is started on therapeutic dose low molecular weight heparin or intravenous unfractionated heparin.*

The need for pre-operative bridging anticoagulation requires careful discussion within an MDT as an RCT involving patients with atrial fibrillation undergoing elective surgery showed that bridging was associated with significantly higher risks of major bleeding and did not reduce thromboembolic events.¹⁴ The Dresden Registry reported similar findings.¹¹⁷ Accordingly, pre-operative bridging with therapeutic dose low molecular weight heparin (LMWH) or unfractionated heparin (UFH) is only indicated in a very small cohort of CEA patients considered high risk of thromboembolism after cessation of VKAs, which would include patients with a recent (≤ 3 months) deep vein thrombosis or pulmonary embolism, or those who suffered a thromboembolic event during previous interruption of oral anticoagulation.³⁴³ If pre-operative bridging is indicated in VKA patients (**Figure 5**), the last dose of LMWH should be ≥ 24 hours pre-operatively. Intravenous UFH can be stopped 4 - 6 hours before CEA.

Figure 5: anticoagulation, antiplatelet and bridging strategies in CEA patients



* Stop VKAs and DOACs according to timings in **Figure 4**. ** If pre-operative bridging is being considered, this decision should involve MDT discussion (preferably involving a specialist in coagulation) and the benefits and risks of bridging must be clearly explained to the patient and documented in the case notes.

VKA = vitamin K antagonist; DOAC = direct oral anticoagulant; LMWH = low molecular weight heparin; UFH = unfractionated heparin. If intolerant of, or allergic to aspirin, 75mg of clopidogrel monotherapy daily or 200mg of dipyridamole modified release monotherapy twice daily are alternatives.

Post-operative bridging is reasonable in CEA patients who have stopped their VKAs and who are considered high risk of thromboembolism. Pre-operative bridging is not, however, recommended in patients on DOACs, as their predictable short half life allows for proper timing of DOAC cessation just before surgery.³⁴³

In CEA patients whose VKAs have been stopped and who are classed as low thromboembolic risk, VKAs can be restarted on day 3. Aspirin (300mg daily) should be continued until either a last dose on day five or when the International Normalised Ratio is therapeutic (**Figure 5**). In CEA patients whose VKAs have been stopped and who are considered high thromboembolic risk, prophylactic subcutaneous LMWH can be prescribed for the first 48 hours after CEA, with VKAs re-started on day 3, when the LMWH is increased to therapeutic doses and continued until the International Normalised Ratio has reached therapeutic levels. In the latter patients, the last dose of aspirin should be on day three (**Figure 5**).

DOAC patients usually do not require post-operative bridging because they achieve full anticoagulation within eight hours of restarting DOACs. Patients at low thromboembolic risk can, therefore, restart DOACs on post-operative day three, with the last dose of aspirin (300 mg) being taken on day three (**Figure 5**). In DOAC patients considered at high thromboembolic risk, the potential for increased bleeding complications needs to be considered. Prophylactic dose LMWH can be started 6 - 24 hours post-operatively and continued until day three when the DOAC is re-started. In these patients, the last dose of aspirin is taken on day 3.

CAS

Decisions about anticoagulation and antiplatelet strategies during CAS depend upon whether unit policy is to (i) stent patients whilst on anticoagulation with the addition of a single antiplatelet agent during the peri-operative period, (ii) stent patients after anticoagulation is stopped with a single antiplatelet agent prescribed during the peri-operative period or (iii) stent patients after anticoagulation is stopped with combination antiplatelet therapy prescribed during the peri-operative period. Much of the debate is driven by concerns about post-operative bleeding complications (especially ICH) if anticoagulation is continued, vs. worries about higher rates of peri-operative ischaemic stroke if antiplatelet therapy is not co-

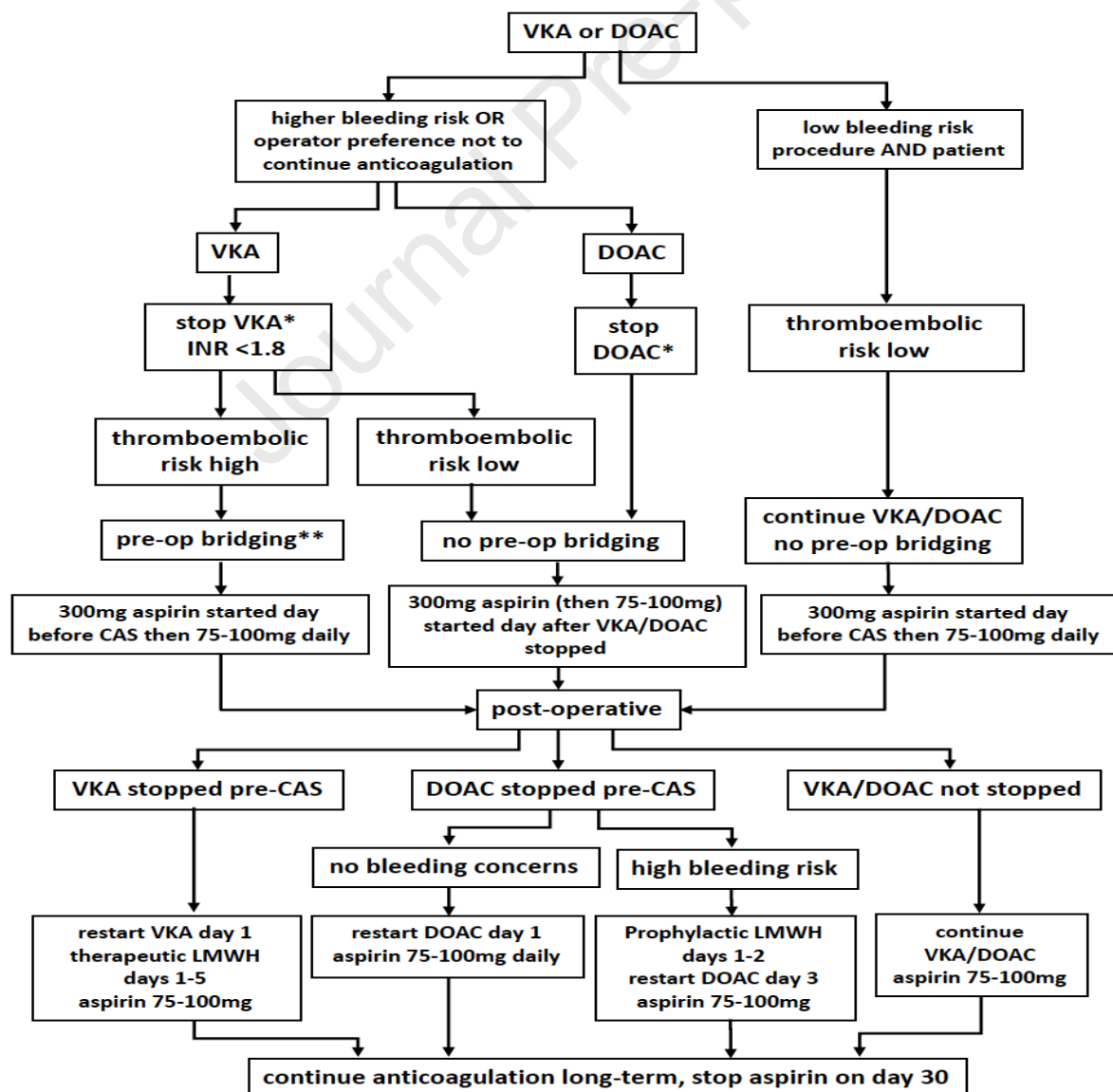
prescribed. Accordingly, individual units will benefit from MDT review, which should ideally include a specialist in coagulation (especially if bridging is being considered) and agreed treatment strategies should be documented in the case notes.

Historically, most CAS procedures were performed with anticoagulation stopped pre-operatively. However, the 2019 Society of Interventional Radiology guidelines advise that anticoagulants do not need to be stopped routinely, unless there are additional high risk of bleeding features.³⁴⁴ This advice has probably not, however, translated into clinical practice in many CAS centres. Whilst there have been no RCTs in CAS patients, evidence from observational studies suggest that CAS can be performed safely whilst the patient is taking anticoagulants plus antiplatelet therapy during the peri-operative period, without increasing bleeding complications,^{345,346} especially if smaller sheaths and ultrasound guided punctures are used.⁹⁷ Extrapolation of data from RCTs in AF patients undergoing percutaneous coronary interventions suggest that dual antithrombotic therapy (anticoagulant plus a single antiplatelet agent) appears to be superior to triple therapy (anticoagulant plus aspirin and clopidogrel) in reducing bleeding events, whilst being non-inferior regarding the associated risks of thromboembolic events.³⁴¹ **Figure 6** provides a pragmatic algorithm for anticoagulation and single agent antiplatelet strategies in CAS patients.

In CAS patients where VKAs and DOACs are to be stopped, the timing is the same as for CEA (**Figure 4**). If bridging is being considered in VKA patients, this decision should involve MDT review (ideally involving a specialist in coagulation) and the benefits vs. risks of bridging must be clearly explained to the patient and documented in the case notes. In the patient algorithm (**Figure 6**), antiplatelet monotherapy (aspirin 300mg the day before CAS, then 75 - 100mg daily until 30 days) is appropriate, given that these patients will also receive intra-operative heparin. If the patient is intolerant of, or allergic to aspirin, 75mg of clopidogrel monotherapy daily or

200mg of dipyridamole modified release monotherapy twice daily are alternatives. After 30 days, antiplatelet therapy is stopped, and anticoagulation continued long term.

Figure 6: anticoagulation and antiplatelet strategies in CAS patients who are taking anticoagulants pre-operatively.



* Stop VKAs/DOACs according to timings in **Figure 4**. ** If bridging is being considered, this decision should involve MDT discussion (preferably involving a specialist in coagulation) and the benefits and risks of bridging must be clearly explained to the patient and documented in the case notes.

VKA = vitamin K antagonist; DOAC = direct oral anticoagulant; LMWH = low molecular weight heparin. If intolerant of, or allergic to aspirin, 75 mg clopidogrel monotherapy daily or 200 mg dipyridamole modified release monotherapy twice daily are alternatives.

In some centres, CAS practitioners prefer to stop anticoagulation therapy pre-operatively and then prescribe combination antiplatelet therapy throughout the peri-procedural period, in order to minimise the risks of embolic stroke from the CAS site. If this is the preferred management strategy, combination antiplatelet therapy should be started on the day after VKA/DOAC cessation (see **section 4.2.2.3** for choice and dosages of combination APRx). However, it is important that the MDT determine exactly when post-operative combination antiplatelet therapy should cease and when anticoagulation should be re-started.

4.2.7 Lipid lowering therapy

4.2.7.1 Statins as secondary prevention

RCTs have evaluated lipid lowering therapy in TIA or minor ischaemic stroke patients (**Table 17**), but only one subgroup analysis included patients with carotid disease.³⁴⁷

Table 17: RCTs evaluating lipid lowering therapy in TIA or minor ischaemic stroke patients

RCT	Treatment	Main findings
Inclusion criteria	strategy	
HPS ³⁴⁸	40mg Simvastatin daily vs. placebo	Simvastatin conferred 20% RR in stroke, non-fatal MI, death from coronary artery disease and/or coronary

3 280 patients with prior TIA (46%), minor ischaemic stroke (63%), prior carotid revascularisation (10%) + cholesterol >3.5mmol/L. Mean interval from symptom onset to randomisation = 4y.		or non-coronary revascularisation in patients with prior cerebrovascular disease $p = .001$). A 19% RR in ischaemic stroke with simvastatin (6.1%) vs. placebo (7.5%) was not significant ($p = .1$) with no statistically significant increase in haemorrhagic stroke with simvastatin (1.3% vs. 0.7%).
FASTER ³¹¹ 392 patients randomised within 24 hours of TIA or minor ischaemic stroke using factorial design	All received aspirin + either Clopidogrel vs. placebo and simvastatin vs. placebo	No significant differences in the 90 day endpoint of any stroke between those who were vs. not taking simvastatin
SPARC ³⁴⁹ 4 731 patients with ischaemic stroke/TIA <6 mths with baseline LDL-C 2.6-4.9mmol/L and no known CAD	80mg Atorvastatin vs. placebo	80mg atorvastatin conferred significantly lower fatal/non-fatal stroke at 5yrs (11.2% vs. 13.1%; HR 0.84, 95% CI 0.71-0.99, $p = .03$). Significant increase in haemorrhagic stroke with atorvastatin vs. placebo (2.3% vs. 1.4%; HR 1.66, 95% CI 1.08-2.55, $p = .02$) which didn't negate the benefit of atorvastatin
SPARCL ³⁴⁷ 1 007 SPARCL patients with carotid stenosis (mean 51%) not undergoing CEA or CAS <30d of randomisation.	80mg Atorvastatin vs. placebo	80mg atorvastatin associated with significant reductions in (i) any stroke (HR 0.67; 95% CI 0.47-0.94, $p = .02$); (ii) late carotid revascularisation (HR 0.44; 95% CI 0.24-0.79, $p = .006$) and (iii) major coronary events (HR 0.57; 95% CI 0.32-1.0, $p = .05$)
TST Trial ⁷ 2 860 patients <3mths of ischaemic stroke (MRS 0-3) or <15 days of TIA (patients randomised within median of six days after TIA/stroke).	Aggressive lipid lowering with statins +/- ezetimibe to achieve lower LDL-C target of <1.8mmol/L	66% in lower LDL-C and 94% in higher LDL-C groups received statins only with 33.8% and 5.8% (respectively) also receiving ezetimibe (10mg daily). Lower LDL-C target (vs. higher target) associated with significant reduction in composite endpoint of any cardiovascular death, stroke, MI, hospitalisation for

Outcomes in SCS patients not reported.	vs. higher LDL-C target of 2.3-2.8mmol/L.	unstable angina requiring urgent CABG or PCI or TIA treated by urgent CEA/CAS at 3.5 years. (8.5% vs. 10.9%; HR 0.78, 95% CI 0.61-0.98, $p = .04$).
STARS ³⁰ 98 patients randomised <12hrs of ischaemic stroke.	40mg simvastatin vs. placebo (only 4% of simvastatin patients and 15% of placebo patients had LAA).	Independence at 90 days (mRS ≤ 2): Simvastatin 69% vs. 70% placebo (OR 0.99; 95% CI 0.35-2.78, $p = .98$). No difference in safety (haemorrhagic transformation, haemorrhagic events, death, infections, serious adverse events).
ASSORT ³⁷ 257 with acute ischaemic stroke + dyslipidaemia or LDL-C >2.6mmol/L randomised to early statin therapy vs. delayed statin therapy.	131 started statin therapy <24hrs (for 12 wks) vs. 126 starting statins on day 7 (for 11 wks). (atorvastatin 20mg/day, pitavastatin 4mg/day or rosuvastatin 5mg/day).	At 90 day, mRS distribution not different between patients receiving early statin therapy vs. delayed (OR 1.1; 95% CI 0.79-1.4). LAA responsible for 43% of strokes at presentation (but no data regarding extracranial vs. intracranial disease or whether they were carotid vs. VA).
EUREKA ²² 316 statin naive patients randomised within 48hrs of acute ischaemic stroke. 33-37% had a 50-99% stenosis of a brain supplying artery, but number with extracranial SCS not reported.	Rosuvastatin 20mg ($n=137$) vs. placebo ($n=152$) over 14 days.	No difference in NIBLs at five or 14 days on DW-MRI (19.7% rosuvastatin vs. 23.6% placebo (RR 0.83; 95% CI 0.53-1.3). Rosuvastatin group had a lower risk of new or worsening haemorrhagic transformation of an infarct (4.4%) vs. 14.5% with placebo ($p = .007$)).

RCT = randomised controlled trial; TIA = transient ischaemic attack; CEA = carotid endarterectomy; CAS = carotid artery stenting; CAD = coronary artery disease; MI = myocardial infarction; CABG = coronary artery bypass graft; PCI = percutaneous coronary intervention; RR = Relative Risk;; LDL-C = low density lipoprotein C; OR (95% CI) = Odds Ratio with 95% confidence intervals; SCS = symptomatic carotid stenosis; mRS = modified Rankin score; NIBLs = new ischaemic brain lesions; DW-MRI = diffusion weighted magnetic resonance imaging; LAA = large artery atherosclerosis.

In most RCTs in patients presenting with TIA/stroke (including those with carotid disease), lipid lowering therapy significantly reduced late cardiovascular events (including stroke). Lower LDL-C targets (< 1.8 mmol/L) were associated with lower stroke rates and greater regression of carotid atherosclerosis, compared with higher LDL-C targets (2.3 - 2.8 mmol/L).⁸

4.2.7.2 Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors

Acute ischaemic stroke patients were excluded from many RCTs involving PCSK9 inhibitors. A secondary analysis of FOURIER assessed outcomes in patients with prior ischaemic stroke who had an LDL-C ≥ 1.8 mmol/L or non-high density lipoprotein cholesterol ≥ 2.6 mmol/L after ≥ 2 weeks stabilisation on a moderate or high intensity statin (3.2 - 3.9% were also on ezetimibe).¹⁸ Median delay between stroke onset and randomisation was 3.3 years, with only 23% randomised within one year of stroke onset and none < 4 weeks. The risk of stroke, MI, cardiovascular death, hospitalisation for unstable angina or coronary revascularisation over a median 2.1 year follow up was significantly lower in 2 686 patients randomised to evolocumab (140 mg every 2 weeks or 420 mg every 4 weeks) vs. 2 651 patients on placebo (HR 0.85; 95% CI 0.72–1.00, $p = .047$). However, the risks of any stroke and ischaemic stroke were no different. Evolocumab did not increase haemorrhagic stroke, despite median LDL-C levels of 0.7 - 0.8 mmol/L.¹⁸ The authors suggested that patients with ischaemic stroke and additional atherosclerotic risk factors may benefit from LDL-C levels below current targets.

4.2.7.3 Lipid targets in stroke/TIA patients

There is sufficient high quality evidence to conclude that patients presenting with TIA or minor ischaemic stroke should be prescribed lipid lowering therapy, unless not tolerated. Both the AHA, ESC, and EAS guidelines recommend high dose Atorvastatin 80mg or Rosuvastatin 20mg, unless not tolerated.^{1,258} As no RCTs have specifically evaluated lipid lowering targets in SCS

or ACS patients, the GWC have mainly adopted targets recommended in the 2021 AHA¹ and the 2019 ESC-EAS guidelines.²⁵⁸ The aim is for a total cholesterol < 3.5 mmol/L (< 135 mg/dL),³⁴⁸ LDL-C < 1.8 mmol/L (< 70 mg/dL),^{348, 7,347} or a 50% reduction in LDL-C vs. baseline.¹ It is reasonable to add ezetimibe (10 mg daily) in SCS patients who fail to achieve lipid targets on maximum doses or maximum tolerated statin doses.^{1,7} The GWC acknowledges that the ESC-EAS guidelines recommend a lower target for LDL-C (< 1.4 mmol/L (< 54 mg/dL)) in very high risk patients with atherosclerotic cardiovascular disease, which includes TIA/stroke patients, as well as significant ACS, but ESC-EAS did not define what significant ACS meant.²⁵⁸ However, due to a significant increase in haemorrhagic stroke with atorvastatin vs. placebo in SPARCL (2.3% vs. 1.4%; HR 1.66, 95% CI 1.08 - 2.55, $p = .02$)³⁴⁹ and the exclusion of patients with TIA/acute stroke from PCSK9 inhibitor trials, the GWC based their recommended LDL-C target of < 1.8 mmol/L on RCTs involving stroke/TIA patients. However, in SCS or ACS patients with additional very high risk factors (eg. CAD, PAD; type II DM with target organ damage, longstanding type I DM), a target LDL-C < 1.4 mmol/L (< 54 mg/dL) should be considered.²⁵⁸ Pending RCT data, in SCS patients who are intolerant of, or not achieving LDL-C targets on statins (with or without ezetimibe), additional or alternative treatment with PCSK9 inhibitors should be considered¹⁸.

Recommendation 34 (Unchanged)	Class	Level	References
For patients with a symptomatic carotid stenosis, statin therapy is recommended for the long term prevention of stroke, myocardial infarction and other cardiovascular events.	I	B	347

Recommendation 35 (New)	Class	Level	References
			ToE

For symptomatic carotid stenosis patients who do not reach their lipid targets on maximum doses or maximum tolerated doses of statins, ezetimibe (10mg daily) is recommended.	I	B	7
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Recommendation 36 (New)	Class	Level	References
			ToE
For symptomatic carotid stenosis patients who are intolerant of, or not achieving target LDL levels on statins, with or without ezetimibe, additional or alternative treatment with PCSK9 inhibitors should be considered	Ila	B	18

4.2.7.4 Statins during carotid interventions

In a meta-analysis (7 observational studies; $n = 610$), statin pre-treatment in patients with > 50% SCS was associated with a significantly lower incidence of MES during TCD monitoring vs. statin naive patients (RR = 0.67; 95% CI 0.45 - 0.98).⁹³ In another meta-analysis (6 observational studies; $n = 7\,503$), patients taking statins prior to CEA had significantly lower peri-operative mortality (0.2% vs. 1.3%) in statin naive patients (OR 0.26; 95% CI 0.1-0.61), plus a non-significant reduction in peri-operative stroke (1.4% vs. 3.0%) in statin naive patients (OR 0.4; 95% CI 0.15-1.09).¹⁰⁰ In a third meta-analysis (11 observational studies; $n = 4\,088$), patients taking statins prior to CAS had significantly lower mortality (OR 0.30; 95% CI 0.10 - 0.96) and procedural stroke (OR 0.39; 95% CI 0.27 - 0.58) vs. statin naive patients.¹⁰¹ Stroke patients prescribed statins should not have this medication withdrawn acutely, because RCTs suggest that stopping statins for three days after acute stroke onset (vs. continuing atorvastatin 20 mg daily) was associated with increased rates of death or dependency at 90 days (OR 4.66; 95% CI 1.46 - 14.91, $p = .043$), after adjusting for age and baseline stroke severity.⁴¹

Recommendation 37 (Unchanged)	Class	Level	References
For patients scheduled to undergo endarterectomy or stenting, it is recommended to commence statin therapy pre-operatively.	I	A	93,100,101

4.2.8 Management of hypertension

4.2.8.1 Secondary prevention in patients with symptomatic carotid stenosis

A Cochrane review (11 RCTs; $n = 38\,742$) reported that anti-hypertensive therapy significantly reduced the relative risk of recurrent stroke by 24% in patients with a prior ischaemic stroke (RR 0.76; 95% CI 0.64 - 0.89).¹¹⁴ A meta-analysis of secondary stroke prevention (14 RCTs; $n = 42\,736$) showed that the extent of SBP and DBP reduction was linearly associated with the magnitude of reduction in recurrent cerebrovascular and cardiovascular events,⁶⁸ emphasising the importance of strict BP control in patients with prior cerebrovascular events. As with ACS patients, the GWC advises readers to refer to ESC-ESH thresholds for treating hypertension (section 3.1.5).²³⁶

4.2.8.2 Blood pressure management during carotid interventions

Because SBP > 180 mmHg is an independent risk factor for stroke after CEA,³⁵⁰ it is reasonable to perform urgent CEA when pre-operative BP is < 180 mmHg. There are no published data for CAS patients, but a similar approach seems reasonable. Symptomatic patients with SBP > 180 mmHg should receive urgent, titrated antihypertensive treatment before undergoing CEA, whilst acknowledging that very rapid BP lowering before CEA and CAS may be inadvisable in patients with severe bilateral stenoses.³⁵¹ Persisting or worsening hypertension after CEA should be treated actively to prevent hyperperfusion syndrome, ICH, bleeding complications, and cardiac events in the early post-operative period³⁰⁹ (section 7.1.3.3).

Recommendation 38 (Unchanged)	Class	Level	References
For patients presenting with a transient ischaemic attack or minor ischaemic stroke with hypertension, antihypertensive treatment is recommended	I	A	236

Recommendation 39 (Unchanged)	Class	Level	References
For symptomatic carotid stenosis patients awaiting endarterectomy or stenting, caution should be considered when rapidly lowering blood pressure in the early time period after onset of symptoms, but uncontrolled hypertension (>180/90 mmHg) should be treated.	Ila	C	350,351

4.2.9 Management of DM

Principles underpinning the management of DM patients with SCS are similar to those with ACS (section 3.1.6). The Prospective Pioglitazone Clinical Trial in macroVascular Events (PROACTIVE) ($n = 5\,238$) investigators reported that pioglitazone (in addition to existing glucose lowering and cardiovascular medications), lowered the risk of stroke in type II DM patients.²⁴² Treatment of DM is important in the acute stroke setting, but it is reasonable to aim for normoglycemia because intensive blood glucose control has not been shown to be beneficial.^{23,352,353} Thereafter, it is reasonable to aim for optimal glycaemic control as per updated guidelines from committees with expertise in treating patients with diabetes.^{243,344}

4.2.10 Adherence to medications

Adherence was analysed in 114 TIA/ischaemic stroke patients who were followed for a median of 1.7 years.³⁵⁴ Letters describing clinical details and a goal directed treatment plan were sent to the patient and referring doctor. The proportion continuing to take prescribed medications was 94% for aspirin, 73% for dipyridamole, 81% for clopidogrel, 88% for statins and 90% for antihypertensive therapy. Overall, 99% reported full adherence the preceding day, while 11%

reported missing at least one medication over the preceding 14 days. Half reported that they never forgot to take their medications.³⁵⁴ The widest variation in adherence involved statins, possibly because of perceived side effects.³⁵⁵ Non-adherence contributes towards patients not achieving LDL-C targets, which increases the risk of recurrent vascular events. The same may apply to aspirin plus dipyridamole therapy (usually dipyridamole induced headache), but this can be reduced by slow dose escalation in the first week of treatment.

4.3 Randomised trials: Endarterectomy vs. medical therapy

4.3.1 30 day and five year outcomes in the randomised trials

Three RCTs (NASCET, ECST, and the Symptomatic Veterans Affairs Co-operative Study (SVACS)) compared CEA vs. BMT in SCS patients reporting carotid territory symptoms within six months.^{188,189,356} The Carotid Endarterectomy Trialists Collaboration (CETC) performed an individual patient meta-analysis of 6 092 patients in the three RCTs, with pre-randomisation angiograms re-measured using the NASCET method. (**Table 18**).³⁵⁷⁻³⁵⁹ CEA (plus BMT) conferred no benefit in patients with < 50% stenoses (see **section 4.10** for management of patients developing recurrent symptoms despite BMT). CEA conferred significant benefit in patients with moderate (50 - 69%) and severe (70 - 99%) stenoses (**table 18**). The benefit conferred by CEA increased with stenosis severity, with the exclusion of CNO. CETC concluded that CNO patients gained no benefit from CEA,^{357,358} and the controversy is discussed further in **section 4.12**.

Table 18: individual patient meta-analysis of five year risks of any stroke (including peri-operative stroke/death) from ECST, NASCET and SVACS RCTs*

	<i>n</i>	5y risk of any stroke (inc peri-operative)	ARR @ 5y	RRR @ 5y		
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stenosis severity (NASCET)		CEA + BMT	BMT			NNT to prevent one stroke @ 5y	strokes prevented per 1 000 CEAs @ 5y
0-30%	1 746	18.4%	15.7%	-2.7%	n/b	n/b	none
30-49%	1 429	22.8%	25.5%	+2.7%	n/b	n/b	27
50-69%	1 549	20.0%	27.8%	+7.8%	28%	13	78
70-99%	1 095	17.1%	32.7%	+15.6%	48%	6	156
CNO	262	22.4%	22.3%	-0.1%	n/b	n/b	none

(*) data derived from the Carotid Endarterectomy Trialists Collaboration³⁵⁷⁻³⁵⁹

CEA = carotid endarterectomy; BMT = best medical therapy; ARR = absolute risk reduction in stroke; RRR = relative risk reduction in stroke; NNT = number needed to treat to prevent one stroke at five years; n/b = no benefit; NASCET = North American Symptomatic Carotid Endarterectomy Trial; SVACS = Symptomatic Veterans Affairs Carotid Study; ECST = European Carotid Surgery Trial; CNO = chronic near occlusion; y = years.

4.3.2 Who is at higher risk of stroke on medical therapy?

Clinical/imaging predictors of increased stroke risk on BMT in the RCTs are detailed in **Table 19**.

Table 19: Clinical and Imaging features that were predictive of a significant increase in late stroke in patients with 50 - 99% stenoses randomised within ECST and NASCET

CLINICAL FEATURES	IMAGING FEATURES
Increasing Age ^{357,358,360} 5y ARR in ipsilateral stroke conferred by CEA <65y = 5.6% (NNT18); 65-75y = 8.6% (NNT 12); >75y = 19.2% (NNT 5)	Irregular vs. Smooth Plaques ³⁵⁸ 5y ARR in ipsilateral stroke conferred by CEA smooth = 8% (NNT 13); irregular = 17% (NNT 6)
Recency of Symptoms ³⁵⁸	Increasing Stenosis Severity ³⁵⁷

5y ARR in ipsilateral stroke conferred by CEA <2w=18.5% (NNT 5); 2-4w=9.8% (NNT 10) 4-12w=5.5% (NNT 18); >12w=0.8% (NNT 125)	5y ARR in ipsilateral stroke conferred by CEA 50-69%=4% (NNT 25); 60-69%=5.9% (NNT 17); 70-79%=15.8% (NNT 6); 80-99%=17.7% (NNT 6); 90-99%=32.4% (NNT 3)
Men vs. Women³⁵⁹ 5y ARR in ipsilateral stroke conferred by CEA males = 11% (NNT 9); females = 2.8% (NNT 36)	Contralateral Occlusion³⁵⁸ 5y ARR in ipsilateral stroke conferred by CEA Contralat occlusion = 24% (NNT 4); no occlusion = 13% (NNT 8)
Hemispheric vs. Ocular Symptoms³⁵⁸ 5y ARR in ipsilateral stroke conferred by CEA ocular = 5% (NNT 20); TIA = 15% (NNT 7); stroke = 18% (NNT 6)	Tandem intracranial disease³⁶² 3y risk of ipsilateral stroke in medically treated patients with tandem intracranial disease increased with extracranial ICA stenosis severity 50-69% = 19% (NNT 5); 70-84% = 29% (NNT 3); 85-99% = 45% (NNT 2)
Cortical vs. Lacunar Stroke³⁶¹ 3y ARR in ipsilateral stroke conferred by CEA non-lacunar stroke 15% (NNT 7); lacunar stroke 9% (NNT 11)	No recruitment of collaterals³⁶³ 2y ARR in ipsilateral stroke conferred by CEA collaterals recruited = 5% (NNT 20); no recruitment = 19% (NNT 5)
Increasing Medical co-morbidities¹⁸⁹ 2y risk of ipsilateral stroke on BMT 0-5 co-morbidities = 17%; 6 = 23%; 7+ = 39% 2y risk of ipsilateral stroke with CEA 0-5 co-morbidities = 11%; 6 = 6%; 7+ = 8%	

NASCET = North American Symptomatic Carotid Endarterectomy Trial; ECST = European Carotid Surgery Trial; CEA = carotid endarterectomy; BMT = best medical therapy; TIA = transient ischaemic attack; ICA = internal carotid artery; ARR = absolute risk reduction; NNT = number needed to treat to prevent one stroke; y = years; w = weeks.

4.4 Randomised trials: Endarterectomy vs. stenting

4.4.1 30 day outcomes

10 RCTs compared CEA vs. CAS (not CA) in 5 797 SCS patients. A meta-analysis of 30 day outcomes is detailed in **Table 20**. CAS (almost exclusively TFCAS) was associated with

significantly higher rates of any stroke, death/any stroke, death/disabling stroke and death/any stroke/MI vs. CEA.⁴⁸

Table 20: Meta-analysis of 30 day outcomes in 10 RCTs* comparing CAS vs. CEA **

	Death	Stroke	Death/ Stroke	Disabling Stroke	Death/ Disabling Stroke	MI	Death/ Stroke/MI
	9 RCTs <i>n</i> =4 257	9 RCTs <i>n</i> =5 535	10 RCTs <i>n</i> =5 797	6 RCTs <i>n</i> =4 855	5 RCTs <i>n</i> =3 534	6 RCTs <i>n</i> =3 980	6 RCTs <i>n</i> =3 719
CAS (95%CI)	1.9% (1.4-2.6)	8.5% (5.9-12.1)	9.3% (6.8-12.6)	3.3% (1.6-6.7)	5.2% (3.0-8.9)	0.8% (0.5-1.4)	8.4% (5.0-13.8)
CEA (95%CI)	1.4% (0.9-2.0)	4.6% (3.3-6.4)	5.1% (3.7-6.9)	1.8% (1.1-3.1)	3.2% (2.5-4.1)	1.6% (1.0-2.3)	5.1% (4.1-6.3)
OR (95%CI)	1.38 (0.8-2.3)	1.73 (1.4-2.1)	1.71 (1.4-2.1)	1.35 (0.9-2.0)	1.42 (1.0-2.0)	0.50 (0.2-1.0)	1.61 (1.2-2.1)

Yellow boxes indicate no statistically significant difference. **Red boxes** indicate a statistically significant result favouring CEA

* CREST-1; EVA-3S; ICSS; Kuliha; Naylor; Brooks; Steinbauer; SPACE-1; SAPHIRE; Wallstent; RCTs = randomised controlled trials; MI = myocardial infarction; CEA = carotid endarterectomy; CAS = carotid artery stenting; OR (95%CI) = odds ratio (95% confidence intervals).

** Reproduced with permission from Batchelder A, Saratzis A, Naylor AR. Overview of Primary and Secondary Analyses from 20 randomised controlled trials comparing carotid artery stenting with carotid endarterectomy. *Eur J Vasc Endovasc Surg* 2019;58:479-493.

Table 21 details a meta-analysis of 30 day outcome data in 4 754 patients from four large multicentre RCTs that randomised > 500 patients including the Endarterectomy versus Stenting in patients with Symptomatic Severe carotid Stenosis (EVA-3S), the Stent-Protected Angioplasty versus Carotid Endarterectomy (SPACE) trial, the International Carotid Stenting Study (ICSS) and the Carotid Revascularisation Endarterectomy vs. Stenting (CREST) Trial.^{314,316,317,364} CAS (almost

exclusively TFCAS) was associated with significantly higher rates of 30 day stroke, death/stroke and death/stroke/MI vs. CEA.⁴⁸ All other endpoints were similar.

Table 21: Meta-analysis of 30 day outcomes after CAS vs. CEA in four RCTs which randomised more than 500 symptomatic patients*

	Death	Stroke	Death/ Stroke	Disabling Stroke	Death/ Disabling Stroke	MI	Death/ Stroke/MI
	3 RCTs <i>n</i> =3 413	4 RCTs <i>n</i> =4 754	4 RCTs <i>n</i> =4 754	4 RCTs <i>n</i> =4 754	3 RCTs <i>n</i> =3 413	3 RCTs <i>n</i> =3 551	2 RCTs <i>n</i> =3 031
CAS	1.2%	7.8%	8.7%	3.3%	4.3%	0.7%	8.0%
(95% CI)	(0.5-2.9)	(6.8-9.0)	(7.6-9.9)	(2.6-4.1)	(3.4-5.4)	(0.4-1.3)	(5.9-10.7)
CEA	0.9%	4.8%	5.5%	2.4%	3.2%	1.0%	5.2%
(95% CI)	(0.5-1.5)	(4.0-5.7)	(4.7-6.5)	(1.8-3.1)	(2.5-4.2)	(0.3-3.1)	(4.2-6.5)
OR	1.67	1.66	1.61	1.39	1.38	0.51	1.60
(95% CI)	(0.9-3.2)	(1.3-2.1)	(1.3-2.0)	(0.9-2.0)	(0.9-2.0)	(0.3-1.0)	(1.2-2.1)

Yellow boxes = no statistically significant difference. Red boxes = statistically significant result favouring CEA.

RCTs = randomised controlled trials; MI = myocardial infarction; CEA = carotid endarterectomy; CAS = carotid artery stenting; OR (95% CI) = odds ratio (95% confidence intervals). *CREST-1; EVA-3S; ICSS; SPACE-1. ** Reproduced with permission from Batchelder A, Saratzis A, Naylor AR. Overview of Primary and Secondary Analyses from 20 randomised controlled trials comparing carotid artery stenting with carotid endarterectomy. *Eur J Vasc Endovasc Surg* 2019;58:479-493.

4.4.1.2 30 day outcomes stratified by age

The Carotid Stenting Trialists Collaboration (CSTC) performed an individual patient meta-analysis of 4 289 SCS patients in ICSS, CREST, EVA-3S and SPACE. There was a strong association between increasing age and higher 30 day death/stroke after CAS, but not CEA (**table 22**).¹⁶⁹

Compared with CEA (**column 3, table 22**), CAS patients aged > 70 years incurred significantly higher rates of death/stroke. Below 70 years, CAS had similar outcomes to CEA.

Table 22: Age and 30 day rates of death/stroke after CEA and CAS in symptomatic patients randomised within ICSS, CREST, EVA-3S, SPACE*

	CAS		CEA		CAS vs. CEA
Age - y	30 day death/stroke	HR (95% CI)	30 day death/stroke	HR (95% CI)	HR (95% CI) ***
<60	13/407 (3.2%)	1.0**	21/407 (5.2%)	1.0 **	0.62 (0.31-1.23)
60-64	20/351 (5.7%)	1.79 (0.89-3.60)	18/341 (5.3%)	1.01 (0.34-1.9)	1.07 (0.56-2.01)
65-69	31/462 (6.7%)	2.16 (1.13-4.13)	18/422 (4.3%)	0.81 (0.43-1.52)	1.61 (0.90-2.88)
70-74	58/480 (12.1%)	4.01 (2.19-7.32)	26/436 (6.0%)	1.20 (0.68-2.13)	2.09 (1.32-2.32)
75-79	48/403 (11.9%)	3.94 (2.14-7.28)	30/461 (6.5%)	1.29 (0.74-2.25)	1.91 (1.21-3.01)
≥80	36/290 (12.4%)	4.15 (2.20-7.84)	16/291 (5.5%)	1.09 (0.57-2.10)	2.43 (1.35-4.38)

* data derived from Howard ¹⁶⁹

** All HR age based calculations compared against age < 60 years

*** age based HR calculation for CAS compared with CEA. If HR is < 1.0, CAS is associated with significantly lower peri-operative death/stroke. If HR is > 1.0, CAS is associated with significantly higher rates of peri-operative stroke/death.

CAS = carotid artery stenting; CEA = carotid endarterectomy; HR (95% CI) = hazard ratio (95% confidence intervals).

4.4.2 Long term outcomes in RCTs

4.4.2.1 Late ipsilateral stroke

Excluding peri-operative risks, a CSTC meta-analysis of four RCTs showed that five year rates of ipsilateral stroke were 3.1% after CEA vs. 3.2% after CAS (HR 1.06; 95% CI 0.73-1.54), giving an average annual ipsilateral stroke rate of 0.62% (CEA) and 0.64% (CAS). Nine year rates of ipsilateral stroke were 3.9% after CEA vs. 4.5% after CAS, giving an average annual ipsilateral stroke rate of 0.43% after CEA and 0.5% after CAS.¹² These data indicate that, as with ACS (section 3.8.2), CAS was as durable as CEA once the peri-operative period had elapsed. Accordingly, the decision to perform CEA or CAS will be largely determined by factors associated with increases in peri-operative stroke/death after CEA or CAS in individual patients (sections 7.1.1.3 and 7.1.2.1).

4.4.2.2 Quality of life

Health Related Quality of life was assessed in CREST.³⁶⁵ CAS patients had better quality of life in the post-operative period, especially physical limitation and pain ($p = .01$), but not at one year. Using disease specific scales, CAS patients reported fewer problems with driving, eating, swallowing, neck pain and headache, but greater difficulty with walking and leg pain ($p < .05$). However, at one year, there was no difference. Peri-operative stroke was associated with poorer one year quality of life across all SF-36 domains, while peri-procedural MI and CNI were not.

4.4.2.3 Survival following peri-operative stroke or MI

The relevance of peri-operative MI (especially non-ST elevation MI with troponin elevation) has

been a source of controversy since its inclusion in the primary endpoint in SAPPHERE and CREST.^{282,316} The rationale was that peri-operative MI and/or troponin elevation were associated with poorer long term survival after non-cardiac surgery.³⁶⁶ At 10 years; CREST patients having a peri-operative stroke had significantly higher mortality vs. patients without peri-operative stroke (HR 1.74; 95% CI 1.21-2.5, $p < .003$).²⁸ Compared with CREST patients who did not have a peri-operative stroke, reduced long term survival was mainly due to deaths occurring in the first 90 days (HR 14.41; 95% CI 5.33-38.94, $p < .0001$). Thereafter, there was a non-significant trend towards increased mortality between 91 days and 10 years (HR 1.40; 95% CI 0.93-2.10). CREST patients with a peri-operative MI had significantly higher mortality at 10 years vs. patients without peri-operative MI (HR 3.61; 95% CI 2.28-5.73, $p = .006$).²⁸ Increased mortality in CREST patients with a peri-operative MI continued through the first 90 days (HR 8.2; 95% CI 1.86-36.2, $p < .001$) and from day 91 to 10 years (HR 3.4; 95% CI 2.09-5.53, $p < .0001$).²⁸

Accordingly, peri-operative stroke and MI are associated with poorer long term survival, emphasising the importance of careful patient selection and optimisation of pre-operative BMT. ESC/European Society of Anaesthesiology guidelines currently do not recommend routine pre- and post-operative troponin measurement in patients undergoing CEA or CAS.³⁶⁷ However, patients with post-operative MI or stroke should be evaluated carefully before discharge. Cardiology review is necessary after a documented MI or where troponin levels have been requested (on clinical grounds) and found to be elevated, as intensification of BMT before discharge (defined as compliance with ESC recommendations for the management of chronic coronary syndromes³⁶⁸) prevents major recurrent cardiac events. Patients with troponin elevation and no post-operative intensification of BMT are significantly more likely to suffer major cardiac events at 12 months vs. patients receiving intensified BMT (HR 2.8; 95% CI 1.05-24.2, $p = .04$).³⁶⁹

4.5 Timing of interventions after onset of symptoms

4.5.1 Risk of recurrent stroke over time

CEA is sometimes delayed in SCS patients because it was believed that this may reduce procedural risks,³⁷⁰ although deferral is advised in patients with disabling stroke (**section 4.7**). However, there is good evidence that CEA confers maximum benefit if performed within 14 days of symptom onset.³⁵⁷⁻³⁵⁹ There is also evidence that the risk of early, recurrent stroke after TIA may be higher than previously thought. Natural history studies suggest the incidence of recurrent stroke after a TIA range from 5 - 8% at 48 hours, 4 - 17% at 72 hours, 8 - 22% at 7 days and 11 - 25% at 14 days (**Table 23**). Recurrent stroke rates at 14 days in the natural history studies are much higher than was reported at five years in BMT patients in ECST, NASCET and SVACS, suggesting that many SCS patients who were destined to suffer an early recurrent stroke were never randomised within the RCTs (which tended to recruit patients somewhat later).

Table 23: Risk of stroke in the early time period after TIA onset in patients with 50 - 99% SCS

	<i>n</i>	48 hours	72 hours	7 days	14 days	5 years
ECST+NASCET+VA 'BMT' patients ^{*358}	1 227					21%
Fairhead ^{**371}	85				20%	
Purroy ^{**372}	90			10%		
Ois ^{**373}	163		17%	22%	25%	
Bonifatì ^{**374}	36	8%				
Johansson ^{**375}	230	5%		8%	11%	

Mono** ³⁷⁶	94		4%			
Merwick** ³⁷⁷	387			8%		
Marnane** ³⁷⁸	44	5%	9%	16%		

NASCET = North American Symptomatic Carotid Endarterectomy Trial; VA = Symptomatic Veterans Affairs Carotid Study; ECST = European Carotid Surgery Trial. * timing relates to time from randomisation; ** timing relates to time from TIA onset; BMT = best medical therapy; SCS = symptomatic carotid stenosis; TIA = transient ischaemic attack.

However, early recurrent stroke in a CSTC meta-analysis of four RCTs (4 754 SCS patients randomised to and then awaiting CEA/CAS) were compared with early recurrent stroke in three older RCTs which randomised patients to CEA or BMT.¹⁶ Recurrent stroke in the more recent RCTs was only 2% at 120 days, which is much lower than in the older RCTs (**table 19**) and in observational studies (**table 23**). CSTC observed that while improvements in BMT, risk factor control and lifestyle may have contributed to reduced early stroke risks in the modern era, RCTs may include patient populations with lower risks of stroke compared with observational cohorts. Accordingly, CSTC concluded that it remained advisable to adhere to recommendations supporting early revascularisation in SCS patients.¹⁶ Other potential reasons for the apparent decline in early stroke after TIA/stroke onset in more recent RCTs include the absence of data on consecutive cases (all of the RCTs in Fisch's meta-analysis included patients already scheduled for CEA or CAS) and early neurological deterioration after the index TIA being missed and, therefore, not reported.³⁷⁹ Natural history studies suggest that rapid institution of BMT after TIA/minor stroke significantly reduces early recurrent stroke, suggesting that emergency carotid interventions are probably unnecessary unless the patient reports crescendo TIAs or stroke in evolution (**section 4.7**).^{144,308,328}

4.5.2 Timing of carotid endarterectomy in national registries and meta-analyses

Five national registries have published median delays from symptom onset to CEA. In the Netherlands, Norway and UK, median delay is 11 days,^{140,142,380} vs. nine days in Germany³⁸¹ and

eight in Sweden.³⁸² Three European countries have published more detailed registry data regarding delays between symptom onset and undergoing CEA (**table 24**).

Table 24: Proportion of patients undergoing CEA in national audits within 0 - 2, 3 - 7, 8 – 14, and > 15 days after onset of symptoms

National Audit	0-2 days	3-7 days	8-14 days	≥15 days
Sweden ³⁸² <i>n</i> = 2 596	148/2 596 (6%)	804/2 596 (31%)	677/2 596 (26%)	967/2 596 (37%)
UK ³⁸⁰ <i>n</i> = 23 235	780/23 235 (3%)	5 126/23 235 (22%)	6 292/23 235 (27%)	11 037/23 235 (48%)
Germany ³⁸¹ <i>n</i> = 56 279	5 198/56 279 (9%)	19 117/56 279 (34%)	16 205/56 279 (29%)	15 759/56 279 (28%)

Table 25 details 30 day rates of death/stroke, stratified for delays from symptom onset to CEA. The 2012 Swedvasc registry attracted the most controversy because when CEA was performed within 48 hours of symptom onset, the 30 day death/stroke rate was 11.5%.³⁸² This significant increase in risk was not, however, observed in the much larger German or UK registries.^{380,381} After 48 hours has elapsed, all three registries showed that CEA could be performed with low procedural risks.³⁸⁰⁻³⁸²

Table 25. 30 day death/stroke after CEA, stratified for delay from symptom onset

National Audit	0-2 days	3-7 days	8-14 days	≥15 days
	% (95%CI)	% (95%CI)	% (95%CI)	% (95%CI)

Sweden ³⁸²	17/148	29/804	27/677	52/967
<i>n</i> = 2 596	11.5% (6.8-17.8)	3.6% (2.4-5.1)	4.0% (2.6-5.8)	5.4% (4.0-7.0)
UK ³⁸⁰	29/780	128/5 126	132/6 292	254/11 037
<i>n</i> = 23 235	3.7% (2.5-5.3)	2.5% (2.1-3.0)	2.1% (1.8-2.5)	2.3% (2.0-2.6)
Germany ³⁸¹	157/5 198	480/19 117	427/16 205	370/15 759
<i>n</i> = 56 279	3.0% (2.6-3.5)	2.5% (2.3-2.7)	2.6% (2.4-2.9)	2.3% (2.1-2.6)

A 2021 meta-analysis (3 RCTs, 68 observational cohorts (*n* = 232 952)) reported that when CEA was performed within 2 days of symptom onset (vs. days 3 - 14), there were significantly higher rates of 30 day stroke (OR 1.57; 95% CI 1.3 - 1.9) and death (OR 5.19; 95% CI 4.1 - 6.6).⁵² When CEA was performed within 7 days (vs. days 8-14), there was a non-significant trend towards increased 30 day stroke (OR 1.2; 95% CI 0.96 - 1.50) and death/stroke (OR 1.22; 95% CI 0.99 - 1.45), but no difference in MI (OR 1.33; 95% CI 0.11 - 15.43) or mortality (OR 1.29; 95% CI (0.88 - 1.88)).

4.5.3 Timing of carotid stenting in national registries and meta-analyses

Two European countries have published registry data on delays between symptom onset and CAS. **Table 26** details the proportion undergoing CAS within each time period, while **table 27** details 30 day death/stroke after CAS, stratified for delays from symptom onset to CAS.

Table 26: Proportion of patients undergoing CAS in national audits within 0 - 2, 3 - 7, 8 - 14, and ≥ 15 days after onset of symptoms

National Audit	0-2 days	3-7 days	8-14 days	≥ 15 days
Sweden ³⁸³	13/323 (4.0%)	85/323 (26.3%)	80/323 (24.8%)	145/323 (44.9%)

Germany ¹⁵⁶	550/4 717 (11.6%)	1 579/4 717 (33.4%)	1 244/4 717 (26.3%)	1 344/4 717 (28.4%)
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Table 27: Procedural death/stroke rates after CAS, stratified for delay from symptom onset to CAS in national audits of practice

National Audit	0-2 days	3-7 days	8-14 days	≥15 days
Sweden ^{*383}	0/13 (0.0%)	4/85 (4.7%)	5/80 (6.3%)	6/145 (4.1%)
Germany ^{**156}	33/550 (6.0%)	70/1 579 (4.4%)	30/1 244 (2.4%)	40/1 344 (3.0%)

* 30 day death/stroke; ** in hospital death/stroke

In the German Statutory Quality Assurance database, performing CAS 3 - 7 days after symptom onset was not associated with reduced in hospital death/stroke vs. when CAS was performed in ≤ 2 days. Performing CAS 8 - 14 days after symptom onset was associated with significantly lower in hospital death/stroke vs. patients undergoing CAS within two days of symptom onset (OR 0.36; 0.20 - 0.67, $p = .001$).¹⁵⁶ In a 2021 meta-analysis (3 RCTs, 68 observational cohorts ($n = 232\,952$)), two studies evaluated outcomes when CAS was performed within 2 days vs. 3 - 14 days of the index symptom⁵². Compared with CAS interventions at 3 - 14 days, CAS within 2 days was not associated with significant increases in 30 day stroke (OR 1.36; 95% CI 0.84 - 2.04), but there was a significantly higher risk of death (OR 2.77; 95% CI 1.39 - 5.52). Two studies compared outcomes when CAS was performed within seven days vs. 8-14 days.⁵² CAS was associated with significantly higher rates of 30 day stroke (OR 1.8; 95% CI 1.14 - 2.84) if performed within 7 days (vs. 8-14 days) after the index event, with no difference in mortality rate (OR 1.70; 95% CI 0.78 - 3.73).⁵²

4.5.4 Comparison of CEA with CAS in the early time period after symptom onset

In a CSTC meta-analysis involving 4 138 SCS patients randomised in CREST, ICSS, EVA-3S and SPACE, only 11% underwent CEA or CAS within 48 hours of symptom onset.¹⁷⁰ Amongst patients treated within seven days of symptom onset, patients undergoing TFCAS were significantly more likely to suffer an adverse 30 day outcome, compared with patients undergoing CEA (table 28).

Table 28: 30 day outcomes following CAS vs. CEA, stratified for timing after symptom onset in a meta-analysis of symptomatic patients randomised in CREST, ICSS, EVA-3S and SPACE*

	30 day outcomes		OR (95%CI)	<i>p</i>
	CEA	CAS		
ANY STROKE/DEATH				
≤7 days	3/226 (1.3%)	24/287 (8.4%)	6.51 (2.00-21.21)	0.002
>7 days	65/1 819 (3.6%)	129/1 806 (7.1%)	2.00 (1.49-2.67)	< .0001
ANY STROKE				
≤7 days	3/226 (1.3%)	23/287 (8.0%)	6.27 (1.92-20.44)	0.002
>7days	62/1 819 (3.4%)	122/1 806 (6.8%)	1.98 (1.47-2.67)	< .0001
FATAL/DISABLING STROKE				
≤7 days	1/226 (0.4%)	9/287 (3.1%)	8.29 (1.07-64.28)	0.04
>7 days	26/1 819 (1.4%)	46/1 806 (2.5%)	1.77 (1.10-2.85)	0.02

* Based on data from Rantner et al¹⁷⁰. CEA = carotid endarterectomy; CAS = carotid artery stenting; OR (95%CI) = odds ratio (95% confidence intervals)

CSTC concluded that for patients undergoing carotid interventions within seven days of symptom onset, CEA was safer than TFCAS.¹⁷⁰ In another CSTC meta-analysis, patients

undergoing TFCAS within 8 - 14 days of their most recent symptom also had significantly higher rates of 30 day death/stroke (8.1%) vs. 3.4% after CEA (OR 2.42; 95% CI 1.0 - 5.7, $p = .04$).³⁸⁴

4.5.5: TCAR outcomes stratified for timing after symptom onset

There has been considerable interest in whether TCAR confers lower procedural risks when performed < 14 days after symptom onset, vs. TFCAS. Only one registry has reported procedural risks after TCAR, stratified for timing after symptom onset.¹¹⁸ In an SVS-VQI audit involving 2 608 SCS patients treated by TCAR, 5.5% were performed within two days of the most recent symptom, 35% at 3 - 14 days, while 59% were performed after > 14 days had elapsed. In hospital outcomes are detailed in **Table 29**. These suggest that in hospital stroke and death/stroke were significantly higher when TCAR was performed within two days of the most recent symptom, while TCAR performed 3 - 14 days after the most recent symptom incurred procedural risks similar to when performed after > 15 days had elapsed. The only significant difference was that patients undergoing TCAR within 14 days were more likely to be discharged to a non-home destination (22% vs. 6.6%; OR 4.2, 95% CI 3.2 - 5.5, $p < .001$).¹¹⁸ These findings are, however, similar to in hospital outcomes reported after TFCAS in the German Statutory Quality Assurance database (**Table 27**).¹⁵⁶

Table 29. In hospital rates of stroke and death/stroke in 2 608 patients undergoing TCAR, stratified for timing after most recent neurological event*.

	<2 days <i>n</i> = 144	3-14 days <i>n</i> = 928	>14 days <i>n</i> = 1 536
In hospital stroke	5.6% OR 2.8; 95% CI 1.3-6.2, $p = .01$	2.5% OR 1.3; 95%CI 1.3-6.4, $p = .4$	2.0% (reference group for calculating OR)**

In hospital stroke/ death	6.5% OR 2.9; 95% CI 1.3-6.4, $p = .01$	2.9% OR 1.2; 95% CI 0.7-2.1, $p = .48$	2.3% (reference group for calculating OR)**
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* based on data from Cui et al¹¹⁸. **OR (95%CI) calculated by comparing outcomes against those performed > 14 days.

OR (95%CI) = Odds Ratio (95% confidence intervals); TCAR = Transcarotid artery revascularisation.

More prospective audits are required to corroborate the SVS-VQI data which are otherwise encouraging. However, 1 169 SCS patients (31%) undergoing TCAR in the SVS-VQI audit did not meet the inclusion criteria, including an unknown proportion with no timing data available. In addition, in hospital endpoints underestimate 30 day procedural risks by 20 - 25%,^{385,386} making direct comparison with 30 day outcomes after TFCAS or CEA less robust.

4.6 Should the 6% risk threshold in symptomatic patients be modified?

Guidelines since 1998 advise that the 30 day risk of stroke/death when performing CEA in patients reporting ipsilateral carotid territory symptoms < 6 months should be 6% or less²⁸³ and that this should be independently audited (**section 2.6**). Recent German-Austrian and ESO guidelines advise that *in hospital* death/stroke following CEA/CAS in SCS patients should be 4% or less.^{2,3} However, this does not mean that the 30 day 6% threshold in SCS patients is being reduced. As with ACS patients (**section 3.9**), it is more an attempt to define acceptable risk thresholds while the patient is still in hospital (ie. easier to audit). RCTs suggest that 19 - 24% of peri-operative strokes and deaths occur after the 8th post-operative day,³⁸⁶ which effectively means the 6% 30 day death/stroke threshold has still been retained by the two guidelines.

One important change in practice over the last 15 years has been awareness that the highest risk period for recurrent stroke is the first 7 - 14 days after symptom onset (**section 4.5.1**).

Previously, provided CEA was performed within six months of symptom onset, a 6% procedural risk was considered appropriate.²⁸³ However, there have been concerns that intervening early in SCS patients might increase peri-procedural risks,³⁷⁰ which could potentially negate any benefits regarding prevention of early recurrent stroke. However, a re-analysis of data from NASCET, ECST and SVACS revealed that even if a surgeon performed CEA within 14 days with a 10% peri-operative risk, more strokes would probably be prevented at five years, compared with delaying CEA for four weeks and then by operating with a theoretical risk of 0%.³⁸⁷ Many countries have reconfigured their services to deliver CEA as soon as possible after symptom onset (**section 4.5.2**). The GWC recognised the importance of promoting early interventions and that most CEAs in Europe are now performed within 7 - 14 days of symptom onset. The GWC concluded that the 30 day risk of stroke/death after CEA or CAS in recently symptomatic patients should be retained at 6% or less, mainly to minimise risk aversion, where surgeons or interventionists might delay interventions to achieve lower complication rates. Such delays could, in turn, lead to increased rates of early recurrent stroke in SCS patients.

Recommendation 40 (Unchanged)	Class	Level	References
For patients reporting carotid territory symptoms within the preceding six months and who have a 70-99% carotid stenosis, carotid endarterectomy is recommended provided the 30 day risk of death/stroke rate is <6%.	I	A	357-359

Recommendation 41 (Unchanged)	Class	Level	References
For patients reporting carotid territory symptoms within the preceding six months and who have a 50-69% carotid stenosis, carotid endarterectomy should be considered provided the documented 30 day risk of death/stroke rate is <6%.	Ila	A	357-359

Recommendation 42 (Unchanged)	Class	Level	References
For patients aged ≥ 70 years who have experienced a carotid territory transient ischaemic attack or ischaemic stroke within the preceding 6 months in association with a 50-99% carotid stenosis, it is recommended that they should be treated by carotid endarterectomy, rather than carotid stenting.	I	A	169

Recommendation 43 (Unchanged)	Class	Level	References
For patients aged < 70 years who have experienced a carotid territory transient ischaemic attack or ischaemic stroke within the preceding 6 months in association with a 50-99% carotid stenosis, carotid artery stenting may be considered an alternative to endarterectomy, provided the documented 30 day risk of death/stroke is $< 6\%$.	IIb	A	169

Recommendation 44 (Unchanged)	Class	Level	References
For symptomatic patients with a 50-99% stenosis in whom a carotid intervention is considered appropriate, it is recommended that this be performed as soon as possible, preferably within 14 days of symptom onset.	I	A	358,359

Recommendation 45 (Unchanged)	Class	Level	References
For patients who are undergoing revascularisation within the first 14 days after onset of symptoms, it is recommended that they should undergo carotid endarterectomy, rather than carotid stenting.	I	A	170,384

4.7 Intervening in neurologically unstable patients

Patients with a disabling stroke ($mRS \geq 3$), or where the area of infarction exceeds one third of the MCA territory and those with altered consciousness should not undergo CEA/CAS until neurological improvement has occurred, due to higher risks of haemorrhagic transformation of

an infarct or ICH.^{388,389} Larger areas of acute cerebral infarction (pre-operatively) are recognised as being an important predictor of post-operative neurological complications. In a series of 646 recently symptomatic patients, 101 (15.6%) had a large area of recent infarction on pre-operative CT/MRI (defined as a maximum axial infarct size $> 4 \text{ cm}^2$). Post-operative non-ischaemic cerebral complications (hyperperfusion syndrome, ICH) were independently associated with large infarcts (adjusted OR 6.839; 95% CI 1.699 - 27.534, $p = .001$).³⁹⁰ Multivariable binary logistic regression showed that infarct size was an independent predictor of post-operative ICH and encephalopathy (infarct size per cm^2 (adjusted OR 1.169; 95% CI 1.067 - 1.128, $p = .001$).³⁹⁰ A similar finding was reported by Pini et al.³⁹¹ In a series of 489 recently symptomatic patients undergoing CEA, an acute cerebral ischaemic lesion volume $\geq 4000 \text{ mm}^3$ on pre-operative CT was predictive of post-operative stroke (OR 4.6; 95% CI 1.1 - 19.1, $p = .03$), with a sensitivity of 75% and a specificity of 63%.³⁹¹

In a meta-analysis of 13 observational studies ($n = 208$), 30 day stroke/death after CEA was 20% (95% CI 12.0 - 28.4) in patients with stroke in evolution and 11% (95% CI 6.1 - 16.7) in patients with crescendo TIAs.³⁹² However, in selected patients with smaller infarcts, emergency CEA can be performed with 2 - 8% rates of death/stroke for stroke in evolution and 0 - 2% for crescendo TIAs. These results compare favourably with the otherwise poor prognosis of these conditions. ESVS recommendations in patients with crescendo TIAs or stroke in evolution are the same as the 2021 SVS and German-Austrian guidelines.^{3,4} There are no RCT data to advise whether i.v. heparin is superior to APRx in preventing early recurrent stroke in patients with stroke in evolution or crescendo TIAs. In a series of 144 patients with non-disabling stroke, a 50 - 99% stenosis and TCD evidence of MES, spontaneous MES rates were reduced in patients on APRx, but not heparin.³⁹⁵ In two RCTs comparing LMWH with aspirin monotherapy in acute stroke patients where APRx or antithrombotic therapy were commenced < 48 hours after stroke onset, there was no evidence that LWMH conferred additional benefits over aspirin.^{396,397} In the

absence of quality evidence, it would seem reasonable to consider heparin (plus aspirin) or combination APRx in patients with recurrent TIAs or crescendo TIAs prior to urgent CEA.

Recommendation 46 (Unchanged)	Class	Level	References
For patients with 50-99% stenoses who experience a disabling stroke (modified Rankin score ≥ 3), or whose area of infarction exceeds one third of the ipsilateral middle cerebral artery territory, or who have altered consciousness/drowsiness, it is recommended to defer carotid interventions to minimise the risks of post-operative parenchymal haemorrhage.	I	C	388,389

Recommendation 47 (Unchanged)	Class	Level	References
For patients with 50-99% stenoses who present with stroke in evolution or crescendo transient ischaemic attacks, urgent carotid endarterectomy should be considered, preferably within 24 hours.	Ila	C	80,392-394

4.8 Timing of CEA and CAS after intravenous thrombolytic therapy (TT)

In the absence of advanced imaging techniques, i.v. TT is recommended in selected patients with acute ischaemic stroke, provided it is started within 4.5 h of stroke onset in patients awake at symptom onset.^{398,399} About 10 - 20% of TT patients will have an underlying 50 - 99% ICA stenosis and may be candidates for CEA or CAS. There are concerns, however, that performing CEA or CAS too soon after TT may increase the likelihood of haemorrhagic transformation of an infarct or neck haematoma formation, with consequent harm to the patient. To balance the risks of early recurrent stroke prevention with the higher risks of ICH, general criteria for selecting patients for early CEA after TT include (1) rapid neurological recovery (mRS 0 - 2); (2) infarction area less than one third the MCA territory; (3) recanalisation of a previously occluded MCA mainstem on repeat CTA; (4) ipsilateral 50 - 99% stenosis and (5) no evidence of parenchymal haemorrhage or significant brain oedema.^{400,401} Contraindications include (1)

severe persistent neurological deficit (modified Rankin score ≥ 3); (2) anticipated high surgical risk; (3) parenchymal haemorrhage on CT and (4) previous radical neck dissection or radiotherapy.⁴⁰² A systematic review identified 25 observational studies ($n = 147\,810$ patients), including 2 557 who underwent CEA ($n = 2\,076$) or CAS ($n = 481$) after TT. **Table 30** details peri-operative outcomes in pooled series.⁶⁶

Table 30: Peri-operative outcomes in pooled series undergoing CEA or CAS after TT*

	CEA ($n = 2\,076$)	CAS ($n = 481$)
Stroke/death	5.2% (95% CI 3.3-7.5)	14.9% (95% CI 11.9-18.2)
ICH	3.4% (95% CI 1.7-5.6)	5.5% (95% CI 3.7-7.7)
Haemorrhage	neck: 3.8% (95% CI 2.9-4.9)	local: 4.9% (95% CI 0.09-16.2)

CEA = carotid endarterectomy; CAS = carotid artery stenting; 95% CI = 95% confidence intervals; TT = thrombolysis; ICH = intracranial haemorrhage. * Data derived from Kakkos⁶⁶

Table 31 details meta-analysed case controlled data comparing peri-operative outcomes in CEA and CAS patients who did (did not) receive TT. TT was associated with significantly higher rates of ICH and neck haematoma in patients undergoing CEA (vs. no TT), while TT was associated with significantly higher stroke/death and ICH in patients undergoing CAS (vs. no TT).⁶⁶

Table 31. Peri-operative outcomes for case control studies in CEA and CAS patients who did (did not) have TT.

	CEA			CAS		
	TT	no TT	OR (95% CI)	TT	no TT	OR (95% CI)
Stroke	4.1%	1.2%	2.74 (0.62-12.07)			
Death	2.1%	0.7%	2.84 (0.85-17.3)			
Stroke/ death	4.3%	1.5%	2.34 (0.74-7.47)	5.2%	1.5%	8.49 (95% CI 2.12-33.95)
Intracranial haemorrhage	2.2%	0.1%	7.82 (4.07-15.2)	5.4%	0.7%	7.48 (95% CI 4.69-11.92)
Neck haematoma	3.6%	2.3%	1.65 (1.17-2.33)			

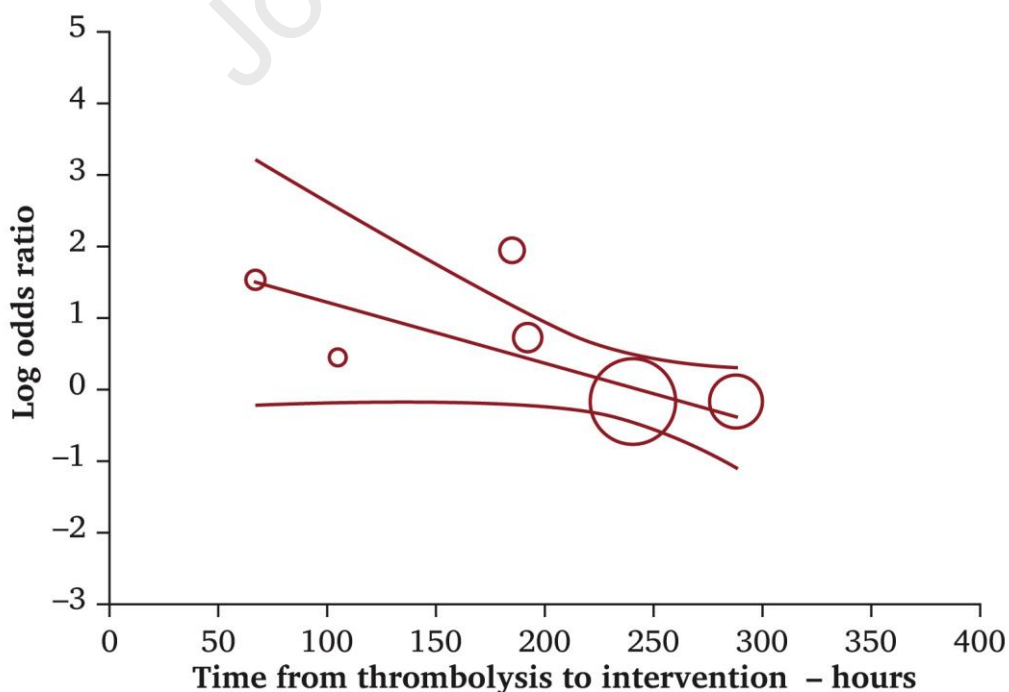
Data derived from Kakkos et al.⁶⁶ CEA = carotid endarterectomy; CAS = carotid artery stenting; OR 95% CI = Odds Ratio and 95% confidence intervals; TT = thrombolysis.

Thrombolysis is associated with complex haematological changes that may make CEA and CAS patients prone to ICH or neck haematoma formation. The half life of i.v. recombinant tissue plasminogen activator (rtPA) is five minutes (Tenecteplase 24 minutes), but fibrinogen and plasminogen levels only revert to > 80% of pre-TT levels \geq 24 hours after rtPA treatment.⁴⁰³ Recombinant tPA increases circulating fibrin degradation products and levels > 200 mg/L may be associated with a five fold increase in parenchymal haemorrhage,⁴⁰⁴ as well as increased permeability across the blood brain barrier (which increases parenchymal haemorrhage).⁴⁰⁵ Vulnerability to haemorrhagic complications after TT will also be compounded by peri-operative APRx and heparin therapy. Guidelines advise that heparin and APRx should be withheld for 24 hours after TT completion and only restarted once a 24 hour CT scan shows no haemorrhagic transformation, after which appropriate APRx can be (re-)commenced before CEA or CAS.³⁹⁹ The optimal timing of carotid interventions after TT remains controversial. A US National Inpatient Sample reported significantly higher rates of post-operative stroke and ICH if CEA was performed early after TT, which then declined to levels comparable to those in non-TT patients

by seven days after TT completion¹⁵⁷. By contrast, the UK National Vascular Registry reported no association between CEA timing after TT and procedural risks.¹³⁶ Meta-regression analyses of published data demonstrated an inverse relationship between the time interval between TT and CEA and the risk of peri-operative stroke/death ($p = .02$); ie. performing CEA early after TT was associated with significantly higher risks of peri-procedural stroke/death.⁶⁶

Using meta-regression analysis (**Figure 7**), peri-operative stroke/death was 13% when CEA was performed three days after TT completion and 10.6% after four days. The risk was predicted to reduce to within the currently accepted 6% threshold after six days had elapsed,⁶⁶ suggesting that CEA should probably be deferred until six days after TT. Unfortunately, there were insufficient case control studies to permit similar analyses in CAS patients, but given the data in **tables 30** and **31**, a similar deferral would seem reasonable.⁶⁶

Figure 7. Regression of Log Odds Ratio on time (hours) of peri-operative death/stroke in patients with stroke undergoing CEA after thrombolysis or without thrombolysis*.



A short deferral permits repeat DUS/CTA imaging to ensure criteria for expedited CEA or CAS have been met (see earlier), and for heparin and APRx to be withheld for 24 hours, before re-starting prior to any intervention. However, one potentially adverse consequence of deferring CEA (even for a short time) is recurrent thromboembolic stroke, which is rarely reported in the literature. In a Finnish study ($n = 128$), the risk of recurrent stroke between TT and undergoing CEA was 5.5% when performed a median of four days after TT (range 0 - 8).⁴⁰⁶ This is lower than the predicted 10.6% risk associated with performing CEA four days after TT in the meta-regression analysis.⁶⁶ Recurrent stroke before deferred CEA in TT patients should be the subject of future audit, which should also include whether the presence/absence of acute infarction influences rates of ICH, to better stratify advice regarding deferral in individual patients as some vascular surgeons and physicians may still opt to proceed to CEA in selected patients less than six days after TT. It is also essential to actively treat post-CEA/CAS hypertension (**section 7.1.3.3**) as poorly controlled BP is a risk factor for ICH and neck haematoma formation. To date, no other guideline has made any recommendation regarding the optimal timing of carotid interventions after thrombolysis.¹⁻³

Recommendation 48 (Unchanged)	Class	Level	References
For symptomatic patients undergoing thrombolysis, it is recommended that intravenous heparin and antiplatelet therapy be withheld for 24 hours after completion of thrombolysis, but antiplatelet therapy should then be commenced before any carotid intervention is undertaken	I	C	399

Recommendation 49 (New)	Class	Level	References
			ToE

For patients with acute ischaemic stroke due to a symptomatic 50-99% carotid stenosis who have received intravenous thrombolysis, delaying carotid endarterectomy or carotid stenting by six days following completion of thrombolysis should be considered.	IIa	B	66,157
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Recommendation 50 (Unchanged)	Class	Level	References
For patients undergoing early carotid interventions after thrombolysis, active treatment of post-interventional hypertension is recommended to reduce the risks of parenchymal haemorrhage.	I	C	402

4.9 Carotid interventions after mechanical thrombectomy (MT)

Based on a meta-analysis of five RCTs ($n = 1\,287$), which showed that MT conferred a twofold improvement in functional outcome,⁴⁰⁷ guidelines recommend emergency MT in selected patients with acute ischaemic stroke.³⁹⁸ About 10 - 20% of MT patients will have embolic MCA occlusion with tandem ICA thrombosis or severe stenosis.⁶¹ Treatment options include (i) synchronous MT + CAS with APRx; (ii) synchronous MT + CAS with no APRx; (iii) synchronous MT + angioplasty (no stent, no APRx) and (iv) MT +/- deferred CEA/CAS. The TITAN registry evaluated all four treatment strategies in 482 patients.¹⁶³ After adjusting for confounding variables, CAS + MT + APRx was independently associated with significantly higher rates of recanalisation, although rates of symptomatic ICH and mortality were similar across all four strategies.^{164,408} The German Stroke Registry recently reported outcomes in 874 MT patients with tandem carotid stenosis or thrombosis, including 607 (69.5%) who underwent synchronous treatment of the extracranial carotid lesion. Synchronous MT + CAS was associated with a significantly higher probability of successful reperfusion vs. MT alone (OR 40.63; 95% CI 30.3 - 70.06), as well as significantly better clinical outcomes (39.5% vs. 29.3%; $p < .001$) and

lower mortality rates (17.1% vs. 27.1%; $p < .001$). MT + CAS was associated with similar complication rates (23.9%) vs. 18.1% ($p = \text{ns}$) in patients undergoing MT alone.¹²⁴

There is, however, no consensus and a survey of clinicians treating acute stroke patients reported that 59% would perform MT + CAS, while 41% wouldn't.⁴⁰⁹ Whilst awaiting data from the TITAN RCT (ClinicalTrials.gov Identifier: NCT03978988), imaging features that might support performing synchronous MT + CAS include poor antegrade ICA flow after MT; poor collateralisation via the CoW after MT and patients with small volume infarcts and lower bleeding risks. Imaging features suggesting that emergency CAS is probably unnecessary (could be deferred) include poor intracranial revascularisation after MT, good filling of ipsilateral intracranial vessels via the VAs and/or contralateral ICA after MT, large volume infarcts and patients at increased bleeding risk.

If synchronous CAS + MT is being considered, should the intervention be intracranial first or extracranial first?⁴¹⁰ Advantages of extracranial first include (i) early flow restoration to the CoW (simply crossing an occluded or stenosed ICA with a large bore catheter can permit sufficient inflow to avoid CAS⁴¹¹); (ii) optimisation of endogenous fibrinolysis by increased intracranial flow; (iii) elimination of a proximal embolic source; (iv) avoiding blind navigation in occluded vessels and (v) reduced risk of re-occluding intracranial vessels.⁴¹² Disadvantages include embolisation during CAS, worsening of any neurological deficit and delay in recanalising intracranial occlusions.^{410,411} A meta-analysis found no difference in either approach regarding mRS scores, procedural complications, symptomatic ICH, revascularisation rates or procedure times,¹⁰⁷ although the German Stroke Registry reported significantly shorter flow restoration times with an intracranial first strategy (53 mins vs. 72 mins, $p < .001$).¹²⁴ Few registries have reported outcomes following staged CEA after MT. In an audit of 63 consecutive cases from

Sweden and Finland, 30 day death/stroke was 0.0%. Carotid endarterectomy was performed a median of seven days after presentation and 75% of patients underwent CEA in < 14 days.¹³⁸

Similarly, there is no consensus regarding optimal APRx and antithrombotic therapy during MT + CAS. CAS mandates peri-procedural APRx (usually combination), which increases the risk of ICH, especially if the patient has also been thrombolysed (common). Conversely, CAS without APRx increases in stent thrombosis, while CA (without stenting) risks secondary embolisation of atherothrombotic debris. Combination APRx usually starts after a post-operative CT scan excludes parenchymal haemorrhage. Combining glycoprotein IIb/IIIa inhibitors and combination APRx provides better stent patency, but with increased ICH risks.^{461,412} A Delphi consensus reported a preference for aspirin monotherapy (or IIb/IIIa receptor inhibitor) during CAS, with combination aspirin plus a P2Y12 inhibitor started post-operatively,⁴¹³ although this has not been tested in RCTs. Another study showed that heparin doses > 3000 iU were only associated with higher bleeding risks when the ASPECTS score was ≤ 7 (indicating a large ischaemic core) and with more than one passage of the MT catheter.⁴¹⁴

Whilst knowledge has increased since 2017, there is no consensus regarding the optimal strategy for treating acute stroke patients undergoing MT who have tandem extracranial stenoses, and few contemporary guidelines have published any recommendations. The 2021 German-Austrian guidelines, however, advise that endovascular treatment with emergency stenting and thrombectomy is indicated.³

Recommendation 51 (New)	Class	Level	References
			ToE
For a patient with acute ischaemic stroke undergoing intracranial mechanical thrombectomy with a tandem 50-99% carotid stenosis and a small area of	IIb	C	Expert Opinion

ipsilateral infarction, synchronous carotid stenting may be considered in the presence of poor antegrade internal carotid artery flow or poor collateralisation via the circle of Willis after mechanical thrombectomy.

4.10 Patients with < 50% stenoses who may benefit from intervention?

In a CETC meta-analysis, CEA conferred no benefit over BMT in patients with < 50% stenoses (**table 19**).³⁵⁷ However, the risk of recurrent ipsilateral stroke in patients with 20 - 49% stenoses at baseline (and treated medically) is about 7.4% at three years.⁴¹⁵ In previously symptomatic patients with < 50% stenosis who experience recurrent TIA/stroke (despite BMT), it is essential to exclude other causes of recurrent symptoms (eg. paroxysmal AF, antiphospholipid syndrome) that would warrant different secondary preventive therapy. If symptoms recur despite optimisation of BMT, it may be reasonable to consider CEA,^{416,417} but only following detailed neurovascular work up and MDT review.

Recommendation 52 (Unchanged)	Class	Level	References
For patients presenting with carotid territory symptoms in the preceding six months and who have a <50% stenosis, a carotid intervention is not recommended	III	A	357

Recommendation 53 (Unchanged)	Class	Level	References
For selected patients experiencing recurrent transient ischaemic attacks or minor stroke, despite best medical therapy and who have a <50% stenosis, carotid endarterectomy may be considered but only following neurovascular work up and multidisciplinary team review	IIb	C	415-417

4.11 'High risk of surgery' symptomatic patients

Certain clinical or anatomical features may be associated with poorer outcomes after CEA and are described as high risk of CEA criteria. However, being high risk of CEA does not mean that superior outcomes are achieved by CAS as, sometimes, procedural risks may be higher. The concept of high risk of CEA is also misinterpreted as being high risk of stroke, which is rarely the case. As will be seen, many studies regarding high risk of CEA criteria are conflicting.

4.11.1 SAPHIRE defined high risk criteria

In SAPHIRE, high risk of CEA criteria included carotid territory symptoms within 180 days and a 50 - 99% stenosis plus more than one of: significant cardiac disease (CHF, abnormal stress test, awaiting cardiac surgery); severe COPD; contralateral occlusion; contralateral RLN palsy; previous radical neck surgery, cervical irradiation; re-stenosis after CEA and age > 80 years.²⁸²

In an SVS Registry, SAPHIRE high risk of CEA patients had similar rates of death/stroke/MI after CAS and CEA (9.1% vs. 7.3%; $p = .11$). No anatomical criteria were associated with poorer outcomes after CEA and there was only a trend towards lower rates of major adverse events after CAS in patients with re-stenosis after CEA (3.5% v.s 7.1%; $p = .10$).⁴¹⁸ VSGNE reported independent risk factors for increased stroke/MI/death one year after CEA as increasing age, pre-admission residence in a nursing home, CHF, DM, COPD, previous stroke/TIA and contralateral occlusion. Three SAPHIRE criteria (abnormal stress test, re-stenosis, and cervical irradiation) were not associated with increased morbidity/mortality.⁴¹⁹ Another retrospective study compared 424 high risk of CEA patients (173 with ≥ 1 physiological high risk criterion; 293 with ≥ 1 anatomical risk criterion) with 424 propensity matched patients with no high risk criteria. There were no significant differences in 30 day death/stroke/MI after CE.⁴²⁰

4.11.2 Increasing age

CSTC¹⁶⁹ reported that age ≥ 70 years was associated with higher peri-operative stroke rates after CAS, but not CEA (**table 22, section 4.4.1.1**), possibly due to increased atherosclerotic burden, aortic arch calcification, changes in vascular anatomy and increasing plaque vulnerability.⁴²¹

4.11.3 Cervical irradiation

Cervical irradiation is cited as conferring poorer outcomes after CEA. However, in a systematic review of 27 observational studies (533 CAS or CEA patients), the risk of 'any cerebrovascular event' was 3.9% with CAS vs. 3.5% after CEA ($p = .77$).⁴²² CNI after CEA was 9.2% vs. 0% after CAS, although few were permanent. After the peri-operative period, recurrent TIA/stroke was more common after CAS than after CEA (4.9/100 vs. 2.8/100 person years; $p = .014$).⁴²²

4.11.4 Re-stenosis after carotid endarterectomy

In an SVS-VQI registry involving 2 863 patients (33% ACS) undergoing redo CEA ($n = 1 047$) or CAS ($n = 1 816$) for re-stenosis after CEA, redo-CEA was associated with a higher mortality rate at 30 days (OR 2.83; 95% CI 1.13 - 7.14, $p = .027$) and at one year (HR 2.17; 95% CI 1.03 - 4.58, $p = .042$). However, there were no differences in peri-operative stroke (OR 0.54; 95% CI 0.20 - 1.45, $p = .22$) or MI (OR 0.98; 95% CI 0.31 - 3.10, $p = .97$).¹⁵ A 2018 meta-analysis involving 13 observational studies (redo CEA = 1 678; CAS = 2 485) reported no difference in 30 day MI (OR 1.32; 95% CI 0.71 - 2.44), mortality (OR 1.82; 95% CI 0.94 - 3.53) or stroke (OR 1.28; 95% CI 0.82 - 2.00). CNIs were significantly higher after redo-CEA (OR 13.61; 95% CI 5.43 - 34.16).¹⁰²

4.11.5 Contralateral carotid occlusion

Contralateral occlusion is another frequently cited high risk of CEA criterion,^{282,316} although data are conflicting. A meta-analysis of 43 RCTs or observational studies ($n = 96 658$) observed that contralateral occlusion was associated with a significant increase in peri-operative stroke/death

after CEA (OR 1.8; 95% CI 1.55 - 2.1, $p < .001$) but not after CAS (OR 1.52; 95% CI 0.95 - 2.44).⁷²

By contrast, an SVS-VQI registry of patients with contralateral occlusion treated by CEA ($n = 3278$) or CAS ($n = 1048$) found that in ACS patients, 30 day death/stroke and two year ipsilateral stroke rates did not differ significantly between CAS and CEA, but the adjusted risk of any stroke/death over two years was significantly higher after CAS (adjusted HR 1.42; 95% CI 1.08 - 1.86, $p = .011$). In SCS patients, CAS was associated with significantly higher 30 day risks of stroke (OR 2.90; 95% CI 1.06 - 7.94, $p = .038$) and death (OR 6.10; 95% CI 2.20 - 16.92, $p = .001$). The two year risk of stroke after intervening in SCS patients was also significantly higher after CAS vs. CEA (adjusted HR 1.94; 95% CI 1.18 - 3.19, $p = .009$).¹⁵¹

Recommendation 54 (New)	Class	Level	References ToE
For recently symptomatic patients with 50-99% stenoses and contralateral carotid occlusion or previous cervical radiation therapy, the choice of carotid endarterectomy or carotid artery stenting should be considered on an individual basis.	Ila	B	72,151,422

Recommendation 55 (Unchanged)	Class	Level	References
For recently symptomatic patients with 50-99% stenoses with anatomical features or co-morbidities that are considered by the multidisciplinary team to be higher risk for carotid endarterectomy, carotid stenting should be considered as an alternative to endarterectomy, providing the documented 30 day risk of death/stroke is <6%.	Ila	B	223,282, 315,316

4.12 Managing patients with carotid 'near occlusion'

The definition of CNO is covered in **section 2.5**. Of the 262 ECST and NASCET patients with CNO, 16 had total distal vessel collapse, while 246 had partial collapse. A CETC meta-analysis

concluded that CEA conferred no significant reduction in stroke at five and eight years (**table 18, section 4.3.1**), largely because of low rates of ipsilateral stroke in BMT patients.³⁵⁷ CETC data significantly influenced the 2017 ESVS carotid guidelines, which advised against CEA in CNO patients¹⁶⁵. However (in NASCET), 33/114 CNO patients (29%) randomised to BMT subsequently underwent CEA but were analysed as BMT on intention to treat analyses. This high rate of cross over may have confounded meaningful data interpretation, leading to a possible underestimation of benefit conferred by CEA. CETC data and ESVS recommendations also led to CNO patients being excluded from RCTs of carotid interventions.

A meta-analysis (32 observational studies) included 703 patients with CNO.⁷⁸ 30 day death/stroke was 1.8% after CEA, 2.2% after CAS and 4.9% with BMT. BMT was associated with significantly higher 30 day death/stroke vs. CEA (OR 5.63; 95% CI 1.3 - 24.45, $p = .021$). No differences were observed between CEA and CAS. One year freedom from stroke/death was 96% following CEA, 94% after CAS and 81% with BMT. However, the number of adverse events was small, precluding robust statistical conclusions.⁷⁸ A subsequent meta-analysis (26 studies, $n = 1\,506$ patients) reported that the late risk of ipsilateral stroke, neurological/cardiac death or MI was 4.26/100 patient years (95% CI 2.92 - 6.2) in CNO patients treated by CEA or CAS, and 13.3/100 patient years (95% CI 5.54 - 31.95) in patients treated medically ($p < .001$)¹¹⁰. However, only five studies directly compared outcomes in CNO patients undergoing CEA or CAS vs. BMT and found no significant difference (HR 2.37; 95% CI 0.97 - 9.75, $p = .23$).¹¹⁰ Xue's meta-analysis did not, however, report data regarding early or late ipsilateral stroke. There is also debate about the relevance of full or partial vessel collapse with CNO. CETC concluded that full collapse was associated with low stroke risks in BMT patients.³⁵⁷ However, a pooled analysis of two studies ($n = 430$) observed that 116 patients (27%) had evidence of CNO, with 47/116 having full distal vessel collapse, while 69 had partial collapse.¹⁹⁴ The 28 day rate of ipsilateral stroke or central retinal artery occlusion was 27% in CNO patients with full collapse vs. 11% in patients

with partial collapse ($p = .047$).¹⁹⁴ By contrast, a Spanish multicentre registry reported no outcome differences between full or partial collapse.¹²⁶ In addition, while some centres have reported increased rates of post-operative ICH following CEA in patients with CNO and full distal vessel collapse,⁴²⁴ others have reported no significant increase.⁴²³ In a single centre study involving 17 CNO patients with full vessel collapse and recurrent carotid territory symptoms (despite BMT), CEA was performed in 15, while two underwent carotid ligation and ECA endarterectomy. Post-operatively, 1/17 (5.8%) died due to haemorrhagic stroke. During a median follow up of 23 months, one died of unknown causes at 90 days, but none of the remainder had recurrent TIA/stroke, suggesting that in selected CNO patients with full vessel collapse in whom BMT has failed, CEA may confer benefit.⁴²³ The 2021 SVS and AHA guidelines made no specific recommendations regarding the management of CNO. ESVS recommendations are similar to the 2021 German-Austrian guidelines.³

Recommendation 56 (Unchanged)	Class	Level	References
For symptomatic patients with carotid near occlusion and distal vessel collapse, carotid endarterectomy and carotid stenting are not recommended, unless as part of a randomised controlled trial.	III	B	357

Recommendation 57 (New)	Class	Level	References
			ToE
For patients with carotid near occlusion and distal vessel collapse with recurrent carotid territory symptoms (despite best medical therapy), carotid endarterectomy or carotid artery stenting may be considered only after multidisciplinary team review	Ib	C	78,110, 126,423

4.13 Management of free floating thrombus

Free floating thrombus (FFT) is defined as elongated thrombus attached to the arterial wall with circumferential blood flow distally.⁴⁹ It is reported in 1.3% of ischaemic stroke patients⁵⁴ and usually occurs on the surface of atherosclerotic plaques.⁵⁴ FFT is more common in men (ratio 2 : 1, $p < .0001$)⁴⁹ and a significant proportion (47%) are hypercoagulable due to thrombophilia, pregnancy, inflammatory or infectious disease or cancer.^{49,54} Optimal management is unclear, with no RCTs to guide practice. In a meta-analysis of 58 case series and 83 case reports ($n = 525$), 345 patients were treated with 'antithrombotic' or 'interventional' methods, in whom 30 day death, TIA/stroke, or silent ischaemia on MRI was 17.1% (95% CI 13.1 - 21.1), with a 30 day risk of stroke/death of 11.1% (95% CI 7.7 - 14.3).⁵⁴ These high event rates presumably reflect high rates of cerebral embolisation. In a Cox regression analysis of relatively poor data, neither anticoagulation vs. no anticoagulation (HR 1.21; 95% CI 0.35 - 4.23, $p = .76$), nor interventions <3 days vs. >3 days after symptom onset (HR 0.78; 95% CI 0.24 - 2.57), $p = .69$) were associated with different risks of silent ischaemia, TIA, or stroke/death at 30 days.⁵⁴ However, patients with FFT undergoing thrombolysis had significantly higher rates of silent ischaemia, TIA or stroke/death (HR 14.79; 95% CI 3.41 - 64.25) $p < .0001$).⁵⁴ Endovascular thrombus aspiration and stent retriever thrombectomy with filter protection are alternatives to open surgery,⁴²⁵ but evidence regarding their safety and efficacy is lacking.

In the absence of better quality evidence, decision making is influenced by (i) probable aetiology (eg. thrombophilia requiring anticoagulation), (ii) whether patients had recurrent events on pre-existing APRx or anticoagulation, (iii) interval since TIA/stroke onset, (iv) size of infarct and (v) whether FFT is located at the carotid bifurcation (accessible) or extends towards the skull base (less accessible). Serial DUS/CTA/MRA can inform clinicians of responses to treatment. Selected patients with recurrent TIA/stroke on optimal anticoagulation therapy (with surgically or endovascularly accessible FFT) may be considered for thrombectomy (open or endovascular), preferably after MDT discussion. Acute stroke patients with FFT who received TT with i.v. rtPA

should be monitored for signs of recurrent thromboembolism. The 2021 SVS, AHA and ESO guidelines provide no advice about the management of symptomatic patients with FFT. The 2021 German-Austrian guidelines advise that (in selected patients), CEA or CAS should be performed within the first hours of the index event after consultation with stroke specialists.³

Recommendation 58 (New)	Class	Level	References
			ToE
For patients presenting with recent carotid territory symptoms and evidence of free floating thrombus within the carotid artery, therapeutic anticoagulation is recommended.	I	C	49,54

Recommendation 59 (New)	Class	Level	References
			ToE
For patients presenting with recent carotid territory symptoms and free floating thrombus who develop recurrent symptoms whilst receiving anticoagulation therapy, surgical or endovascular removal of the thrombus may be considered.	IIb	C	Expert Opinion

Recommendation 60 (New)	Class	Level	References
			ToE
For patients presenting with recent carotid territory symptoms and evidence of free floating thrombus, intravenous thrombolysis is not recommended.	III	C	54

4.14 Management of carotid webs

A carotid web (CaW) is a ridge like filling defect in the posterior aspect of the carotid bulb and studies suggest it may be an intimal variant of fibromuscular dysplasia. Its incidence is unknown, but in non-selected patients with ischaemic stroke, the prevalence was 1.2% (0.7% ipsilateral).⁴²⁶

In a cohort of the Mr CLEAN RCT and registry (which randomised acute stroke patients to intra-arterial treatment plus usual care vs. usual care alone (see **section 4.9**), 30/3 439 (0.9%) patients with an anterior circulation stroke due to large vessel occlusion who had CTA of the carotid bifurcation and two years surveillance post-MT had CaW.¹⁹ In another cohort of 466 patients undergoing MT for large vessel occlusion stroke, 10.7% with embolic stroke of undetermined source had CaW vs. 0.7% in those with a known source of embolism.⁴²⁷ Logistic regression analysis showed a significant association between embolic stroke of undetermined source and ipsilateral CaW after adjusting for age, sex and vascular risk factors (OR 12.5; 95% CI 2.1 – 71, $p = .005$).⁴²⁷

CaW may act as a pocket for thrombus accumulation and cerebral embolisation. Antiplatelet monotherapy may be insufficient to prevent recurrent events and there is no current evidence supporting anticoagulation.^{69,112} A systematic review identified 37 observational studies ($n = 158$). Median age was 46 years (range 16 - 85), 68% were female and 76% symptomatic. In the symptomatic cohort, 56% of those initially treated medically had recurrent stroke at a median of 12 months after symptom onset (range 0 - 97) and 72% ultimately underwent an intervention (50% CAS, 50% CEA)¹¹². In the Mr CLEAN cohort, 1% of patients with anterior circulation stroke due to large vessel occlusion and no CaW had recurrent ipsilateral stroke by two years, vs. 13% in CaW patients (adjusted HR 8.1; 95% CI 1.4 -46.8).¹⁹ Treatment includes CAS or web resection plus patching or segmental resection and anastomosis. No guideline has made any recommendation regarding the optimal management of symptomatic patients with carotid webs, although the AHA identified it as an area warranting future research.¹

Recommendation 61 (New)	Class	Level	References
			ToE

For symptomatic patients with a carotid web in whom no other cause for stroke can be identified after detailed neurovascular work up, carotid endarterectomy or carotid artery stenting may be considered to prevent recurrent stroke.	IIb	C	19,69,241, 426,427
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4.15 Management of chronic ocular ischaemia syndrome

Chronic ocular ischaemia syndrome presents with progressive visual impairment/loss, with dilated conjunctival or episcleral vessels and narrowing of retinal arteries with or without dilated retinal veins.⁴²⁸ It is usually associated with 90 - 99% stenoses but has been reported with > 50% stenoses.⁴²⁹ Patients may develop pain due to elevated intra-ocular pressure and neovascular glaucoma, rubeosis iridis (coarse dilated vessels on the surface and stroma of the iris)⁴³⁰ or retinal haemorrhages from fragile retinal neovascularisation.⁴²⁹ Ocular ischaemia syndrome may also present with ipsilateral monocular blurring, dimming or whiteout of vision in response to haemodynamic triggers or sudden bright lights due to low flow retinopathy.

Management requires expert ophthalmic treatment to limit neovascularisation and control elevated intra-ocular pressures and neovascular glaucoma, along with risk factor control and BMT (**section 4.2**). Carotid interventions can preserve visual acuity by limiting further ischaemia induced neo-vascularisation, which leads to worsening neovascular glaucoma or retinal haemorrhages. CEA may reverse rubeosis iridis and improve visual acuity in 60%, with no change in 40%.⁴³¹ Carotid revascularisation is less likely to improve visual acuity in patients with established neovascularisation related glaucoma due to severe ocular hypoperfusion,⁴²⁹ but treatment options have not been subject to randomised comparison. In a systematic review of 14 observational studies ($n = 589$), revascularisation led to significant increases in peak systolic velocity in the ipsilateral ophthalmic artery, with improvement in ocular ischaemic symptoms

in 93%.⁸³ No other international guidelines have provided any recommendations regarding the optimal management of ocular ischaemia syndrome.

Recommendation 62 (New)	Class	Level	References
			ToE
For patients with confirmed ocular ischaemia syndrome and a 50-99% ipsilateral carotid stenosis, carotid endarterectomy or carotid stenting should be considered to prevent further ischaemia induced retinal neovascularisation.	Ila	C	83,431

4.16 Symptomatic patients with > 50% carotid stenosis and atrial fibrillation

A 2021 meta-analysis (20 observational studies) reported that 12% of AF patients had a > 50% carotid stenosis, while in 25 observational studies, 9% of patients with > 50% carotid stenosis had AF⁸⁴. This suggests that about one in ten patients with > 50% carotid stenosis will have AF and vice versa. Not all strokes in AF patients are cardio-embolic. In six stroke registries (1 720 AF patients with acute ischaemic stroke), 14% were deemed atherothrombotic.⁴³² Regarding long term stroke risk in AF patients with a 50 - 99% stenosis, the FibStroke registry reported that at 3.5 years, the risk of stroke was 21.2% in patients with AF plus a > 50% carotid stenosis at baseline, vs. 12.7% with AF alone ($p = .005$). After multivariable analysis, stenosis > 50% was an independent predictor of late stroke recurrence (HR 2.02; 95% CI 1.37 - 3.01, $p = .001$).¹⁴⁵

This highlights a conundrum as to whether patients presenting with a recent carotid territory TIA or ischaemic stroke with an ipsilateral 50 - 99% carotid stenosis and newly diagnosed or known AF should undergo carotid revascularisation followed by long term anticoagulation, or anticoagulation alone, without carotid revascularisation. There are no RCTs to guide practice (ECST, NASCET, ICSS, CREST excluded patients with a potential cardio-embolic source) and a

pragmatic approach is required. This is greatly aided by MDT involvement. Investigations should aim to determine whether the TIA/ischaemic stroke was probably cardio-embolic (ie. the carotid stenosis is asymptomatic and an urgent carotid intervention is unnecessary) or probably atherothrombotic (expedited carotid intervention appropriate, followed by post-operative anticoagulation). If it is not possible to determine the probable aetiology, TOAST would define these TIA/strokes as being of undetermined aetiology as there are two potential causes (**section 2.3**).

There are no definitive diagnostic tests for discriminating between cardio-embolic or carotid sources of embolisation and management decisions will have to be based on probability, guided by access to basic or more complex investigative modalities. If CT/MRI shows acute ischaemia or infarction in additional territories (contralateral carotid or VB) other than the ipsilateral symptomatic carotid, then cardiac embolism is the likeliest cause. The patient should be anticoagulated, and the carotid stenosis treated as asymptomatic. Although ipsilateral carotid territory ischaemia/infarction supports a diagnosis of carotid embolism, cardiac embolism cannot be excluded. In this situation, centres with access to more complex neurovascular work up may be able to gain additional diagnostic information.

More complex imaging strategies might include T1 fat saturated MRI to look for IPH in the carotid plaque, which is associated with acutely symptomatic carotid plaques. Transoesophageal echocardiography can diagnose left atrial appendage thrombus or other cardiac sources of embolism. Transoesophageal echocardiography (plus bilateral TCD) with i.v. microbubble contrast media in conjunction with a Valsalva manoeuvre can diagnose a patent foramen ovale (suggesting paradoxical embolisation). Finally, 30 - 60 minutes of bilateral simultaneous TCD monitoring of both MCAs can diagnose spontaneous embolisation. In a series of 123 recently symptomatic patients with 50 - 99% stenoses, 40% of patients undergoing 30

minutes of TCD monitoring within seven days of TIA/stroke onset had ongoing ipsilateral MCA embolisation.⁴³³ Bilateral embolisation, however, suggests a cardio-embolic source. To date, no guidelines have offered advice regarding the management of patients with recent carotid territory symptoms, an ipsilateral carotid stenosis and AF.

Pragmatic decision making

1. Acute ischaemia/infarction in multiple vascular territories suggests cardio-embolism. Patients should be anticoagulated, and the carotid stenosis considered asymptomatic.
2. Acute ischaemia/infarction in the ipsilateral carotid territory is suggestive of a carotid source of embolism and (in some centres) this would be considered sufficient to recommend CEA/CAS. However, this diagnosis can be made with greater certainty if supported by ipsilateral embolism on TCD, IPH in the ipsilateral carotid plaque and no evidence of left atrial appendage thrombus.
3. If a patient is anticoagulated (on the basis that cardio-embolism was the likeliest aetiology) but then suffers recurrent event(s) in the territory ipsilateral to the 50 - 99% carotid stenosis whilst on therapeutic anticoagulation, it is reasonable to consider CEA or CAS (see **section 4.2.6.3** for management of peri-operative anticoagulation).
4. If investigations are neither diagnostic nor informative and more complex imaging is unavailable, the MDT will have to make an empirical management decision, following discussion of diagnostic uncertainties and potential implications with the patient.

Recommendation 63 (New)	Class	Level	References ToE
For patients presenting with a transient ischaemic attack or minor ischaemic stroke in the presence of newly diagnosed or known atrial fibrillation and an ipsilateral 50-99% carotid stenosis, comprehensive neurovascular work up with	I	C	Expert opinion

multidisciplinary team review is recommended to determine whether urgent carotid revascularisation or anticoagulation alone is indicated.

Recommendation 64 (New)	Class	Level	References
			ToE
For patients who have been started on anticoagulation (on the basis that cardiac embolism was considered the most likely cause of their transient ischaemic attack or stroke) but who then report recurrent event(s) in the territory ipsilateral to a 50-99% carotid stenosis whilst on therapeutic levels of anticoagulation, carotid endarterectomy or carotid artery stenting is recommended.	I	C	Expert opinion

Section 5: Open surgical techniques

5.1 Carotid endarterectomy

5.1.1 Pre-operative check list

Responses to key questions should be documented in the casenotes prior to CEA. The aim is to minimise morbidity/mortality and lessen medicolegal censure. They include: has the indication for CEA been documented? Are there atypical symptoms warranting further investigation? Is the degree of stenosis appropriate for CEA? Have procedural risks quoted to the patient been documented? Is the patient prescribed optimal BMT? Is high carotid disease possible? Are there pre-existing CNIs? Has the operation side been marked?

Four of these are particularly important; (i) has the surgeon quoted their own procedural risks during the consent process, rather than RCT data? (ii) If the patient has previously undergone contralateral CEA, total/partial thyroidectomy or radical neck surgery, indirect laryngoscopy must exclude contralateral RLN palsy as bilateral RLN palsies can be fatal (as can bilateral hypoglossal). If a contralateral vocal cord palsy is identified, the rationale for CEA must be

reviewed. If the patient is asymptomatic, CEA should be cancelled, and CAS considered (if still deemed appropriate). If the patient is symptomatic, CAS should still be considered. If it is not possible to safely perform CAS and the indication for intervening is compelling, the patient must be warned about the consequences of bilateral RLN palsies (permanent tracheostomy) and an Ear Nose and Throat surgeon should be present at extubation. In addition, the surgeon should avoid a retrojugular approach to the bifurcation, as this is associated with higher risks of temporary RLN injury (**section 5.1.6**). (iii) It is important to ensure the patient is receiving optimal medical therapy (**section 3.1** and **4.2**) and (iv) the surgeon must anticipate the possibility of distal ICA disease. If this is considered likely, the surgeon must ensure that CEA can be done safely. It may be necessary to plan a more complicated exposure (**section 5.1.14**).

5.1.2 Staged or synchronous bilateral carotid interventions?

Some patients present with bilateral severe stenoses. Most will be asymptomatic, or one side will be symptomatic and the other asymptomatic. It is extremely rare for both stenoses to be simultaneously symptomatic. Some have suggested that synchronous bilateral CEAs should be considered,⁴³⁴ but the most dangerous complication is injury to both RLNs or hypoglossal nerves, which can be fatal. Accordingly, if bilateral revascularisation is deemed necessary, it is safer to consider bilateral CAS, unilateral CEA + contralateral CAS⁴³⁵ or staged bilateral CEAs.

5.1.3 CEA under general (GA) vs. locoregional anaesthesia (LRA)?

There is controversy whether to perform CEA under LRA or GA. The General Anaesthesia Local Anaesthesia trial ($n = 3\,526$) was the largest RCT and reported no difference in peri-operative death, stroke, or MI between GA (4.8%) and LRA (4.5%).⁴³⁶ However, pooled data from five CEA vs. CAS RCTs showed reduced 30 day stroke/death for CEA under LRA (adjusted RR 0.70; 95% CI 0.50 - 0.99)⁷⁰, while NIBLs were commoner with GA (17.1% vs. 6.7%; $p = .031$).⁴³⁷ In the American College of Surgeons National Surgical QIP, LRA incurred lower CNI rates, shorter

operation times and hospital stays, fewer re-admissions, less post-operative pneumonia, and reduced blood transfusion.^{130,149} However, LRA attracted lower patient satisfaction (65% vs. 93%) and future preference (61% vs. 97%).⁴³⁸ In a large meta-analysis (25 observational studies, six RCTs ($n = 152\ 376$), LRA was associated with significantly shorter operation times, lower peri-operative stroke (OR 0.76; 95% CI 0.62 - 0.92, $p = .006$); fewer cardiac complications (OR 0.59; 95% CI 0.47 - 0.73, $p = .00001$) and lower mortality (OR 0.72; 95% CI 0.59 - 0.90, $p = .003$) in observational studies.⁶⁰ However, there were no significant differences in any endpoint in RCTs⁶⁰. Some believe that RCTs lack statistical power,⁵⁸ but an alternative interpretation may be that CEA under GA may be more challenging surgically (suggested by higher CNI rates, longer operation times, increased blood transfusion) and that observational study data reflect selection biases which are avoided in RCTs.

Most studies on CEA under LRA include patients on aspirin monotherapy. However, with the increasing use of combination APRx (**section 4.2.2.2**), there are concerns about neck haematoma formation. In a systematic review of 69 observational studies ($n = 10\ 081$), combined deep + superficial cervical plexus blockade was associated with significantly higher complication rates (OR 2.13; $p = .006$) vs. superficial or intermediate blockade.⁴³⁹ No guidance has been published regarding neck haematoma risks after deep cervical plexus blockade in LRA patients. In a working party consensus on LRA in patients with coagulation abnormalities, there was no mention of adverse events relating to combination APRx and no advice about performing CEA under deep cervical plexus blockade.⁴⁴⁰ There are no published data on whether it is safe to perform deep cervical plexus blockade in CEA patients on combination APRx.⁴⁴¹ Given that an increasing proportion of symptomatic patients undergo CEA on combination APRx, surgeons and anaesthetists need to establish protocols regarding APRx strategies and choice of anaesthesia. It would be inappropriate to stop clopidogrel and delay CEA for 7 - 10 days to perform deferred CEA under LRA, as this increases the likelihood of

recurrent embolic stroke. Intra-operative DUS may enable safer infiltration of LRA, with visualisation of the cervical transverse processes and VAs. ESVS recommendations regarding LRA vs. GA are the same as in the SVS and German-Austrian guidelines.^{3,4}

Recommendation 65 (Unchanged)	Class	Level	References
In patients undergoing carotid endarterectomy, decisions regarding choice of anaesthesia (locoregional, general) should be considered at the discretion of the surgeon/anaesthetist performing the procedure, taking account of local experience, patient preference and preferred antiplatelet strategy.	Ila	B	58,70,70, 130,149,436

5.1.4 Hospital and surgeon volumes

Interpretation of data is confounded by inter-study heterogeneity regarding presentation (symptomatic vs. asymptomatic), urgency (emergency vs. elective) and non-standardised definitions of low vs. high volume surgeons or hospitals (actual numbers vs. quintiles). A meta-analysis of 25 studies (900 000 USA based CEAs) reported significant benefit when CEA was performed in higher volume centres, with a threshold of 79 CEAs per centre per year.⁴⁴² In a similar analysis of 18 248 UK CEAs, there was a significant volume-outcome relationship favouring higher volume centres,⁴⁴³ with an annual threshold of 35 CEAs per hospital. The differing thresholds probably relate to higher operative risks in symptomatic patients. Most UK CEAs involve SCS patients, while in the USA most are asymptomatic.

A systematic review of 233 411 CEAs in Europe reported an inverse relationship between hospital volume and peri-operative stroke/death in elective patients (no threshold reported), but no association with emergency CEAs. Univariable analyses suggested an inverse relationship between surgeon volume and outcome, but this did not persist after adjusting for confounding variables.⁸⁸ AbuRahma analysed the influence of surgeon volume on 30 day stroke/death in 953

CEAs. High volume surgeons (≥ 30 CEAs/year) had significantly lower 30 day stroke/death (1.3%) than 4.1% in surgeons performing < 30 CEAs/year. 30 day death/stroke was significantly higher when CEA was performed by non-vascular surgeons vs. vascular trained surgeons in ACS patients (3.2% vs. 0.72%; $p = .033$).⁴⁴⁴ In an Australia and New Zealand audit ($n = 16\,765$), there was a small but significant inverse association between operator volume and in hospital stroke/death, which was 2.2% for the lowest three volume quintiles (≤ 17 CEAs per year), vs. 1.76% in surgeons with the two highest volume quintiles (≥ 18 CEAs per year). There was, however, no hospital volume-outcome relationship.¹²⁸

In a meta-analysis of 25 studies on hospital volume, nine on surgeon volume and seven on surgeon specialty, there was no association between hospital volume and outcome, but the definition of a high volume hospital ranged from > 20 to > 164 CEAs annually. Similarly, 7/9 studies showed a significant inverse relationship for surgeon volume, but the definition of a high volume surgeon ranged from > 10 to > 50 CEAs per year,⁴⁴⁵ making it difficult to establish the optimal volume threshold. Finally, 7/8 studies reported that specialist vascular training was associated with lower death/stroke after CEA vs. non-vascular training, but only in low volume surgeons. For high volume surgeons, specialty had no impact.⁴⁴⁵ In a Canadian study ($n = 14\,301$), 30 day stroke was significantly higher when CEA was performed by non-vascular surgeons (3.6%), than 2.5% by vascular surgeons (OR 1.38; 95% CI 1.11 - 1.71).¹³³

The situation regarding hospital and/or surgeon volume thresholds is now being confounded by temporal changes in vascular workload. In 2012, the UK centralised major arterial procedures (including CEA) into larger volume centres, each serving a population of $\geq 800\,000$. At the time, it was advised that each vascular unit should perform ≥ 50 CEAs per year.¹⁵⁸ However, the UK has seen a 25% decline in CEA numbers in symptomatic patients between 2011 - 2017 and a 65% decline in ACS patients, which was not associated with parallel increases in CAS

numbers.¹³⁵ The decline in CEA numbers in the UK, attributed to improvements in primary and secondary cardiovascular prevention, was the main reason for the Vascular Society of Great Britain and Ireland to recommend (in 2021) that the minimum annual hospital volume of CEAs should now be reduced from 50 to 35 (which will inevitably influence individual surgeon volumes as well).¹⁶⁰

While there is evidence that better outcomes are achieved when vascular surgeons perform CEA vs. non-vascular surgeons, data regarding hospital and surgeon volume outcomes are conflicting. Only the German-Austrian guidelines have made a recommendation about annual caseload, advising CEA should only be performed in hospitals performing > 20 CEAs per year.³

Recommendation 66 (New)	Class	Level	References
			ToE
For patients undergoing carotid endarterectomy, it is recommended that the operation be performed by trained vascular surgeons, rather than by surgeons from other specialties.	I	B	133,444, 445

5.1.5 Transverse or longitudinal incision?

The standard approach is a longitudinal anterior sternomastoid incision, but CEA can be performed via a transverse skin crease incision which may confer better cosmesis and a lower CNI rate.⁴⁴⁶ Others, however, have reported no difference in CNI and it may be more difficult to insert a shunt with transverse incisions.⁴⁴⁷ A modified approach involves DUS marking of the bifurcation and a smaller longitudinal incision, which is extended as required. This reduces incision length and offers good cosmesis.⁴⁴⁸ Surgeons can, therefore, use whichever incision they prefer. If DUS suggests the bifurcation is not too high with a focal stenosis, a transverse

crease incision will probably give the best cosmetic result. If there is any question about the bifurcation being high, or if the lesion is extensive, a longitudinal incision is preferable.

5.1.6 Antegrade or retrojugular exposure?

A retrojugular approach avoids mobilizing the hypoglossal nerve and may optimise access to the distal ICA, by sweeping (anteriorly) the sternocleidomastoid artery, hypoglossal nerve and ansa cervicalis.⁴⁴⁹ A meta-analysis (four observational studies, two RCTs [740 CEAs]) found no evidence that retrojugular (vs. antegrade) exposure reduced peri-operative death (0.6% vs. 0.5%) or stroke (0.9% vs. 0.7%). However, a retrojugular approach was associated with higher rates of RLN palsy (8.1% vs. 2.2%) and no reduction in hypoglossal injury (1.3% vs. 1.3%).⁴⁵⁰

Recommendation 67 (Unchanged)	Class	Level	References
For patients undergoing carotid endarterectomy, decisions regarding carotid exposure (antegrade, retrojugular) should be left to the operating surgeon	Ila	B	450

5.1.7 Carotid sinus nerve blockade?

The hypothesis that carotid sinus nerve blockade reduces hypotension, hypertension, or dysrhythmias during/after CEA was not supported by a meta-analysis of four RCTs.⁴⁵¹ A fifth single centre RCT led to similar conclusions.⁴⁵²

Recommendation 68 (Unchanged)	Class	Level	References
For patients undergoing carotid endarterectomy, routine carotid sinus nerve blockade is not recommended.	III	A	451,452

5.1.8 Protamine reversal of heparin?

Evidence supports more routine use of protamine during CEA. A 2016 meta-analysis in 3 817 patients undergoing CEA who received protamine and 6 070 patients undergoing CEA who did not receive protamine, reported that protamine significantly reduced re-exploration for neck haematomas (OR 0.42; 95% CI 0.22 - 0.8, $p = .008$), with no evidence that protamine increased peri-operative stroke (OR 0.71; 95% CI 0.49 - 1.03, $p = .07$).⁴⁵³ The proportion of US surgeons using protamine increased from 43% (2003) to 62% (2010)⁴⁵⁴ and 73% by 2018.¹⁵⁴ VSGNE (10 059 CEAs) also reported that protamine significantly reduced re-exploration for neck haematoma (0.6% vs. 1.4%; $p = .001$), without increasing peri-operative stroke/death (1.1% vs. 1.0%) or MI (1% vs. 1.2%).⁴⁵⁴ In a 2020 SVS-VQI audit (72 787 elective CEAs for ACS), re-operation for bleeding was significantly higher in patients not receiving protamine (1.4% vs. 0.7%; OR 2.0, 95% CI 1.8 - 2.6).¹⁵⁴ This is important as re-interventions for neck haematoma are associated with significant increases in peri-operative MI, stroke, and death.¹³⁷ ESVS recommendations regarding protamine reversal of heparin are the same as the 2021 SVS and German-Austrian guidelines.^{3,4}

Recommendation 69 (Unchanged)	Class	Level	References
For patients undergoing carotid endarterectomy, protamine reversal of heparin should be considered.	Ila	B	154, 453,454

5.1.9 Shunting: routine, never, selective?

Carotid clamping can cause haemodynamic stroke, which is prevented by shunt insertion. Surgeons tend to be routine, selective or never shunters, based on training. There is a paucity of quality data for guiding practice. Whilst there are numerous methods for monitoring brain perfusion during clamping (electroencephalography (EEG), stump pressure, backflow, TCD, transcranial cerebral oximetry, near infrared spectroscopy), the only reliable method is the patient's neurological status with CEA under LRA. A Cochrane review (6 RCTs; 1 270 CEAs)

concluded that (based on poor data) no meaningful recommendations could be made regarding shunt strategies.⁴⁵⁵ Analysis of 28 457 CEAs from a SVS-VQI audit (4 128 routine, 1 740 never, and 12 489 selective) found no differences in peri-operative TIA/stroke.¹⁶² A VQI update included 5683 CEA procedures performed within 14 days of symptom onset showed no difference in peri-operative stroke rates following routine vs. no shunting (OR 1.39; 95% CI 0.91 - 2.13).¹⁴⁶ Shunting was a risk factor for increased 30 day stroke/death in patients undergoing CEA in the CSTC database⁷⁰. ESVS recommendations regarding shunting are the same as the SVS and German-Austrian guidelines.^{3,4}

Recommendation 70 (Unchanged)	Class	Level	References
For patients undergoing carotid endarterectomy, decisions regarding shunting (routine, selective, never) should be considered at the discretion of the operating surgeon.	Ila	C	146, 162,455

5.1.10 Patching: routine, never, selective?

A meta-analysis of 23 RCTs compared primary closure ($n = 753$), eversion CEA ($n = 431$), vein patch ($n = 973$), polytetrafluoroethylene (PTFE) patch ($n = 948$), polyester patch ($n = 828$), bovine pericardial patch ($n = 249$) and polyurethane patch ($n = 258$). Eversion CEA (eCEA) and patched CEA (PTFE, bovine pericardium) had the lowest 30 day stroke/death rates, with primary closure having the highest 30 day death/stroke rate. Lowest re-stenosis rates were observed with eCEA, then patched CEA (PTFE, bovine pericardium), with the highest rates in patients with primary closure or polyester patching. Vein patch blow out and patch infection were reported in 0.2%.⁷³

A meta-analysis of 10 RCTs ($n = 2\,157$) observed that routine patching (vs. routine primary closure) was associated with significant reductions in 30 day ipsilateral stroke (1.5% vs. 4.5%; OR 0.2, 95% CI 0.1 - 0.6, $p = .001$) and 30 day ICA thrombosis (0.5% vs. 3.1%; OR 5.6, 95% CI 2.4 - 12.5, $p = .0011$). Patients randomised to primary closure were more likely to return to theatre within 30 days (3.1% vs. 1.1%; OR 2.9, 95% CI 1.3 - 6.3, $p = .01$). There were no significant differences regarding peri-operative death, fatal stroke, death/stroke and CNI.^{456,457} An SVS-VQI registry reported significantly lower peri-operative stroke/TIA when the arteriotomy was closed with bovine pericardium (OR 0.59; 95% CI 0.48 - 0.72) or polyester patches (OR 0.56; 95% CI 0.43 - 0.72) vs. vein patch, PTFE patch or primary closure. Bovine pericardial patches (OR 0.57; 95% CI 0.44 - 0.75), polyester patches (OR 0.70; 95% CI 0.50 - 0.98) and vein patches (OR 0.72; 95% CI 0.53 - 0.98) had significantly lower one year re-stenosis rates vs. primary closure.¹²²

Routine patching (vs. routine primary closure) was associated with significant reductions in late ipsilateral stroke (1.6% vs. 4.8%; OR 0.3, 95% CI 0.2 - 0.6, $p = .001$), late any stroke (2.4% vs. 4.6%; OR 0.49, 95% CI 0.3 - 0.9, $p = .002$) and late re-stenosis (4.3% vs. 13.8%; OR 0.2, 95% CI 0.2 - 0.3, $p < .01$). No RCTs have compared routine with selective patching.^{456,457} No RCTs have evaluated selective patching strategies. ESVS recommendations regarding patching are similar to 2021 SVS guidelines,⁴ while the German-Austrian guidelines advise that the choice of CEA technique (eCEA vs. patched CEA) should be left to the operating surgeon.³

Recommendation 71 (Unchanged)	Class	Level	References
For patients undergoing conventional carotid endarterectomy, routine patch closure is recommended, rather than routine primary arteriotomy closure.	I	A	73, 456,457

Recommendation 72 (Unchanged)	Class	Level	References
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For patients undergoing carotid endarterectomy, the choice of patch closure material should be considered at the discretion of the operating surgeon.

IIa

A

73

5.1.11 Eversion (eCEA) vs. conventional (cCEA) endarterectomy?

During eCEA, the ICA is transected obliquely at its origin and a cylinder of atheroma expelled by eversion of the outer media and adventitia. The distal intimal step is examined for flaps, which are excised. The ICA can be shortened and then reanastomosed to the bifurcation. Advantages include no prosthetic infection, it is quicker than patched CEA, bifurcation geometry is preserved, and the distal ICA is shortened where necessary. Disadvantages are that a shunt cannot be inserted until eCEA is completed and there may be problems accessing the distal ICA.

A meta-analysis (one RCT, six observational studies ($n = 1\,275$)) reported that eCEA was associated with significantly more post-CEA hypertension than cCEA (OR 2.75; 95% CI 1.82 - 4.16). Conversely, cCEA was associated with significantly higher rates of hypotension (OR 11.37; 95% CI 1.95 - 66.46).⁴⁵⁸ In an SVS-VQI audit ($n = 72\,787$), eCEA was an independent risk factor for re-interventions for bleeding (OR 1.4; 95% CI 1.1 - 1.7), possibly because of more extensive dissection.¹⁵⁴ In a systematic review of five RCTs and 20 observational studies (16 249 eCEA and 33 251 cCEA), outcomes were different between RCTs and observational studies.⁸⁶ In five RCTs, eCEA (vs. cCEA) was not associated with reduced 30 day stroke, death/stroke, or death/stroke MI, but eCEA was associated with fewer restenoses (OR 0.40; $p = .001$). In 20 observational studies, eCEA (vs. cCEA) was associated with significant reductions in 30 day death (OR 0.46; $p < .0001$), stroke (OR 0.58; $p < .0001$), death/stroke (OR 0.52; $p < .0001$) and late re-stenosis (OR 0.49; $p = .032$). However, when eCEA outcomes were compared with patched CEA in observational studies, there were no significant differences in 30 day death, stroke or death/stroke,⁸⁶ suggesting cCEA provides equivalent outcomes to eCEA, provided the

arteriotomy is patched. ESVS recommendations regarding eCEA vs. cCEA, are similar to SVS guidelines.⁴ The German-Austrian guidelines advise that the choice of eCEA vs. cCEA should be left to the operating surgeon.³

Recommendation 73 (Unchanged)	Class	Level	References
For patients undergoing carotid endarterectomy, eversion endarterectomy or patched endarterectomy is recommended over routine primary arteriotomy closure.	I	A	86

Recommendation 74 (Unchanged)	Class	Level	References
For patients undergoing carotid endarterectomy, the choice between eversion or patched endarterectomy should be considered at the discretion of the operating surgeon.	Ila	A	86

5.1.12 Management of coils, kinks and loops

In DUS studies involving 19 804 patients aged > 25 years, 13.5% had coils, kinks or loops.⁴⁵⁹ Half had histology consistent with fibromuscular dysplasia⁴⁶⁰ in whom an increased incidence of spontaneous dissection was observed⁴⁶¹. One RCT compared surgical correction vs. BMT in 182 patients with hemispheric or non-hemispheric symptoms and isolated ICA coils or kinks, with independent neurologist assessment.⁴⁶⁰ Patients randomised to surgery had 0% thrombosis at 5.9 years, vs. 5.5% with BMT ($p = .02$). Late stroke was 0% after surgery, vs. 6.6% with BMT ($p = .01$). ESVS recommendations regarding treatment of coils/kinks are similar to SVS guidelines.⁴

Recommendation 75 (Unchanged)	Class	Level	References
For patients with asymptomatic isolated coils/kinks of the internal carotid artery, surgical correction is not recommended.	III	C	Expert Opinion

Recommendation 76 (Unchanged)	Class	Level	References
For symptomatic patients with isolated coils/kinks, surgical correction may be considered, but only following multidisciplinary team review and provided no other cause for transient ischaemic attack or stroke symptoms can be identified.	IIb	B	460

5.1.13 Monitoring and quality control (QC) after CEA

QC is not the same as monitoring. The role of monitoring is to ensure adequate brain perfusion, (especially during clamping or shunting), using TCD, CEA under LRA, stump pressure, ICA backflow or near infrared spectroscopy. Loss of cerebral electrical activity is assessed by somatosensory evoked potentials (SSEPs) or EEG. The aim of QC is to identify and correct technical error, such as embolisation during carotid mobilisation (TCD), ensuring the shunt is functioning (TCD, CEA under LRA), identifying luminal thrombus *before* flow restoration (angiography), identifying luminal thrombus *after* flow restoration (DUS, angiography), diagnosing intimal flaps (angiography, DUS, angiography), diagnosing residual stenoses (DUS, angiography) and diagnosing the rare patient thrombosing the operated ICA during neck closure (increasing embolisation followed by declining MCA velocities on TCD).³⁰⁹

A meta-analysis of 34 observational studies compared procedural risks in patients undergoing (vs. not undergoing) completion imaging after CEA (angiography = 53 218; DUS = 20 030; flowmetry = 16 812; angiography = 2 291). No study evaluated combination completion imaging and no RCTs have been performed. Completion angiography and DUS significantly reduced peri-operative stroke (RR 0.83; 95% CI 0.76 - 0.91) and death (RR 0.86; 95% CI 0.76 - 0.98). Flowmetry conferred no benefit. Completion angiography was associated with reductions in peri-operative stroke (RR 0.48; 95% CI 0.033- -0.68, $p = .0001$).⁷¹ ESVS recommendations regarding monitoring

and QC are similar to the German-Austrian guidelines.³ The SVS guidelines concluded there was insufficient evidence to recommend completion imaging.⁴

Recommendation 77 (New)	Class	Level	References
			ToE
For patients undergoing carotid endarterectomy, intra-operative completion imaging with angiography, duplex ultrasound or angioscopy should be considered in order to reduce the risk of peri-operative stroke.	Ila	B	71

5.1.14 Management of high internal carotid artery lesions

High bifurcation or disease extending behind the jaw poses technical challenges and increases operative risks. If DUS cannot image above the lesion, CTA/MRA must be performed to evaluate operability. Distal disease should prompt the surgeon to reconsider whether CEA remains appropriate in ACS patients. If the patient is symptomatic and the surgeon is concerned about their ability to complete the procedure, referral to a more experienced surgeon is advised. CAS is an alternative, but longer lesions increase stroke rates after CAS.^{44,171} Simple measures to facilitate distal access include nasopharyngeal intubation (which opens up the angle between the mastoid process and the jaw), division of various ECA branches and division of the posterior belly of the digastric muscle. More complex strategies, including temporomandibular subluxation, must be planned in advance as it cannot be done once CEA is underway. An alternative operative strategy (which can be used intra-operatively) involves extending the incision anterior to the ear with mobilisation of the superficial lobe of parotid.⁴⁶² This increases access to the upper ICA, but usually requires input from Ear Nose and Throat or Maxillofacial colleagues. ESVS recommendations regarding distal disease extension are similar to SVS guidelines.⁴

Recommendation 78 (Unchanged)	Class	Level	References
For patients undergoing carotid endarterectomy, it is recommended that the surgeon should anticipate the presence of distal disease extension pre-operatively and plan for this in advance.	I	C	Expert Opinion

5.1.15 Wound drainage

Drain placement after CEA should (in theory) prevent haematoma formation which can compromise the airway and increase peri-operative death/stroke,¹³⁷ as well as predisposing to abscess formation and patch infection. There is controversy about whether drains make a difference, with one RCT showing no difference in drain volumes or haematoma size on DUS.⁴⁶³ In 47 752 CEA patients in a VQI database, 41% had drain placement. However, drains did not reduce re-interventions for neck haematoma (1% vs. 0.83%; OR 1.28, 95% CI 1.03 - 1.58) but were associated with increased length of stay (2.4 vs. 2.1 days; OR 2.2, 95% CI 1.5 - 3.7).¹⁵³ In a meta-analysis of five observational studies (drain = 19 832; no drain = 28 465), wound drainage was associated with significantly higher rates of re-exploration, vs. no drains (OR 1.24; 95% CI 1.03 - 1.49, $p = .02$),⁸⁹ while in a VQI audit ($n = 28\,683$), wound drainage did not protect against re-operation for bleeding (OR 1.06; 95% CI 0.76 - 1.48, $p = .72$).¹³⁷ ESVS recommendations regarding wound drainage are similar to SVS guidelines.⁴

Recommendation 79 (New)	Class	Level	References
			ToE
For patients undergoing carotid endarterectomy, selective wound drainage should be considered	Ila	B	89, 153

5.1.16 Ward, high dependency or intensive care after CEA?

Patients benefit from 3 - 6 hours of close neurological and intra-arterial BP monitoring in theatre recovery. Few need overnight monitoring in a high dependency unit (HDU) or intensive care unit (ICU). Most are then transferred to the vascular ward for hourly non-invasive BP and neurological monitoring for the first 24 hours (4 - 6 hourly thereafter until discharge). Up to 40% may require treatment for post-CEA hypertension,⁴⁶⁴ with half needing treatment in the first three post-operative hours (**section 7.1.3.3**). If there are no additional hypertensive surges, patients can return to the ward 2 - 3 hours later. Patients requiring ongoing *i.v.* hypertensive therapy should remain in theatre recovery or go to HDU/ITU for intra-arterial BP monitoring. Two hours after *i.v.* treatment has been completed (with no further BP surges), it is reasonable to transfer patients to the vascular ward for ongoing monitoring. Anyone suffering a major intra-operative cardiac event should be transferred to ICU or coronary care for further evaluation.

5.2 Carotid bypass

5.2.1 Indications

Carotid bypass may be indicated in the treatment of patch infection, carotid stent explantation, re-stenosis or technical problems during CEA (arterial wall thinning, damage to arterial wall). Other indications include extensive atherosclerotic disease, ICA fibrosis secondary to radiotherapy, or revascularisation after *en bloc* removal of a neck tumour.⁴⁶⁵⁻⁴⁷⁴

5.2.2 Technique

There are several techniques including interposition with proximal and distal end to end anastomoses, or end to side anastomosis to the distal common carotid artery (CCA) and either end to side or end to end anastomosis to the distal ICA. The ECA can be preserved or ligated.

Conduits include reversed saphenous vein (from the thigh),^{466,467,470,474} PTFE,^{465,466,468,469,472,474} or polyester.⁴⁷¹

5.2.3 Results

Outcomes from observational studies are detailed in **Table 32**. Late patency of prosthetic and vein grafts appeared comparable to CEA. Late prosthetic graft infection was rare (3/987; 0.3%).

Table 32: Thirty day and late outcomes following carotid bypass

author	<i>n</i>	conduit type	30 day death/stroke	primary patency	late infection
Ricco ⁴⁶⁵	198	PTFE	1/198 (0.5%)	98% @ 10y	none
Dorafshar ⁴⁶⁶	31	PTFE	1/31 (3.2%)	90% @ 4 y	1/31
Roddy ⁴⁷⁸	22	PTFE	0/22 (0.0%)	95% @ 2y	none
Veldenz ⁴⁶⁹	51	PTFE	1/51 (1.9%)	96% @ 2y	none
Illuminati ⁴⁷²	66	PTFE	0/66 (0%)	93% @5y	none
Ricco ⁴⁷³	42	PTFE (31), GSV (11)	0/42 (0%)	n/a	none
Stilo ⁴⁷⁴	13	PTFE (7), GSV (6)	0/13 (0%)	100% @41m	n/a
Koncar ⁴⁷¹	292	Polyester	19/292 (6.5%)	96% @ 32m	2/292
Dorafshar ⁴⁶⁶	10	GSV	1/10 (10%)	80% @ 4y	n/a
Lauder ⁴⁶⁷	50	GSV	3/50 (6.0%)	83% @ 3y	n/a
Branchereau ⁴⁷⁰	212	GSV	14/212 (6.6%)	92% @10y	n/a

PTFE = polytetrafluoroethylene; GSV = greater saphenous vein

5.3. Extracranial to intracranial (EC-IC) bypass.

The rationale for EC-IC bypass in patients with extracranial ICA occlusion (usually from the superficial temporal artery to the ipsilateral MCA), is that it reduces long term ipsilateral ischaemic stroke. A Cochrane review (2 RCTs, 19 observational studies (*n* = 2 591)) concluded

that EC-IC bypass conferred no benefit over BMT regarding late stroke prevention (RCTs: OR 0.99; 95% CI 0.79 - 1.23, $p = .91$; non-RCTs: OR 0.80; 95% CI 0.54 - 1.18, $p = .25$).⁴⁷⁵ A third RCT included patients with recently symptomatic ICA occlusion and haemodynamic impairment in the ipsilateral hemisphere⁴⁷⁶. The two year risk of ipsilateral stroke (including 30 day death/stroke) was 21% (95% CI 12.8 - 29.2) after EC-IC bypass, vs. 22.7% (95% CI 13.9 - 31.6) with BMT ($p = .78$). There is currently no role for EC-IC bypass in patients with atherosclerotic ICA occlusion.

Recommendation 80 (Unchanged)	Class	Level	References
For recently symptomatic patients with an extracranial atherosclerotic internal carotid artery occlusion, extracranial to intracranial bypass surgery is not recommended.	III	A	475,476

Section 6. Carotid Artery Stenting

6.1 Adjuvant medical therapy

Most operators administer 5000iu i.v. heparin to prevent thrombosis, plus 0.6 - 1.2mg atropine (0.6mg glycopyrrolate) before balloon inflation to prevent hypotension, bradycardia, or asystole.^{477,478}

Recommendation 81 (Regraded)	Class	Level	References
For patients undergoing carotid artery stenting, intravenous atropine or glycopyrrolate is recommended prior to balloon inflation to prevent hypotension, bradycardia or asystole	I	C	477,478

6.2 Access

6.2.1 Transfemoral

Access in RCTs comparing CEA vs. CAS was mostly via the common femoral artery (CFA), with other routes reserved for CFA disease, tortuosity or disease of both iliac arteries and distal aorta. Unfavourable arch anatomy (type III, bovine arch) and severe atheromatous disease of the aortic arch or supra-aortic arteries increase the risk of cerebral embolisation during catheter navigation via the CFA, which has encouraged the development of alternative access strategies.

6.2.2 Transcarotid

Direct access to the proximal CCA (via a cervical incision) avoids manipulation of wires and catheters in the arch. TCAR provides cerebral protection via proximal CCA clamping plus ICA flow reversal via an extracorporeal circuit from the CCA to femoral vein⁴⁷⁹ or ipsilateral jugular vein (allowing the stenosis to be stented during protected flow reversal) with significantly fewer NIBLs (13%) vs. 33% after TFCAS ($p = .03$).⁴⁸⁰ No RCTs have evaluated TCAR, but registries have reported outcomes. ROADSTER-2 enrolled 692 patients deemed high risk of CEA with 99.7% technical success, despite 81% of operators being TCAR naive.⁴⁸¹ Procedural success (technical success without death/stroke/MI < 30 days) was 96.5%, with 30 day stroke rates of 1.9%, mortality 0.4%, MI 0.9% and CNI 1.4%. 30 day stroke/death was 2.3%. However, only a minority (26%) were symptomatic.⁴⁸¹ An SVS-VQI registry compared TCAR ($n = 638$) with TFCAS ($n = 10136$) and reported that TFCAS was associated with significantly higher in hospital TIA/stroke/death vs. TCAR (OR 2.1; 95% CI 1.08 - 4.08, $p = .03$).¹⁴⁸ However, only 33% of the TCAR cohort were symptomatic, vs. 42% in the TFCAS cohort ($p < .001$). A second SVS-VQI registry compared TCAR with CEA and reported fewer CNIs after TCAR (0.6% vs. 1.8%; $p < .001$), but no difference in in hospital stroke/death (OR 1.3; 95% CI 0.8 - 2.2, $p = .28$).¹⁵² Only 32% of the TCAR cohort were symptomatic. An SVS-VQI study developed a TCAR risk score calculator to aid patient selection, but recency of symptoms was excluded.¹⁴⁷ A systematic review of TCAR (18 observational studies; $n = 8380$) reported low 30 day stroke rates (1.2% - 5.2%), MI (0% - 2.1%) and death (0% - 2.7%),⁵¹ while another meta-analysis of 13 observational studies ($n = 837$)

reported that carotid dissection following TCAR was 2% (95% CI 1 - 3).⁸² Outcome data when TCAR was performed < 14 days of symptom onset are detailed in **section 4.5.5**.

6.2.3 Radial and brachial

RADCAR (RADial access for CARotid artery stenting) randomised 260 patients to transradial access (TRA) or TFCAS. Procedural success was 100%, with 10% crossover during TRA and 1.5% with TFCAS ($p < .05$).³⁵ Access complications were low (0.9% vs. 0.8%), as were major cardiac and/or cerebral events (0.9% vs. 0.8%), but radiation doses to the patient were significantly higher with TRA.³⁵ In a single centre series (101 TRA; 674 TFCAS), in hospital cardiac and/or cerebral events were similar (2% vs. 3.6%), with a crossover of 4.9% from TRA to TFCAS.⁴⁸² Navigating from the right radial artery (RA) into the CCA (especially the left) is challenging. In a multicentre series ($n = 214$) undergoing TRA CAS, distal filter deployment was not possible in 7%, while proximal protection was not possible in 1.6%.⁴⁸³ A meta-analysis of seven observational studies involving 723 ACS and SCS patients undergoing TRA CAS, reported minor stroke/TIA in 1.9% (95% CI 0.6 - 3.8), major stroke rate 1.0% (95% CI 0.4 - 1.8) and RA occlusion rates of 5.9%; 95% CI 4.1 - 8.0).⁶⁴

Recommendation 82 (New)	Class	Level	References ToE
For patients selected to undergo carotid artery stenting, transradial or transcarotid artery revascularisation should be considered as an alternative to transfemoral carotid artery stenting, especially where transfemoral access may confer a higher risk of complications.	Ila	B	35,64,148, 481-483

6.3 Wires, catheters and stent design

Access to the CFA, brachial or RA is secured and a .035" hydrophilic guide wire used to access the CCA. 6 - 8 Fr long sheaths or guiding catheters secure a stable position in the CCA, typically after exchange of a .035" support wire in the ECA. For stent placement and balloon angioplasty (requiring rapid exchange systems) .014" floppy tip guide wires are advised.

6.3.1 Stent design

Carotid stent design is summarised in **Table 33** as open cell (more flexible, suited for tortuous anatomy), closed cell (more rigid, better plaque coverage), or hybrid (closed cell in middle, open cell at the edges).

Table 33: Characteristics of open cell, closed cell and hybrid design stents

	open	closed	hybrid
Free cell area	large	small	mid segment=small; edges=large
Strut interconnections	few	many	mid segment=many; edges= few
Flexibility	good	limited	moderate
Plaque coverage	limited	good	good

There are conflicting data regarding open vs. closed cell stents. Two small RCTs reported no outcome differences,^{484,485} although NIBLs were commoner with open cell stents ($p = .02$).⁴⁸⁵ A CSTC meta-analysis ($n = 1\,557$) reported that open cell stents incurred significantly higher 30 day stroke/death (10.3%) vs. 6% with closed cell (RR 1.7; 95% CI 1.23 - 2.52, $p = .002$) after adjusting for age and symptom status.¹⁰⁸ However, after the peri-operative period, late stroke risks are similar (HR 0.78; 95% CI 0.35 - 1.75).³³ In the German CAS registry ($n = 13\,086$) there was a non-significant trend towards lower in hospital stroke/death with closed cell stents (RR 0.86; 95% CI 0.65 - 1.14, $p = .30$),¹⁴¹ while in an SVS-VQI registry (1 384 closed cell vs. 1 287 open

cell), multivariable analyses revealed that closed cell stents were associated with higher stroke/death when deployed across the bifurcation (OR 5.5; 95% CI 1.3 - 22.2, $p = .02$).¹²³ In a meta-regression analysis ($n = 46\,728$), open cell stents were associated with significantly higher 30 day death/stroke and NIBLs (RR 1.25; $p = .03$), with no differences regarding re-stenosis, stent fracture, or intraprocedural haemodynamic depression.⁵³

Dual layer mesh covered stents (DLS) combine the close vessel wall apposition of open cell stents (soft nitinol outer layer) and prevention of plaque prolapse associated with closed cell stents (micromesh inner layer with very small cell size). A small RCT ($n = 104$ with lipid rich plaques) reported that proximal protection reduced MES by 76% - 83% vs. distal filter protection ($p < .0001$), while DLS reduced MES by 13% - 29% vs. closed cell stents ($p = .02$).⁴⁸³ A meta-analysis of four observational studies revealed one year death/stroke rates of 3.8% with DLS and 2.1% re-stenosis.⁹⁸ A Japanese study enrolled 140 DLS patients (39% SCS), reporting that the risk of peri-operative death/stroke/MI and/or ipsilateral stroke at one year was 1.4%. Outcomes were similar irrespective of age, CEA risk and presentation.⁴⁸⁶ Caution should be exercised if considering DLS in acute stroke treatment, as a registry has reported higher rates of acute stent thrombosis with DLS (45%) vs. 3.7% with single layer stents ($p = .001$).⁴⁸⁷

Recommendation 83 (New)	Class	Level	References
			ToE
For patients undergoing carotid artery stenting, decisions regarding stent design (open cell, closed cell) should be considered at the discretion of the operator.	Ila	B	53,123, 141

Recommendation 84 (New)	Class	Level	References
			ToE

For patients undergoing elective carotid artery stenting, dual layer mesh covered stents may be considered.

IIb

C

486

6.4 Pre- and post-dilation

Pre-dilation of the target lesion facilitates advancement of distal protection systems and stent catheters, as well as allowing stent expansion, which is also the aim of post-dilation. Pre-dilation is generally avoided unless the stent or protection device cannot cross a tight lesion. Severe calcification (circumferential or exophytic) is a contraindication to CAS due to high procedure failure rates.¹⁷² Pre- and post-dilation may also cause embolisation and vessel injury. In a CSTC meta-analysis ($n = 1\,557$), 30 day death/stroke was unaffected by pre-dilation (RR 0.96; 95% CI 0.67 - 1.44, $p = .92$) or post-dilation (RR 0.87; 95% CI 0.47 - 1.62, $p = .67$).¹⁰⁸ However, another meta-analysis (6 observational studies ($n = 4\,652$)) reported greater haemodynamic instability when post-dilation was performed (OR 1.69; 95% CI 1.14 - 2.56).¹¹³ Single vs. double dilation was associated with significantly fewer neurological events (RR 0.67; 95% CI 0.47 - 0.97, $p = .03$), as was less aggressive pre-dilation (balloon diameter < 5 mm) vs. > 5mm balloons (RR 0.27; 95% CI 0.09 - 0.86, $p = .026$). In a series of 255 ACS and SCS patients, primary stenting (without pre- or post-dilation), was associated with a 1.2% 30 day risk of death/stroke⁴⁸⁸. In an SVS-VQI audit, primary stenting was associated with similar 30 day stroke/death vs. CAS with pre- and/or post-dilation (OR 1.15; 95% CI 0.72183, $p = .55$).¹³¹

Recommendation 85 (New)	Class	Level	References
			ToE
For patients undergoing carotid artery stenting, when pre-dilatation is planned, balloon diameters <5 mm should be considered in order to reduce the risk of peri-procedural stroke or transient ischaemic attack.	IIa	C	113

Recommendation 86 (New)	Class	Level	References
			ToE
For patients undergoing carotid artery stenting, post-dilatation is not recommended when the residual stenosis is <30%, in order to reduce haemodynamic instability.	III	B	113

6.5 Cerebral protection devices (CPDs)

The role of CPDs is controversial, despite embolic material being regularly retrieved from filters.⁴⁸⁹ In a meta-analysis of 13 RCTs and 193 registries ($n = 54\,713$), 22 studies ($n = 11\,655$) reported lower peri-operative stroke/death favouring CPDs (OR 0.57; 95% CI 0.43 - 0.76, $p < .01$).⁴⁹⁰ However, a CSTC meta-analysis of three RCTs ($n = 1\,557$) reported that CPDs did not reduce 30 day stroke/death (RR 1.1; 95% CI 0.71 - 1.70, $p = .67$).¹⁰⁸ The German National registry ($n = 13\,086$) observed that CPDs were associated with lower rates of major stroke/death (RR 0.60; 95% CI 0.43 - 0.84) and any stroke (RR 0.57; 95% CI 0.43 - 0.77).¹⁴¹ An SVS-VQI audit ($n = 10\,074$) also reported higher 30 day stroke/death when CPDs were not used (OR 3.97; 95% CI 2.47 - 6.37).¹³¹

Proximal CPDs protect the brain by reversing blood flow in the bifurcation during stenting (**section 6.2.2**). Proximal CPDs should, however, be avoided in patients with severe ECA or CCA disease.⁴⁹¹ The best CAS results in RCTs involving asymptomatic patients were reported by CREST-1 and ACT-1, where CPDs were mandatory and practitioners were trained in their use.^{224,316} Contradictory reports have led to conflicting opinions amongst CAS practitioners, with some claiming CPDs are unnecessary, while others would never perform unprotected CAS. Given the lack of RCTs, ESVS recommendations are based on a consensus amongst CAS practitioners that CPDs should be considered when performing CAS. ESVS recommendations

regarding access for CAS, protection devices and pre- and post-dilation are similar to the 2021 SVS guidelines.⁴

Recommendation 87 (Unchanged)	Class	Level	References
For patients undergoing carotid artery stenting, cerebral protection systems should be considered	Ila	C	224,316, 490

Recommendation 88 (New)	Class	Level	References
			ToE
For patients undergoing carotid artery stenting, decisions regarding choice of cerebral protection (filter, proximal flow reversal) should be considered at the discretion of the operator.	Ila	B	108,131, 141,224, 316,490

Recommendation 89 (Unchanged)	Class	Level	References
For patients undergoing carotid artery stenting, it is not recommended to deploy proximal cerebral protection devices in patients with advanced common carotid disease or external carotid artery disease (if an occlusion balloon is to be positioned in the external carotid artery) or in patients with contralateral occlusion and insufficient collateralisation.	III	C	491

6.6 Hospital and individual operator volumes

Low volume hospitals (< 20 CAS/year) had a significantly higher 30 day stroke rate than higher volume hospitals (HR 1.5; 95% CI 1.06 - 2.12, $p = .023$).¹³² In a Healthcare Cost and Utilisation Project, higher CAS volumes were associated with lower mortality/morbidity, shorter length of stay and reduced hospital costs.⁴⁹² In a high risk of CEA registry, a lifetime experience of 72 procedures was required to achieve 30 day death/stroke rates < 3% in non-octogenarian ACS patients.⁴⁹³ 30 day mortality in Centre for Medicare and Medicaid beneficiaries was higher if practitioners performed < 6 CAS/year, vs. > 24 (OR 1.9; 95% CI 1.4 - 2.7, $p < .001$).⁴⁹⁴ In a single

centre series ($n = 2\,124$), a lifetime experience of > 100 interventions was associated with fewer peri-operative strokes (OR 0.81; 95% CI 0.67 - 0.95), whilst < 50 procedures was a predictor for increased peri-operative stroke ($p < .001$).⁴⁹⁵

A CSTC meta-analysis of three European RCTs ($n = 1\,557$ SCS patients) reported 30 day death/stroke was not influenced by lifetime CAS experience,⁴⁹⁶ but 30 day death/stroke was significantly higher with lower volume operators (≤ 3.2 CAS/year) vs. higher volume operators (> 5.6 CAS/year) (OR 2.3; 95% CI 1.36 - 3.87).⁴⁹⁶ CSTC concluded that a minimum of six CAS procedures per year was necessary to remain competent.⁴⁹⁶ However, others advise that in an era of low CAS volumes, 25 lifetime procedures is reasonable to achieve competency, plus 10 - 15 procedures annually.⁴⁹⁷ A 2021 audit from Australia and New Zealand ($n = 1\,350$) demonstrated significantly higher peri-operative stroke/death rates with lower volume CAS operators (2.63% for operators doing < 11 annual cases) vs. 0.37% for operators performing ≥ 12 cases annually (OR 6.11; 95% CI 1.27 - 29.33, $p = .024$).¹²⁸ In the CHOICE registry ($n = 5\,841$), operator volume (but not hospital volume) was an independent predictor of 30 day death/stroke/MI, with a 5% increase in adverse outcomes per additional month between consecutive CAS procedures (OR 1.05; 95% CI 1.02 - 1.09, $p = .005$).⁴⁹⁸ SVS guidelines made no recommendation regarding annual CAS volumes, but the German-Austrian guidelines advised that CAS should only be performed in hospitals performing > 10 CAS procedures per year.³

Recommendation 90 (New)	Class	Level	References
			ToE
For patients undergoing transfemoral carotid stenting, at least twelve carotid stent procedures per year (per operator) may be considered an appropriate operator volume threshold in order to maintain optimal outcomes.	IIb	C	128,492,498

Section 7: Complications after carotid interventions

7.1 Peri-operative period

7.1.1 Stroke after carotid endarterectomy

7.1.1.1 Intra-operative stroke

Intra-operative stroke is a new neurological deficit (worsening of pre-existing deficit), apparent following recovery from anaesthesia (or during CEA under LRA), lasting > 24 hours. Most follow intra-operative embolisation (carotid mobilisation, shunt insertion, flow restoration, accumulation of thrombus on endarterectomy zone). A minority (20%) are haemodynamic after carotid clamping or shunt malfunction.⁴⁹⁹ In a 21 year audit ($n = 2\,300$), most intra-operative strokes followed embolisation of luminal thrombus at flow restoration, with the source being bleeding from transected vasa vasorum onto the endarterectomised surface.³⁰⁹ One advantage of CEA under LRA is that the timing of new deficits can be accurately determined. For patients undergoing CEA under GA, abrupt EEG changes predict the likeliest time of onset.⁵⁰⁰ Patients with a triad of hemiplegia, homonymous hemianopia, and higher cortical dysfunction on recovery from anaesthesia are likely to have suffered ICA or MCA occlusion. If 1 - 2 triad components are present, occlusion of one or more MCA branches is likely.⁵⁰¹

Previously, patients recovering from anaesthesia with a new neurological deficit underwent immediate re-exploration to exclude thrombus within the endarterectomy zone. This remains the recommendation in the 2021 SVS guidelines.⁴ However, a recent Delphi consensus study concluded that immediate re-exploration remained appropriate in patients experiencing a new deficit when flow was restored with CEA under LRA, but in all other peri-operative phases, rapid imaging of carotid vessels and brain was advised before re-exploration.⁵⁰² In ACST-1, there was no difference in rates of disabling/fatal stroke between patients who underwent immediate re-exploration vs. those who did not.⁵⁰³ The priority, therefore, is to quickly identify patients with

ICA thrombosis, as they will benefit from immediate re-exploration. TCD aids decision making, as MCA velocities with ICA thrombosis are identical to those during carotid clamping. Thrombosis is also preceded by increasing rates of embolisation.³⁰⁹ DUS can confirm flow in the endarterectomy zone, but subcutaneous air makes it difficult to interpret early post-operative findings. At re-exploration, thrombus should be removed. If thrombus extends distally, it should be carefully removed with a Fogarty catheter. Following thrombectomy, technical errors are corrected, and a completion angiogram performed. Embolic occlusion of the ipsilateral anterior or middle cerebral artery can be treated by re-exploration (to remove thrombus in the endarterectomy zone) followed by intra-arterial thrombolysis.⁵⁰⁴ Emergency MT is another option in patients with embolic MCA mainstem occlusion. No RCTs have been done, but targeted intra-operative neuromonitoring (TCD, EEG) and QC assessment (completion angioscopy, DUS, angiography) have been associated with significant reductions in intra-operative stroke.^{71,309,500,505}

7.1.1.2 Post-operative stroke

This is defined as a new neurological deficit (or worsening of a pre-existing deficit) after an uneventful recovery from anaesthesia, with symptoms lasting > 24 hours. In the first six hours, the commonest cause is ICA thrombosis or embolism from mural thrombus in the endarterectomy zone. A Delphi consensus recommended rapid imaging before re-exploration.⁵⁰² After six hours, CT and extracranial and intracranial CT/CTA will exclude ICA thrombus, cerebral oedema, or parenchymal haemorrhage. In ICSS, the commonest cause of post-operative stroke was hyperperfusion syndrome (HS).³⁸⁵ HS is discussed in more detail in **section 7.1.3.5.**

7.1.1.3 Predictors of stroke after CEA

In ECST, predictors included (i) female sex (10.4% vs. 5.8%, $p = .0001$); (ii) PAD (12.0% vs. 6.1%, $p = .0001$); (iii) pre-operative SBP (< 120 mmHg = 3.4%; 121 - 159 = 6.5%; 160 - 180 = 7.7%; > 180 mmHg = 13.0%, $p = .04$) and (iv) presentation (retinal (3.2%), hemispheric stroke (6.3%), TIA (9.1%) $p = .006$).³⁵² Predictive features in NASCET were (i) hemispheric vs. retinal events (6.3% vs. 2.7%; OR 2.3; 95% CI 1.1 - 5.0); (ii) left vs. right CEA (6.7% vs. 3.0%; OR 2.3, 95% CI 1.4 - 3.6); (iii) contralateral occlusion (9.4% vs. 4.4%; OR 2.2, 95% CI 1.1 - 4.5); (iv) ipsilateral CT/MR infarct (6.3% vs. 3.5%; OR 1.8; 95% CI 1.2 - 2.8) and (v) irregular vs. smooth plaques (5.5% vs. 3.7%; OR 1.5, 95% CI 1.1 - 2.3).⁵⁰⁶ In ICSS, stroke was more frequent in females (RR 1.98; 95% CI 1.02 - 3.87, $p = .05$) and with increased DBP (RR 1.30 per +10mmHg; 95% CI 1.02 - 1.66, $p = .04$), but unrelated to CEA method or GA vs. LRA.⁵⁰⁷ In a multivariable model, increased DBP was the only independent predictor of stroke, MI or death.⁵⁰⁷ In ACST-1, DBP was also an independent predictor for stroke.¹³

Recommendation 91 (New)	Class	Level	References ToE
For patients experiencing a peri-operative stroke, it is recommended to differentiate between an intra-operative and a post-operative stroke.	I	C	502

Recommendation 92 (New)	Class	Level	References ToE
For patients who develop an ipsilateral neurological deficit after flow is restored following carotid clamp release when carotid endarterectomy is performed under locoregional anaesthesia, immediate re-exploration of the carotid artery is recommended.	I	C	502

7.1.2 Stroke after carotid artery stenting

In a meta-analysis of SCS patients in RCTs, the risk of stroke on the day of CAS was 4.7% with an additional 2.5% during days 1 - 30. Most were ischaemic (94%), with 91% ipsilateral to the stented ICA.⁴⁸ Important causes include embolisation, in stent thrombosis, ICA/CCA dissection, HS and ICH. Prevention of embolic stroke is a role for CPDs (**section 6.5**), but embolism can still occur due to incomplete deployment, malpositioning, or incomplete aspiration of debris. If a neurological deficit occurs during CAS, no additional imaging is required prior to MT or intra-arterial TT. In patients developing a stroke after CAS, the usual rules of acute stroke management should be followed, which includes ICH exclusion (and other stroke mimics) and assessment of cerebral perfusion.

Treatment options in patients developing a new neurological deficit during CAS include MT with or without intra-arterial TT. Mechanical removal of embolic material from the distal ICA out to the distal M2 MCA segment is possible using dedicated neuro-interventional retrieval devices.⁵⁰⁸ Accordingly, most interventionists now advocate MT in CAS patients suffering acute stroke due to ICA or M1/M2 MCA branch occlusions. Intra-arterial TT is less effective in acute stroke during CAS as the embolus usually comprises plaque, rather than fibrin clot. In patients with acute stent thrombosis, TT should be considered with rTPA delivered as a 5mg bolus, followed by slow infusion (maximum dose 20mg), ensuring the catheter remains positioned within the thrombus. If the thrombus dissolves, the microcatheter tip is advanced into the remaining thrombus. Selective intra-arterial administration of 5mg abciximab followed by an i.v. bolus of 5mg abciximab has been effective in treating distal embolisation during CAS.⁵⁰⁸

While no RCTs have addressed the treatment of acute stroke due to ICA thrombosis, or M1/M2 embolic branch MCA occlusions, management should be no different to stroke occurring without a prior carotid intervention. It would be preferable that, in the future, a neuro-interventional service is available in any institution performing CAS.

Recommendation 93 (New)	Class	Level	References
			ToE
For patients who develop an ipsilateral or contralateral stroke at any time period following carotid endarterectomy or carotid artery stenting, urgent diagnostic neurovascular imaging of both carotid arteries and the brain is recommended.	I	C	Expert opinion

7.1.2.1 Predictors of stroke after CAS

A Delphi consensus identified anatomic features associated with increased difficulty for CAS novices including (i) type III arch; where the vertical distance between the brachiocephalic artery origin and top of the arch exceeds two left CCA diameters; (ii) bovine arch (where the brachiocephalic artery shares a common origin with the left CCA); (iii) severe arch atheroma; (iv) diseased or occluded ECA; (v) angulated distal ICA (severity not specified); (vi) long stenoses and (vii) pinhole stenoses.⁵⁰⁹ The Delphi Anatomical Risk score was validated in 883 CAS patients and a score in the highest quartile was an independent predictor for stroke/TIA (OR 3.79; 95% CI 1.7 - 8.3, $p = .001$).¹⁶⁸ However, in ICSS there was no correlation between the Delphi Anatomical Risk score and peri-operative stroke.¹³ In CREST, plaque features associated with increased stroke risk after CAS included plaque length > 13 mm or sequential lesions extending remotely from the ICA stenosis¹⁷¹. However, in an ICSS-MRI substudy, none of the CREST plaque features were associated with higher rates of NIBLs on MRI.⁵¹⁰ In ICSS, features associated with significantly higher rates of NIBLs included arch type II/III (OR 2.8; 95% CI 1.1 - 7.1, $p = .027$) and a greater ICA angle ($\geq 60^\circ$ vs. $< 60^\circ$; OR 4.1, 95% CI 1.7 - 10.1, $p = .002$).³²

In a CSTC meta-analysis (**section 2.3.5**), CAS incurred significantly higher rates of death/stroke (vs. CEA) in the first 7 days after symptom onset (8.3% vs. 1.3%; RR 6.7, 95% CI 2.1 - 21.9).¹⁷⁰ In a propensity matched analysis involving octogenarians undergoing CEA or CAS, urgent interventions (OR 2.12; 95% CI 1.68 - 2.69, $p < .001$); COPD (OR 1.52; 95% CI 1.11 - 2.09, $p =$

.009); and ASA grade > 3 (OR 1.46; 95% CI 1.15 - 1.86, $p = .002$) were independent predictors of post-operative stroke.¹²⁰ ICSS reported that CAS patients with an age related white matter change (ARWMC) score ≥ 7 on CT/MRI had higher rates of peri-operative stroke, vs. patients whose ARWMC score was < 7 (HR 2.76; 95% CI 1.17 - 6.51, $p = .021$). There was no association between ARWMC score and stroke after CEA (HR 1.18; 95% CI 0.4 - 3.55, $p = .76$).¹⁷³ CAS was associated with significantly higher rates of peri-operative stroke (vs. CEA) if the ARWMC score was > 7 (HR 2.98; 95% CI 1.29 - 6.93, $p = .011$), with no difference between CEA and CAS when the ARWMC score was < 7.¹⁷³ Of interest, a high ARWMC score was also associated with silent cerebral embolisation during transcatheter aortic valve implantation.⁵¹¹

7.1.3 Haemodynamic instability

7.1.3.1 Post-endarterectomy hypotension

Post-CEA hypotension is attributed to exposure of carotid sinus baroreceptors to the pulse pressure, without the dampening effect of the excised plaque.⁵¹² Its relevance is variable, with some reporting increases in peri-operative stroke/MI,⁵¹³ while others consider it a benign phenomenon.⁵¹² There is no consensus regarding what BP threshold should be used for treatment. Management of post-CEA hypotension is the same as for CAS.

7.1.3.2 Post-stenting hypotension

In a meta-analysis of 27 observational studies ($n = 4\,204$), 12% of CAS patients were treated for hypotension, 12% for bradycardia, while 13% had treatment for both. Persistent haemodynamic instability (more than one hour vasopressor support) affected 19% of CAS patients.⁵¹⁴ There was a significant association between persistent haemodynamic depression after CAS and a history of ipsilateral CEA,⁵¹⁴ calcification, involvement of the carotid bulb, severe stenosis, eccentric plaque^{515,516} and nitinol stents,⁵¹⁵ although the latter was not corroborated

in a meta-analysis of two RCTs and 66 cohort studies ($n = 46\,728$).⁵³ Avoiding post-dilation was protective against persistent haemodynamic depression in a meta-analysis of six cohort studies involving 4 652 patients (RR 0.59; 95% CI 0.39 - 0.87, $p = .03$).¹¹³ Meta-analysis of 27 observational studies ($n = 4204$) suggested no differences in peri-operative stroke in CAS patients with or without haemodynamic instability (OR 1.0; 95% CI 0.57 - 1.75).⁵¹⁴

Preventing haemodynamic instability during CAS involves hydration, withholding antihypertensive medications on the morning of CAS, continuous ECG/BP monitoring and venous access. Glycopyrrolate (synthetic atropine derivative) was compared with atropine in a retrospective study ($n = 115$) and was more effective in preventing post-operative bradycardia (30% vs. 72%, $p = .002$), and hypotension (2.5% vs. 36%, $p = .001$), with lower rates of compensatory hypertension (2.5% vs. 16%, $p = .047$).⁵¹⁷ Treatment of hypotension includes i.v. crystalloid and volume expanders, but this may be inadequate due to decreased peripheral vascular resistance with loss of sympathetic tone, rather than hypovolaemia. Titrated i.v. vasopressors (norepinephrine, dobutamine, phenylephrine) may be necessary to maintain SBP > 90 mmHg. Major adverse events (MI, dysrhythmia, cardioversion) were more common in patients receiving dopamine vs. norepinephrine/phenylephrine ($p = .04$). Midodrine (selective α -1 agonist) causes arteriolar and venous vasoconstriction without stimulating cardiac β adrenergic receptors and is as effective as dopamine for treating hypotension after CAS.⁵¹⁸

7.1.3.3 Post-endarterectomy hypertension

Post-CEA hypertension can affect up to two thirds of patients, depending on its definition.⁴⁶⁴ Causes include carotid bulb denervation and increased norepinephrine and/or renin production.⁵¹⁹⁻⁵²¹ Post-CEA hypertension is associated with pre-operative hypertension,^{464,522} GA⁵²³ and eCEA.⁴⁵⁸ The association between GA and post-CEA hypertension is attributed to increased neuroendocrine stress hormone levels, while the association with eCEA is attributed

to carotid bulb denervation.⁵²⁴ In a meta-analysis of six observational studies, patients undergoing eCEA were significantly more likely to require vasodilator therapy in the early post-operative period vs. cCEA (OR 2.75; 95% CI 1.82 - 4.16).⁴⁵⁸ However, evidence suggests that (in the long term) there is no significant difference in BP measurement between eCEA and cCEA.⁴² In a prospective study ($n = 100$), poorly controlled pre-operative BP and impaired baroreceptor function (but not impaired autoregulation) were associated with post-CEA hypertension.⁴⁶⁴ Intra-operative predictors include poorly controlled or labile hypertension at induction of anaesthesia. No other variable (including magnitude of MCA velocity increase with flow restoration) was predictive of post-CEA hypertension.⁵²⁵ Poorly treated post-CEA hypertension is associated with increased rates of post-operative TIA/stroke^{309,522,526} and is a risk factor for neck haematoma, HS and ICH.^{309,527} There are various published strategies for when and how to treat post-CEA hypertension^{309,528} but because units tend to adopt different thresholds for intervening, it is difficult to define a consensus treatment protocol. However, it is important that units performing CEA/CAS have written guidance for the treatment of post-CEA hypertension,^{309,528} so that management decisions are not delayed.

7.1.3.4 Post-stenting hypertension

Post-CAS hypertension required treatment in 9.9% of CAS patients in an SVS-VQI database and was associated with higher rates of stroke/death (OR 3.39; 95% CI 2.3 - 5.0, $p < .0001$). The management of post-CAS hypertension is the same as for CEA.

7.1.3.5 Hyperperfusion syndrome

There are no consensus criteria for diagnosing HS, which affects 1% of CEA and 3% of CAS patients.^{529,530} HS may be characterised by headache, confusion, atypical migraineous phenomena, seizures, hypertension, decreased consciousness, nausea and vomiting, and (ultimately) a neurological deficit, which can be due to vasogenic oedema, ischaemia or haemorrhage.⁵²⁹ The average time of symptom onset is 12 hours post-operatively, although it

can occur up to four weeks later.^{63,531} MRI typically shows vasogenic oedema (not always located in the ipsilateral carotid territory) with evidence of perfusion within the oedema (ie. this is not an evolving ischaemic infarct⁵³²). Other MRI features include hyperintense signal change on T2 weighted and fluid attenuated inversion recovery (FLAIR) MRI, without restricted diffusion on DWI. There may also be a high T1 signal with hyperacute haemorrhage.

Pathophysiological mechanisms include impaired baroreceptor function and disturbances to the trigeminovascular reflex. Female sex, older age, chronic kidney disease, and a treated left carotid artery were associated with HS after CAS.¹²⁹ Impaired CVR increased the risk of HS after CAS, while hypertension and a significant contralateral stenosis (both risk factors for HS after CEA) and male sex did not.⁶³ Risk factors for HS after CEA include female sex, recent major stroke, CAD and a contralateral stenosis $\geq 70\%$.¹⁶¹ Several imaging modalities have been proposed as predictors for HS including TCD, SPECT, near infrared spectroscopy, perfusion CT and quantitative MRA. However, TCD is probably the most reliable, with studies suggesting that 99% of patients with increases in mean MCA velocity $< 100\%$ at 24 hours (compared with baseline) did not develop HS.⁵³³

HS associated ICH appears commoner after CAS than CEA,^{63,134} possibly because CAS is associated with intraprocedural hypotension followed by compensatory hypertension, which may persist beyond discharge and also because CAS patients are routinely prescribed DAPT.^{63,134} In a meta-analysis of 41 observational studies ($n = 28\,956$) hypertension and ipsilateral high grade stenosis were risk factors for ICH after both CEA and CAS.⁴⁵ Untreated HS progresses through regional vasogenic oedema to petechial haemorrhages then ICH.⁵³¹ Any patient with suspected HS should have elevated BP reduced urgently (**section 7.1.3.3**), while seizures should be controlled with appropriate anti-epileptic drugs. ESVS recommendations regarding the

management of post-intervention hypotension, hypertension and HS are similar to the 2021 SVS and German-Austrian guidelines.^{3,4}

Recommendation 94 (Unchanged)	Class	Level	References
For patients with post-carotid hypotension, administration of intravenous crystalloids and volume expanders should be considered as first line treatment. If this fails to improve blood pressure, titrated intravenous vasopressors should be considered to maintain systolic blood pressure >90 mmHg.	Ila	C	517,518

Recommendation 95 (Unchanged)	Class	Level	References
For patients undergoing carotid interventions, regular blood pressure monitoring is recommended for the first 3-6 hours after carotid endarterectomy, as well as in carotid stent patients who develop haemodynamic instability during the procedure.	I	C	Expert Opinion

Recommendation 96 (Unchanged)	Class	Level	References
For carotid stenting patients who develop haemodynamic instability during the procedure, regular blood pressure monitoring is recommended for the first 24 hours after carotid revascularisation.	I	C	Expert Opinion

Recommendation 97 (Unchanged)	Class	Level	References
In centres performing carotid interventions, it is recommended that they have written criteria for treating post- procedural hypertension.	I	C	309

7.1.4 Neck haematoma after carotid endarterectomy

Most neck haematomas occur in the first six hours post-operatively, usually following untreated hypertension.⁵²⁷ In a meta-analysis of six RCTs ($n = 2\,988$), 2.2% (95% CI 1.2 - 3.9) developed a

haematoma requiring re-exploration.⁴⁸ In GALA, the incidence of haematoma needing re-operation was 2.6% under GA vs. 2.3% under LRA ($p = ns$).⁴³⁶ In an SVS-VQI registry ($n = 72\,787$), eCEA was an independent risk factor for re-exploration for neck haematoma (OR 1.4; 95% CI 1.1 - 1.7, $p = .002$).¹⁵⁴ In another SVS-VQI audit ($n = 28\,683$), re-exploration for neck haematoma was associated with significantly higher in hospital risks vs. patients not re-explored (stroke: 3.7% vs. 0.8%, $p < .001$); (MI: 6.2% vs. 0.8%, $p < .001$); (death: 2.5% vs. 0.2%, $p < .001$); (stroke/death: 5.0% vs. 0.9%, $p < .001$).¹³⁷ The effect of combination APRx on neck haematoma after CEA is discussed in **section 4.2.2.4**, while the role of protamine in reducing re-exploration for neck haematoma is discussed in **section 5.1.8**. Recommendations regarding wound drains are in **section 5.1.15**. ESVS recommendations regarding the management of neck haematoma are similar to the 2021 SVS and German-Austrian guidelines.⁴

Recommendation 98 (Unchanged)	Class	Level	References
For a patient who develops a post-operative neck haematoma associated with stridor or tracheal deviation, immediate re-exploration is recommended.	I	C	Expert Opinion

7.1.5 Cranial nerve injury (CNI)

CNI refers to partial or total loss of function of one or more of the 12 cranial nerves. In a meta-analysis of 7 535 patients in 13 RCTs, CNI after CAS was 0.5% (95% CI 0.3 - 0.9) vs. 5.4% (95% CI 4.7 - 6.2) after CEA (OR 0.07; 95% CI 0.04 - 0.1).⁴⁸ In ICSS, CNI occurred in 5.5% of patients, but only 1.3% had symptoms at 30 days and only one patient (0.12%) had a disabling CNI six months after CEA.⁵³⁴ In CREST, CNI was observed in 4.6% after CEA. Overall, one third resolved in < 30 days, with 81% resolved in less than one year. CNI impacted on swallowing at 2 - 4 weeks, but not thereafter.⁵³⁵ In a meta-analysis of four RCTs and 22 observational studies ($n = 16\,749$), CNIs affected the RLN (4.2%), hypoglossal (3.8%), mandibular branch of facial nerve (1.6%), glossopharyngeal (0.2%) and the spinal accessory (0.2%), with CNI prevalence declining over

the last 30 years.⁵³⁶ CNI predictors include urgent procedures, re-exploration for bleeding or neurological deficit.⁵³⁶ GA (OR 1.68; 95% CI 1.19 - 2.39),¹³⁰ previous neck radiation⁵⁶ and redo CEA (OR 13.61; 95% CI 5.43 - 34.16).¹⁰²

7.1.6 New ischaemic brain lesions (NIBLs)

In ICSS, a subgroup ($n = 161$) underwent DWI-MRI pre-operatively, with a second MRI scan 1 - 3 days post-operatively and a third at 27 - 33 days to evaluate the incidence of NIBLs.⁵³⁷ Sixty-two of 124 CAS patients (50%) and 18/107 CEA patients (17%) had ≥ 1 NIBL at the first post-operative scan (OR 5.21; 95% CI 2.78 - 9.79, $p < .0001$). At 1 month, there were persisting FLAIR-MRI changes in 28/86 CAS patients (33%) vs. 6/75 (8%) after CEA (OR 5.93; 95% CI 2.25 - 15.62, $p = .0003$).⁵³⁷ In a meta-analysis (two RCTs, 18 observational studies), NIBLs were commoner after CAS vs. CEA (40% vs. 12%; OR 5.17, 95% CI 3.31 - 8.06, $p < .00001$).⁵³⁸ In a meta-analysis of two RCTs and 44 observational studies ($n = 5\,018$), predictors for NIBLs after CEA included prior TIA/stroke, impaired CVR and raised inflammatory markers. Predictors for NIBLs after CAS included increasing age, plaque vulnerability and complex carotid and aortic arch anatomy.⁹² In a third meta-analysis (five RCTs, three observational studies ($n = 357$), proximal protection vs. filter CPDs was associated with significantly fewer NIBLs.⁹⁸

The clinical relevance of NIBLs is unclear. In carotid RCTs, there was no evidence of any association with cognitive impairment,⁴⁸ possibly because cohorts were too small. The NeuroVISION study, which reported the incidence and significance of NIBLs after non-cardiac surgery in 1 114 patients (but not including CEA patients), observed that 7% developed NIBLs, of whom 42% developed cognitive impairment at one year vs. 29% in patients with no NIBLs (HR 1.98; 95% CI 1.22 - 3.2).¹⁶⁶ In ICSS, five year recurrent stroke/TIA was 22.8% in patients with NIBLs vs. 8.8% in patients without NIBLs (HR 2.85; 95% CI 1.05 - 7.72, $p = .04$).¹⁶⁷ NeuroVISION also reported increased rates of stroke/TIA at one year in patients with NIBLs (HR 4.13; 95% CI

1.14 - 14.99).¹⁶⁶ ICSS concluded that NIBLs may be a marker of recurrent cerebrovascular events and that patients may benefit from more aggressive and prolonged combination APRx,¹⁶⁷ although this has not been tested in RCTs. In future, NIBLs might become a surrogate endpoint in carotid intervention trials as they have a plausible biological relationship with stroke.⁹² A meta-analysis of 9 RCTs and 76 observational studies ($n = 6\,970$) concluded that for an underlying 3% ARR in procedural stroke among revascularisation techniques, a 90% sample size reduction could be achieved if NIBLs were used, instead of 30 day death/stroke.¹⁰⁴ No guidelines have made any recommendations about the prevention or management of NIBLs.

7.2 Late complications

7.2.1 Prosthetic patch and stent infection

Patch infection complicates 1% of CEAs.^{74,106,539-541} About half present within three months of CEA (abscess/neck mass), with 55% presenting after > 6 months (usually with a draining sinus).⁵⁴² Patch rupture or anastomotic dehiscence with pseudoaneurysm formation is relatively rare (11%), and mostly occurs in the first three months.^{74,106,540-542} *Staphylococci* and *Streptococci* are the infecting organism in 90% of cases, with *S. aureus* predominating in early infections and *S. epidermidis* in later infections.^{74,106,539-542} Antibiotic therapy should be determined by an MDT approach, based on likely micro-organisms in the absence of cultures. DUS (first line) may reveal patch corrugation (can precede overt infection by 11 months⁵⁴³), deep collections or pseudo-aneurysm formation. DUS should be followed by CTA/MRI in patients being considered for re-exploration.

Conservative therapy is not advised in fit patients, due to the high risk of secondary haemorrhage or tracheal compression following anastomotic dehiscence or wall necrosis.⁵⁴⁴ It is helpful to review the original operation note to establish whether the patient developed

ipsilateral neurological symptoms, coma, or seizures during carotid clamping (if CEA was performed under LRA) or had EEG/SSEP abnormalities or MCA velocities < 15 cm/sec on TCD during clamping under GA. If the answer is 'YES' to any of these, the patient is highly likely to suffer a stroke should ligation or endovascular coil embolisation of the carotid artery become necessary.⁵⁴² Patch excision with autologous reconstruction (vein patch, bypass) remains the gold standard.^{74,106,539,542,544} Reconstruction with prosthetic material should be avoided because of high reinfection rates.⁵⁴² Limited case reports ($n = 18$), but with good early and midterm results (10 - 60 months), suggest that selected patients may be treated with covered stents, especially in an emergency. Stent insertion can be combined with EndoVAC or wound drainage.^{74,541} The EndoVAC technique is a novel, three step strategy, involving relining the infected reconstruction with a stent graft, followed by debridement, vacuum assisted therapy and long term antibiotic therapy to allow granulation and secondary healing. Where radical surgery or conservative management is not considered safe, EndoVAC may be an option.⁵⁴⁵ Carotid ligation should only be considered as a last resort, unless the artery is already thrombosed, or the patient tolerated carotid clamping at the original operation (see above). Peri-operative risks are increased (vs. primary CEA) and this needs to be discussed with the patient (mortality = 3.6%, stroke = 6.4%, CNI = 13%). The long term re-infection rate is 3.5% following autologous reconstruction.^{74,106,539-542}

Only 9 carotid stent graft infections have been reported, culturing *S. aureus*, *Streptococcus* and *Candida*.^{74,546} Clinical presentation included abscess/neck mass, bleeding, and septic embolisation. Treatment involves excision of infected material and autologous reconstruction. In four cases, stent grafts were removed without reconstruction (known carotid thrombosis). In another, stent excision was followed by EC-IC bypass.⁵⁴⁶ There were three peri-operative deaths, two strokes, one major bleeding event and one late reinfection.⁷⁴ ESVS

recommendations regarding patch infection are similar to SVS and German-Austrian guidelines^{3,4}.

Recommendation 99 (Unchanged)	Class	Level	References
For patients with prosthetic patch infection or carotid stent infection excision and autologous venous reconstruction is recommended.	I	C	74,542

Recommendation 100 (Unchanged)	Class	Level	References
For patients with carotid patch or stent infection, excision and prosthetic reconstruction is not recommended.	III	C	74,542

Recommendation 101 (New)	Class	Level	References ToE
In selected high risk of surgery or emergency patients with suspected prosthetic patch infection, insertion of a covered stent may be considered, as part of the three stage EndoVAC technique	IIb	C	74,541,545

7.2.2 Re-stenosis after carotid interventions

7.2.2.1 Pathophysiology

‘Recurrent’ lesions within six weeks represent residual atherosclerotic disease. In a meta-analysis of 13 observational studies ($n = 4\,163$ CEA and CAS patients), factors associated with re-stenosis after CEA included DM, dyslipidaemia, chronic kidney disease, SCS, stenosis > 70% and primary arteriotomy closure. Female sex and smoking were associated with re-stenosis after CEA, but not after CAS.¹⁰³ In a multivariable analysis of data from ICSS, older age, female sex, current or past smoking, non-insulin dependent DM, history of angina, a greater severity of stenosis in the contralateral carotid artery at randomisation, raised SBP and DBP at

randomisation, and higher total serum cholesterol at randomisation increased the risk of re-stenosis independently of each other and for both CEA and CAS patients.³⁹

7.2.2.2 DUS criteria for diagnosing re-stenosis

DUS criteria for diagnosing re-stenosis may be different to diagnosing primary atherosclerotic stenoses. After CEA, it has been proposed that peak systolic velocity (PSV) thresholds for diagnosing > 50% re-stenosis should be 213 cm/sec and 274 cm/sec for > 70% re-stenosis.⁵⁴⁷ DUS velocities after CAS are more difficult to interpret as the stent causes increased in stent velocities, even when fully deployed.⁵⁴⁸ Higher PSV thresholds have been proposed including > 220cm/sec (ICA/CCA ratio ≥ 2.5) for diagnosing > 50% re-stenosis and ≥ 300 cm/sec (end diastolic velocity ≥ 90 cm/sec; ICA/CCA ratio ≥ 3.8) for diagnosing > 70% re-stenosis.^{549,550} However, ICSS (which compared DUS derived PSV with CTA in re-stenosis patients after CAS) found no evidence that PSV thresholds needed to be increased when diagnosing > 50%.⁵⁵¹

7.2.2.3 DUS surveillance after carotid interventions

No evidence supports routine surveillance in all CEA/CAS patients. It is, therefore, reasonable to assume that subgroups with increased risks of re-stenosis, (DM, chronic kidney disease, females, smokers) might benefit from surveillance out to two years. Two high risk subgroups do warrant DUS surveillance, because an asymptomatic re-stenosis > 70% would be an indication for re-do CEA or CAS. The first includes patients developing neurological symptoms during carotid clamping under LRA, or during balloon inflation or proximal flow reversal during CAS. The second are patients with significant EEG/SSEP changes during carotid clamping, or MCAV < 15cm/sec on TCD monitoring during carotid clamping under GA. A threshold of 15 cm/sec has been shown to correlate with loss of cerebral electrical activity on EEG.⁵⁵² In both subgroups, progression to occlusion could cause a major haemodynamic stroke.

7.2.2.4 DUS surveillance of the contralateral carotid artery

Surveillance allows monitoring of disease progression in the contralateral ICA, with progression depending on disease severity at the time of CEA. With DUS surveillance of the contralateral asymptomatic ICA in 599 patients after CEA, there was progression to severe stenosis in 48% with a moderate ICA stenosis at baseline. Only 1% with a mild stenosis progressed to severe stenosis. The rate of neurological events ipsilateral to the contralateral ICA was 3.2% (19/599) with most affecting patients with progression from moderate to severe stenoses.⁵⁵³ The cost effectiveness of contralateral surveillance has, however, been questioned. In a series of 151 patients undergoing serial imaging of the non-operated ICA, cumulative freedom from stroke in the non-operated hemisphere was 99%, 96% and 86% at one, five and 10 years respectively (mean stroke incidence 1% per year). No late stroke was associated with a > 70% contralateral ACS⁵⁵⁴, indicating that none could have been prevented by surveillance.⁵⁵⁴ It would, however, be reasonable to offer DUS surveillance to patients with > 50% contralateral ACS, as those progressing to a 60 - 99% stenosis with ≥ 1 clinical or imaging feature that make them higher risk of stroke on BMT, would then be considered for a carotid intervention (**section 3.3.5**).

7.2.2.5 Incidence of re-stenosis

In a Cochrane review (9 RCTs; $n = 5\,477$), CAS had significantly higher re-stenosis rates > 50% than CEA (HR 2.0; 95% CI 1.12 - 3.6, $p = .02$).⁷⁹ **Table 34** details rates of re-stenosis > 70% in various meta-analyses. In ICSS, the cumulative incidence of $\geq 50\%$ re-stenosis at one year was 18.9% (patch closure), 26.1% (primary closure) and 17.7% after eversion CEA⁴³. At five years, the cumulative incidence of re-stenosis $\geq 50\%$ was 25.9%, 37.2% and 30% respectively. Primary arteriotomy closure incurred a significantly higher risk of re-stenosis $\geq 50\%$ than patch angioplasty (HR 1.45; 95% CI 1.06 - 1.98, $p = .019$), while there was no significant difference in re-stenosis rates between patched and eversion CEA.⁴³

Table 34. Meta-analyses of rates of re-stenosis > 70% after CEA and CAS

Author	Procedure	No RCTs	No non-RCTs	<i>n</i>	Mean FU	Re-stenosis >70% or occlusion
Kumar ⁵⁵⁵	any CEA	11		4 249	47mths	5.8% (95% CI 4.1-8.2)
	patched CEA	5		1 078	32mths	4.1% (95% CI 2.0-8.4)
	CAS or CA	6		2 916	60mths	10.3% (95% CI 6.4-16.4)
	CAS	5		2 716	62mths	10.0% (95% CI 6.0-16.3)
Xin ¹⁰⁹	CEA	15	12		6mths	2.04%
	CAS	15	12		6mths	4.12%
	CEA vs. CAS			20 479		OR 0.49 (95% CI 0.29-0.86) <i>p</i> = .013
Xin ¹⁰⁹	CEA	15	12	1 578	120mths	8.4%
	CAS	15	12	1 610	120mths	10.2%
	CEA vs. CAS					OR 0.92 (95% CI 0.42-2.04)
Li ⁷⁵	CEA	8		3 136	48mths	8.0%
	CAS	8		3 869	48mths	11.3%
	CAS vs. CEA					OR 1.48 (95% CI 0.93-2.35) <i>p</i> =0.10
Jung ⁶⁵	CEA	8		2,798	>10yrs	7.1%
	CAS	8		2,757	>10yrs	9.9%
	CEA vs. CAS					OR (0.68 (95% CI 0.48-0.97)

RCTs = randomised controlled trials; FU = follow up; CEA = carotid endarterectomy; CAS = carotid artery stenting; 95% CI = 95% confidence

intervals; mths = months; yrs = years.

7.2.2.6 Asymptomatic re-stenosis and recurrent ipsilateral symptoms

Table 35 details stroke rates ipsilateral to an asymptomatic > 70% re-stenosis from a meta-analysis of DUS surveillance involving 7 RCTs (2 839 CEA patients) and four RCTs (1 964 CAS patients). The Principal Investigator of each RCT provided additional data about re-stenosis severity on the surveillance scan *preceding* stroke onset.⁵⁵⁵ The five year ipsilateral stroke was 0.8% in CAS patients with re-stenosis > 70% vs. 2% without re-stenosis > 70% (OR 0.87; 95% CI

0.24 - 3.21, $p = .8339$).⁵⁵⁵ By contrast, > 70% asymptomatic re-stenosis after CEA was associated with a significantly higher risk of ipsilateral stroke (5.2%) at three years vs. 1.2% without re-stenosis > 70% (OR 4.77; 95% CI 2.29 - 9.92).⁵⁵⁵

Table 35: meta-analysis of late ipsilateral stroke in CEA and CAS patients with and without an asymptomatic re-stenosis > 70% in RCTs*

Procedure	Mean follow up (mths)	Stroke ipsilateral to >70% re-stenosis or occlusion**	Stroke ipsilateral to re-stenosis <70%	OR (95% CI)
Any CEA 7 RCTs*** ($n = 2\ 810$)	37	7/135 5.2%	40/2704 1.2%	4.77 (95%CI 2.29-9.92)
CAS 4 RCTs**** ($n = 1\ 964$)	50	1/125 0.8%	37/1839 2.0%	0.87 (0.24-3.21)

* Data derived from Kuma;⁵⁵⁵ ** re-stenoses had been asymptomatic prior to stroke onset; *** EVA-3S; SPACE-1; CREST-1; AbuRahma 2002; AbuRahma 2008; Naylor 2004; Stone 2014; **** EVA-3S; SPACE-1; CREST-1; Steinbauer; Mths = months; CEA = carotid endarterectomy; CAS = carotid artery stenting; RCTs = randomised controlled trials; OR (95% CI) = odds ratio (95% confidence intervals).

7.2.2.7 Management of re-stenosis

Symptomatic re-stenosis

No RCTs have been performed. It is, however, customary to adopt similar management to SCS patients with atherosclerotic stenoses (**section 4.3**). If a patient reports carotid territory symptoms with an ipsilateral 50 - 99% re-stenosis, they should be considered for re-do CEA or CAS within 14 days of symptom onset. Recently symptomatic patients with < 50% ipsilateral re-stenosis should be treated medically unless they develop recurrent symptoms on BMT.

Asymptomatic re-stenosis

The management of asymptomatic re-stenosis is controversial, with no RCTs to guide practice. Despite being considered benign,²⁵⁶ a meta-analysis of 13 observational studies ($n = 1\,132$) found that two thirds undergoing re-intervention were asymptomatic.⁵⁵⁶ A meta-analysis (**table 35**) suggested that patients with asymptomatic re-stenosis $> 70\%$ after CAS would gain little benefit from re-intervening, as stroke risks were very low (0.8% over four years) and 97% of late ipsilateral strokes involved patients with $< 70\%$ re-stenosis.⁵⁵⁵ Asymptomatic re-stenosis $> 70\%$ after CEA was associated with a 5.2% risk of ipsilateral stroke over three years. Operating on 100 patients might prevent five ipsilateral strokes,⁵⁵⁵ but at a cost of 2 - 3 peri-operative strokes,⁵⁵⁶ and 85% of late ipsilateral strokes would still occur in patients with re-stenosis $< 70\%$.

Re-do endarterectomy or stenting?

Once a decision has been made to re-intervene, options include surgery (re-do CEA, bypass) or CAS, neither tested in RCTs. In a meta-analysis (13 observational studies; 4 163 patients), 30 day stroke was 2.6% after redo CEA vs. 2% after CAS ($p = ns$). Permanent CNI was 3.3% after redo CEA vs. 0% after CAS.¹⁰² In an SVS-VQI database on treating in stent re-stenosis after CAS (117 CEA; 511 redo CAS); 30 day stroke after CEA was 1.5% vs. 1.4% after redo CAS ($p = .91$), while death/stroke was 4.5% after CEA vs. 1.9% after redo CAS ($p = .09$).¹¹⁶

Recommendation 102 (Regraded)	Class	Level	References
For patients experiencing a late ipsilateral stroke or transient ischaemic attack in the presence of an ipsilateral 50-99% re-stenosis, re-do carotid endarterectomy or carotid artery stenting is recommended.	I	B	357

Recommendation 103 (Regraded)	Class	Level	References
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For patients experiencing a late ipsilateral stroke or transient ischaemic attack in the presence of an ipsilateral <50% re-stenosis, medical therapy is recommended	I	B	357
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Recommendation 104 (Unchanged)	Class	Level	References
For carotid endarterectomy patients with an asymptomatic 70-99% re-stenosis, re-intervention may be considered following multidisciplinary team review.	IIb	A	555

Recommendation 105 (Unchanged)	Class	Level	References
For carotid stent patients who develop an asymptomatic re-stenosis >70%, medical management is recommended.	I	A	555

Recommendation 106 (Unchanged)	Class	Level	References
For patients who developed focal neurological symptoms or seizures during carotid clamping when carotid endarterectomy is performed under local anaesthesia, or during balloon inflation (or proximal flow reversal) during carotid stenting, serial post-operative surveillance and re-intervention for asymptomatic restenoses >70% is recommended.	I	C	Expert Opinion

Recommendation 107 (Unchanged)	Class	Level	References
For carotid endarterectomy patients who develop significant electrophysiological changes during carotid clamping, or whose mean middle cerebral artery velocities fell below 15cm/sec on transcranial Doppler monitoring during carotid clamping under general anaesthesia, serial post-operative surveillance and re-intervention for asymptomatic re-stenoses >70% is recommended.	I	C	Expert Opinion

Recommendation 108 (Unchanged)	Class	Level	References
For patients with re-stenosis in whom a decision has been made to undertake revascularisation, it is recommended that the choice of re-do endarterectomy or stenting be based on multidisciplinary team review, local surgeon and interventionist preference and patient choice.	I	C	Expert Opinion

The SVS and German-Austrian guidelines, regarding post-operative DUS surveillance, differ from the ESVS. German-Austrian guidelines recommend DUS before discharge, again at six months and then annually (unless a re-stenosis develops, when it remains every six months).³ The SVS recommends DUS at three months and then annually for two years, then biennially unless a re-stenosis develops.⁴ The management of re-stenosis also differs slightly. The SVS and German-Austrian guidelines advise re-intervening in patients with a symptomatic 50 - 99% re-stenosis^{3,4} (same as ESVS). For asymptomatic 70 - 99% re-stenoses, German-Austrian guidelines advise that re-intervention may be considered in patients having ESVS criteria that make them high risk of stroke if a re-stenosis progressed to occlusion.³ The SVS advises that early asymptomatic re-stenoses after CEA should be treated conservatively, unless they become symptomatic, progressive or pre-occlusive (80 - 99%). After CAS, the SVS recommends that early asymptomatic 70 - 99% restenoses be treated medically, unless they are progressive or symptomatic. The SVS also advised that CEA and CAS patients with late re=stenoses should be treated as if they had primary atherosclerosis.⁴

Section 8 Management of concurrent coronary & carotid disease

8.1 Stroke after cardiac surgery

The incidence of stroke after CABG is 1 - 2%⁵⁵⁷ and differentiation between intra- and post-operative stroke is helpful, as the aetiologies differ. Most intra-operative strokes (70 - 80%) follow thromboembolism, usually after aortic manipulation/cannulation. A minority (20 - 30%) follow hypoperfusion secondary to hypotension. Post-operative stroke within seven days is usually due to dysrhythmias, while those between 7 - 30 days are usually due to generalised atherosclerosis. Peri-operative stroke also impacts on survival. In a meta-analysis of 174 000 cardiac operations, patients with intra-operative stroke had a 30 day mortality of 29%, vs. 18% with post-operative stroke, vs. 2.4% in patients with no stroke ($p < .001$). At eight years, mortality was 12% in patients with intra-operative stroke who survived 30 days vs. 9% after post-operative stroke vs. 3% with no stroke.⁵⁵

8.2 Is carotid disease an important cause of stroke during cardiac surgery?

The prevalence of > 50% carotid stenosis in CABG patients is 9%. The prevalence of stenosis > 80% is 7%.⁵⁵⁷ A meta-analysis of 106 observational studies reported that CABG patients with > 50% stenosis had a 7% risk of peri-operative stroke, increasing to 9% with > 80% stenosis.⁵⁵⁸ While these risks appear high (and supportive of a role for synchronous/staged carotid interventions), the data need to be interpreted carefully, as stroke risks vary with unilateral vs. bilateral disease, symptomatic vs. asymptomatic stenoses and stenoses vs. occlusion.

CABG patients with prior TIA/stroke or carotid occlusion have the highest rates of post-operative stroke. D'Agostini reported post-CABG stroke in 18% of patients with an unoperated symptomatic unilateral 70 - 99% stenosis, increasing to 26% with bilateral 70 - 99% stenoses (or contralateral occlusion).⁵⁵⁹ CABG patients with carotid occlusion had an 11% risk of post-CABG stroke.⁵⁵⁷ In a systematic review (106 observational cohorts) which excluded patients with occlusion (not candidates for CEA) and SCS patients, the risk of peri-operative stroke was $\leq 2\%$ in patients undergoing isolated CABG with a unilateral (non-operated) 50 - 99% ACS, 70 - 99%

ACS or 80 - 99% ACS.⁵⁵⁸ In the same systematic review, 6.5% with bilateral 50 - 99% ACS had a post-CABG stroke, while 9.1% died or had a stroke.⁵⁵⁸ In a pooled series of 23 557 patients undergoing isolated CABG, 95% of 476 post-CABG strokes could not be attributed to carotid disease.⁵⁶⁰⁻⁵⁶² A carotid bruit is a significant predictor of severe aortic arch disease,⁵⁶³ while > 70% stenosis is also an independent predictor of severe aortic arch disease.⁵⁶⁴ In a 2019 systematic review of 36 observational studies ($n = 174\,969$), meta-regression analyses revealed that prior stroke was the most important predictor of peri-operative stroke ($p < .0001$), while carotid stenoses were not significantly predictive ($p = .1271$).⁵⁵ The evidence suggests no causal relationship between unilateral ACS and post-CABG stroke in most cases, ie. other aetiologies play a more important role, particularly aortic arch athero-embolism, for which ACS is a marker.^{563,564} As CABG patients increase in age, so too does the incidence of severe ACS, severe aortic arch disease, and post-CABG stroke (**table 36**).

Table 36: Prevalence of post-CABG stroke and its association with age and prevalence of carotid and aortic arch disease.

Age	Post-CABG stroke ⁵⁵⁷	Carotid stenosis >70% on screening* ²⁰⁶	Severe aortic arch disease ⁵⁶⁵
50-59	1-2%	0.2% M : 0.1% F	9%
60-69	2-3%	0.8% M : 0.2% F	18%
70-79	4-7%	2.1% M : 1.0% F	22%
≥80	8-9%	3.1% M : 0.9% F	33%

*M = male; F = female; CABG = coronary artery bypass graft, * prevalence of carotid stenosis based on population screening (section 2.2.2.4)*

rather than screening in CABG patients

8.3 Screening cardiac surgery patients for ACS

Given the lack of a causal association between ACS and post-CABG stroke, routine screening for ACS before CABG cannot be supported. However, selective screening in CABG patients aged > 70, or with a history of TIA or stroke, or who have a carotid bruit or left mainstem disease,⁵⁶⁶ allows the patient to be better informed about increased peri-operative mortality in CABG patients with concurrent carotid disease.

8.4 Are carotid interventions indicated in cardiac surgery patients?

In 22 355 patients in the Society of Thoracic Surgeons Adult Cardiac Surgery Database (where two thirds undergoing staged or synchronous carotid procedures were neurologically asymptomatic and 73% had unilateral ACS), there was no difference in in hospital stroke in patients undergoing CABG + CEA (OR 0.93; 95% CI 0.72 - 1.21, $p = .6$) or 30 day mortality (OR 1.28; 95% CI 0.97 - 1.69, $p = .08$), vs. patients undergoing isolated CABG.⁵⁶⁷ A similar observation was made for in hospital stroke (OR 0.8; 95% CI 0.37 - 1.69, $p = .55$) and 30 day mortality (OR 0.78; 95% CI 0.35 - 1.72, $p = .54$) in patients undergoing off bypass CABG with/without CEA.⁵⁶⁷ In a review of 5 924 cardiac surgery patients, 2 482 underwent a pre-operative carotid DUS and 7.4% had a > 70% carotid stenosis (majority unilateral and asymptomatic).⁵⁶⁸ Patients undergoing CEA prior to cardiac surgery had significantly higher peri-operative stroke (10.3%) vs. 1.4% after isolated CABG in patients with confirmed or presumed normal ICAs ($p = .008$), plus significantly higher rates of peri-operative MI (13.8% vs. 0.4%; $p < .001$). Patients undergoing isolated CABG with confirmed or presumed normal ICAs had similar rates of peri-operative stroke (1.4%) vs. 3.2% in CABG patients with known severe ICA disease who did not undergo CEA ($p > .05$).⁵⁶⁸

Two RCTs have evaluated synchronous or staged CEA in CABG patients with unilateral ACS. Illuminati randomised 185 patients with unilateral 70 - 99% ACS to CEA prior to or synchronous

with CABG vs. isolated CABG followed by deferred CEA. 30 day mortality was 1% in each group, while 30 day death/stroke was 4% (deferred CEA) vs. 1% (staged/synchronous CEA) ($p = ns$). 90 day death/stroke was 9% for deferred CEA vs. 1% for staged/synchronous CEA ($p = .02$). The authors concluded that prophylactic CEA was potentially beneficial in CABG patients with unilateral 70 - 99% ACS in order to reduce 90 day ipsilateral stroke, rather than peri-operative stroke.⁵⁶⁹ CABACS (involving 17 centres in Germany and the Czech Republic) randomised 129 CABG patients with unilateral 80 - 99% ACS to synchronous CEA + CABG vs. CABG alone. Patients undergoing synchronous CEA + CABG had a 30 day stroke/death rate of 18.5% vs. 9.7% after isolated CABG (ARI 8.8%; 95% CI 3.2 - 20.8, $p = .12$).³⁶ For secondary endpoints at 30 days and one year, there was no significant difference, although patients undergoing isolated CABG tended to have better outcomes.³⁶ Unfortunately, CABACS was terminated after funding was withdrawn.

8.5 What surgical and endovascular options are available?

Options include (1) staged CEA then CABG; (2) staged CABG then CEA; (3) synchronous CEA plus CABG; (4) staged CAS then CABG and (5) same day CAS + CABG. **Table 37** summarises data from meta-analyses of non-randomised studies. The majority (> 80%) were neurologically asymptomatic with unilateral ACS. **Table 38** presents similar data from administrative dataset registries. 30 day death/stroke ranged from 6 - 10% in predominantly ACS patients, with the highest rates of death/stroke being observed in patients with a history of stroke/TIA undergoing staged or synchronous CEA + CABG (14%) or CAS then CABG (44%).⁵⁷⁰ Performing CABG off pump was associated with lower rates of post-CABG stroke, possibly due to avoiding cannulation of a diseased aortic arch.^{567,571}

Table 37: Meta-analyses of 30 day outcomes from non-randomised studies regarding revascularisation strategies in patients with combined carotid and cardiac disease

Procedure	n	Death	Stroke	MI	Death/ stroke	Death/ stroke/MI
Staged CEA then CABG (all)						
Brener 1996 ⁵⁷²	407	9.4%	5.3%	11.5%		
Borger 1999 ⁵⁷³	920	2.9%	3.2%		5.7%	
Naylor 2003 ⁵⁷⁴	917	3.9%	2.5%	6.5%	6.1%	10.2%
Sharma 2015 ⁵⁷⁵	7 552	3.4%	1.9%		6.2%	
Staged CABG then CEA (all)						
Brener 1996 ⁵⁷²	213	3.6%	10.0%	2.7%		
Naylor 2003 ⁵⁷⁴	302	2.0%	5.8%	0.9%	7.3%	
Synchronous CEA + CABG (all)						
Brener 1996 ⁵⁷²	2 308	5.6%	6.2%	4.7%		
Borger 1999 ⁵⁷³	844	4.7%	6.0%		9.5%	
Naylor 2003 ⁵⁷⁴	7 753	4.6%	4.6%	3.6%	8.7%	11.5%
Sharma 2015 ⁵⁷⁵	17 469	4.0%	4.3%	3.6%	7.9%	
Giannopoulos 2019 ⁵⁸	16 712	4.0%	3.0%	5.0%		
Synchronous CEA + CABG (symptomatic)						
Naylor 2003 ⁵⁷⁶	514	5.8%	6.8%	1.9%	7.6%	8.1%
Synchronous CEA + CABG (asymptomatic)						
Naylor 2003 ⁵⁷⁶	925	3.6%	3.7%	2.2%	4.5%	4.5%
Synchronous CEA + CABG (off bypass)						
Fareed 2009 ⁵⁷¹	324	1.5%			2.2%	3.6%
Synchronous CEA + CABG						

(pre-bypass)						
Naylor 2003 ⁵⁷⁶	5 386	4.5%	4.5%	3.6%	8.2%	11.5%
Synchronous CEA + CABG (on bypass)						
Naylor 2003 ⁵⁷⁶	844	4.7%	2.1%	2.9%	8.1%	9.5%
Same day CAS + CABG (all)						
Paraskevas 2016 ⁵⁷⁷	531	4.5%	3.4%	1.8%	5.9%	6.5%
Staged CAS-CABG (all)						
Guzman 2008 ⁵⁷⁸	277	6.8%	7.6%		12.3%	
Naylor 2009 ⁵⁷⁹	760	4.2%	5.5%	1.8%	9.1%	9.4%
Paraskevas 2016 ⁵⁷⁷	2 196	4.8%	5.4%	4.2%	8.5%	11.0%
Giannopoulos 2019 ⁵⁸	985	2.0%	3.0%	5.0%		

* *synch* = synchronous; *MI*: myocardial infarction; *CABG*: Coronary artery bypass graft; *CAS*: carotid stenting; *CEA*: carotid endarterectomy; *off*

bypass means CABG done without cardiopulmonary bypass; *pre-bypass*, *on bypass* indicates when CEA was performed relative to

cardiopulmonary bypass

Table 38: 30 day procedural risks after CEA + CABG stratified for treatment strategy in administrative dataset registries

Procedure	Registry	<i>n</i>	Death	Stroke	Death/ stroke
Staged CEA + CABG					
All cases					
Gopaldas 2011 ⁵⁸⁰	NIS 1998-2007	6 153	4.2%	3.5%	7.1%
Feldman 2017 ¹²⁵	NIS 2004-2012	6 297	3.8%	1.9%	5.4%
Off bypass					
Gopaldas 2011 ⁵⁸⁰	NIS 1998-2007	2 004	4.0%		7.0%
On bypass					
Gopaldas 2011 ⁵⁸⁰	NIS 1998-2007	4 149	4.3%		7.7%

Staged or synchronous					
CEA + CABG					
All cases					
Dubinsky 2007 ⁵⁸¹	NIS 1993-2002	7 073	5.6%	4.9%	9.7%
Timaran 2008 ⁵⁷⁰	NIS 2000-2004	25 249	5.4%	3.9%	8.6%
Symptomatic*					
Timaran 2008 ⁵⁷⁰	NIS 2000-2004	948		14.2%	
Synchronous CEA + CABG					
All cases					
Gopaldas 2011 ⁵⁸⁰	NIS 1998-2007	16 639	4.5%	3.9%	7.7%
Feldman 2017 ¹²⁵	NIS 2004-2012	15 402	4.4%	2.8%	6.8%
Klarin 2020 ⁵⁶⁷	STS ACSD	3 972	6.0%	6.2%	
Off bypass					
Gopaldas 2011 ⁵⁸⁰	NIS 1998-2007	5 280	4.2%		
Klarin 2020 ⁵⁶⁷	STS ACSD	566	2.1%	2.3%	6.5%
On bypass					
Gopaldas 2011 ⁵⁸⁰	NIS 1998-2007	11 359	4.5%		7.4%
Klarin 2020 ⁵⁶⁷	STS ACSD	3 406	3.9%	3.9%	
Staged CAS then CABG					
All cases					
Feldman 2017 ¹²⁵	NIS 2004-2012	802	1.9%	3.0%	4.2%
Symptomatic*					
Timaran 2008 ⁵⁷⁰	NIS 2000-2004	25		44%	

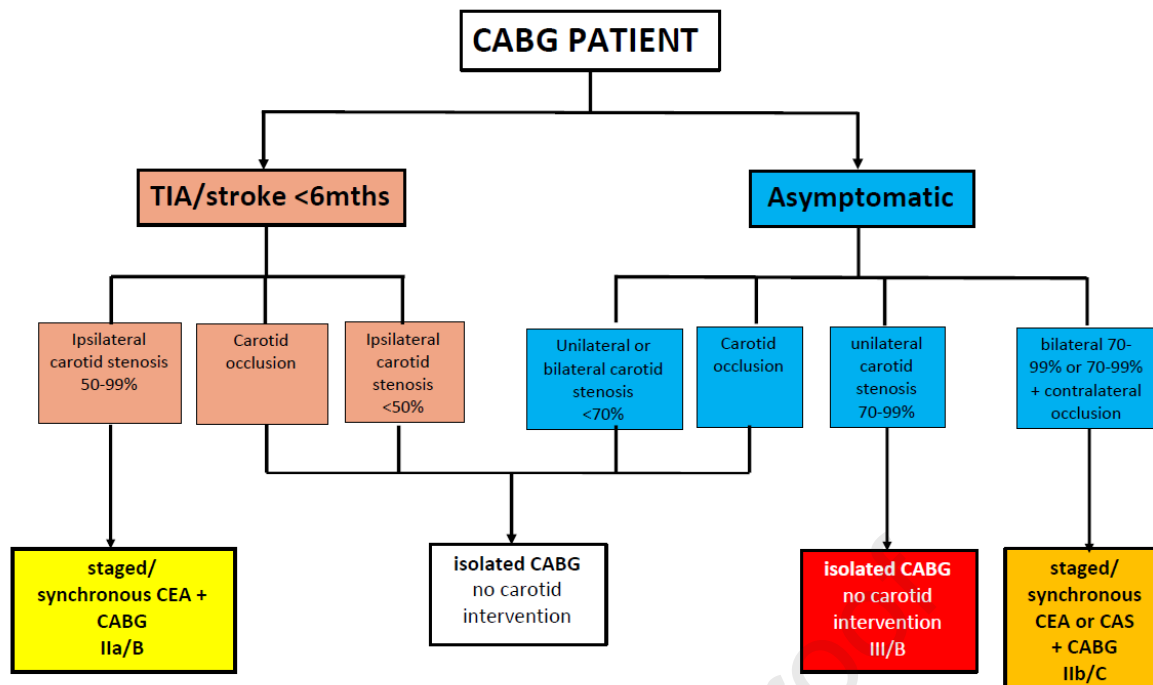
n = number of cases; CEA = carotid endarterectomy; CAS = carotid artery stenting; CABG = coronary artery bypass graft; NIS = National Inpatient Sample; STS ACSD = Society of Thoracic Surgeons Adult Cardiac Surgery Database; * = prior stroke or transient ischaemic attack

A 2017 meta-analysis of 31 observational studies included 2 727 patients undergoing staged or same day CAS-CABG, reported a 30 day death/stroke rate of 7.9%.⁵⁷⁷ The majority (80%) were neurologically asymptomatic with unilateral ACS, in whom 30 day death/stroke was 6.7%. Given

the low risk of stroke attributable to unilateral ACS (**section 8.2**), it is unlikely that CAS + CABG will benefit CABG patients with unilateral ACS any more than CEA + CABG. Staged or same day CAS + CABG in patients with a history of TIA/stroke was associated with 15% rates of 30 day death/stroke.⁵⁷⁷ In another meta-analysis of five observational studies, ($n = 16\,712$), outcomes following synchronous CEA + CABG were compared with staged CAS followed by CABG in patients with ACS and SCS (**table 37**). Rates of peri-operative stroke (3.0% vs. 3.0% and MI (5.0% vs. 5.0% were not significantly different, but patients undergoing synchronous CEA + CABG incurred significantly higher mortality (OR 1.8; 95% CI 1.05 - 3.06).⁵⁸ The need for aspirin + clopidogrel combination APRx with CAS can complicate staged CAS-CABG, as it increases MI risk during the delay between each procedure and increases bleeding risks during CABG. Evidence suggests that CAS can be performed on the same day as CABG using aspirin or heparin, with thienopyridine APRx starting 6 - 12 hours after CABG.⁵⁷⁷

The Agency for Healthcare Research and Quality Healthcare Cost and Utilisation Project evaluated outcomes in 22 501 CABG patients (95% ACS, 5% SCS); (i) 15 402 (68%) had synchronous CEA + CABG; (ii) 6 297 (28%) staged CEA then CABG, while (iii) 802 (4%) had staged CAS then CABG.¹²⁵ Peri-operative stroke rates were comparable (synchronous CEA + CABG 2.8%; staged CEA + CABG 1.9%; staged CAS + CABG 3.0% ($p_{\text{trend}} = .37$), but adjusted stroke rates were lower in both surgical groups vs. CAS + CABG: (CEA + CABG: OR 0.65; 95% CI 0.42 - 1.01, $p = .06$), (staged CEA + CABG: OR 0.50; 95% CI 0.31 - 0.8, $p = .004$).¹²⁵ In summary, the literature supports staged or synchronous carotid interventions in CABG patients with a prior history of stroke/TIA⁵⁵⁹ and in patients with bilateral 70 - 99% ACS, or 70 - 99% ACS with contralateral occlusion **Figure 8**.

Figure 8. Managing CABG patients with symptomatic and asymptomatic carotid disease.



CABG = coronary artery bypass graft; TIA = transient ischaemic attack; CEA = carotid endarterectomy; CAS = carotid artery stenting.

8.6 Managing patients with unstable coronary artery disease

The Carotid Artery Revascularisation and Endarterectomy (CARE) registry involved 255 urgent CABG patients undergoing CAS and 196 undergoing CEA. 30 day death/stroke/MI was 15% after CAS vs. 22% after CEA. CARE did not differentiate between staged or synchronous CEA + CABG, regional practice variations existed and 60% of interventions involved ACS patients.⁵⁸²

Recommendation 109 (Unchanged)	Class	Level	References
For patients undergoing open heart surgery, routine screening for carotid disease is not recommended.	III	C	Expert Opinion

Recommendation 110 (Unchanged)	Class	Level	References
For patients undergoing coronary artery bypass surgery, duplex ultrasound screening for carotid disease should be considered in patients aged >70 years, and those with a history of transient ischaemic attack or stroke or who have a carotid bruit or left mainstem disease, so that the patient can be better	IIa	C	557,566

informed of the increased risks associated with coronary artery bypass if they have concurrent carotid disease.

Recommendation 111 (Unchanged)	Class	Level	References
For coronary artery bypass surgery patients with a history of stroke or transient ischaemic attack in the preceding six months and a 50-99% carotid stenosis, a staged or synchronous carotid intervention should be considered	Ila	B	557,559

Recommendation 112 (Unchanged)	Class	Level	References
For coronary artery bypass surgery patients with a history of stroke or transient ischaemic attack in the preceding six months and a 50-99% carotid stenosis, a staged or synchronous carotid endarterectomy should be considered instead of carotid stenting plus coronary bypass surgery.	Ila	B	570,574, 577,579

Recommendation 113 (Unchanged)	Class	Level	References
For coronary artery bypass patients with an asymptomatic unilateral 70-99% carotid stenosis, a staged or synchronous carotid intervention is not recommended for the prevention of post-operative stroke.	III	B	558,567, 568

Recommendation 114 (Unchanged)	Class	Level	References
For coronary artery bypass patients with bilateral asymptomatic 70-99% carotid stenoses, or a 70-99% stenosis with contralateral occlusion, a staged or synchronous carotid intervention may be considered.	Ilb	C	558

Recommendation 115 (Unchanged)	Class	Level	References
For asymptomatic carotid stenosis patients in whom a carotid intervention is deemed necessary if they are undergoing coronary artery bypass surgery, the choice between carotid endarterectomy or carotid stenting should be considered based on the urgency of performing surgery, choice of antiplatelet	Ila	C	58,125

therapy during coronary bypass, individual patient characteristics, symptom status and local expertise.

The German-Austrian guidelines made no recommendation regarding CABG patients with a unilateral 70 - 99% ACS, whilst the rest were identical to ESVS.³ The SVS recommendations were also identical to ESVS, the only exception being that SVS indicated that managing CABG patients with unilateral 70 - 99% ACS was controversial but did not make any further recommendation.⁴

Section 9. Carotid disease and major non-cardiac surgery

Vascular surgeons are often asked whether prophylactic CEA or CAS should be considered in ACS patients scheduled for major non-cardiac surgery, in order to prevent peri-operative stroke.

9.1 Incidence of stroke after major non-cardiac surgery

The incidence of peri-operative stroke depends upon the nature and complexity of the procedure, risk factors and timing after recent TIA/stroke (**table 39**). The incidence of stroke was < 1% in all but two cohorts, suggesting that stroke is rarely a problem after major non-cardiac surgery.

Table 39. Incidence of peri-operative stroke stratified for type of procedure

Author	Population	<i>n</i>	Stroke risk
Axelrod ⁵⁸³	major vascular surgery	5 296 aortic operations	0.5%
		7 299 lower limb bypasses	0.4%
		7 442 major amputations	0.6%

Sharifpour ⁵⁸⁴	major vascular surgery	8 077 major amputations 21 962 lower limb bypasses 7 888 open aortic 9 823 EVAR	0.7% 0.5% 0.8% 0.5%
Jorgensen ⁵⁸⁵	non-cardiac, including vascular	481 113	0.1%
Sonny ⁵⁸⁶	non-cardiac including vascular	2 110	2.6%
Kikura ⁵⁸⁷	general, orthopaedic, thoracic, non-carotid vascular	36 634	0.3%
Parvizi ⁵⁸⁸	knee arthroplasty	1 636	0.4%
Bateman ⁵⁸⁹	hemicolectomy hip replacement lung resection	131 067 201 235 39 339	0.7% 0.2% 0.6%
Huang ⁵⁹⁰	Caesarian section	303 862	0.05%
Mashour ⁵⁹¹	non-cardiac (low risk) general, orthopaedic, urology, ENT, plastics, thoracic, gynaecology	523 059	0.1%
Biteker ⁵⁹²	non-cardiac, non-vascular	1 340	2.3%

* EVAR = endovascular aortic aneurysm repair; ENT = Ear Nose and Throat.

9.2 Predicting stroke after major non-cardiac surgery.

Table 40 summarises predictors for peri-operative stroke after non-cardiac surgical procedures.

The most consistent were increasing age and a history of stroke.

Table 40. Predictors for peri-operative stroke following major non-cardiac procedures

Author	Population	Stroke predictors	OR (95% CI)
Axelrod ⁵⁸³	major vascular surgery	aortic operation vs. lower extremity	1.7 (1.0-2.8)

Sharifpour ⁵⁸⁴	major vascular surgery	each one yr increase in age cardiac history vs. none female sex vs. male history of stroke vs. no stroke acute/chronic renal failure vs. no history	1.02 (1.01-1.04) 1.4 (1.1-1.9) 1.5 (1.1-1.9) 1.7 (1.3-2.3) 2.0 (1.4-3.0)
Kikura ⁵⁸⁷	general, orthopaedic, thoracic, non-carotid vascular	age >70 yrs vs <70 yrs diabetes vs. no diabetes coronary disease vs. none CCF vs. no CCF AF vs. no AF prior stroke vs. no stroke	23.6 (9.6-58.1) 2.2 (1.4-3.3) 2.3 (1.3-4.1) 1.7 (1.1-2.7) 5.5 (2.8-10.9) 7.1 (4.6-11)
Bateman ⁵⁸⁹	hemicolectomy, hip replacement, lung resection	renal impairment vs. none AF vs. no AF prior stroke vs. no stroke valvular heart disease vs. none CCF vs. no CCF Diabetes vs. no diabetes	3.0 (2.5-3.5) 2.0 (1.7-2.3) 1.6 (1.3-2.1) 1.5 (1.3-1.9) 1.4 (1.2-1.7) 1.2 (1.0-1.4)
Mashour ⁵⁹¹	non-cardiac, non- neurosurgery, general, orthopaedics, urology, ENT, plastics, thoracic, gynaecology, minor vascular	acute renal failure vs. none history of stroke vs. none history of TIA vs. none on dialysis vs. not on dialysis hypertension vs. no COPD vs. no COPD Smoking vs. non smoking	3.6 (2.3-5.8) 2.9 (2.3-3.8) 1.9 (1.3-2.6) 2.3 (1.6-3.4) 2.0 (1.6-2.6) 1.8 (1.4-2.4) 1.5 (1.1-1.9)
Biteker ⁵⁹²	non-cardiac, non-vascular	history of stroke vs. no stroke	3.6 (1.2-4.8)
Jorgensen ⁵⁸⁵	non-cardiac	stroke <3 months vs. no stroke stroke 3-6 months vs. no stroke	67.6 (52.3-87.4) 24.0 (15.0-38.4) 10.4 (6.2-17.4)

		stroke 6-12 months vs. no stroke	
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BMI = body mass index; OR (95% CI) = odds ratio (95% confidence intervals); CCF = congestive cardiac failure; AF = atrial fibrillation; TIA = transient ischaemic attack; COPD = chronic obstructive pulmonary disease; ENT = Ear, Nose and Throat operations.

9.3 Timing of major surgery after recent stroke

In a study of 481 183 adults undergoing elective, non-cardiac surgery, 7 137 (1.5%) had a history of stroke, in whom the rate of peri-operative stroke was 11.9% if operations were performed within three months of the stroke, declining to 4.5% where 3 - 6 months had elapsed and 1.8% where 6 - 12 months had elapsed vs. 0.1% in patients with no history of stroke.⁵⁸⁵

9.4 Is there a role for prophylactic CEA or CAS?

Patients undergoing major non-cardiac surgery with 3 - 4 cardiovascular risk factors (age, CAD, renal failure, hypertension, DM, smoking, BMI > 35 kg/m², COPD, prior stroke/TIA) had a 0.7% risk of peri-operative stroke. With ≥ 5 risk factors, peri-operative stroke increased to 1.9%,^{591,592} emphasising the importance of optimising cardiovascular risk prior to major non-cardiac surgery.^{590,593} Most strokes were ischaemic and secondary to cardiac embolism. The peri-operative period also involves complex haemodynamic stresses involving hypercoagulable and systemic inflammatory responses, which increase the risks of peri-operative stroke, especially if anticoagulation or antiplatelet therapies are withdrawn.

ACS patients undergoing major non-cardiac surgery were evaluated in one RCT and one observational study. Seventy-nine patients with 70 - 99% ACS were randomised to CEA within one week of the scheduled procedure ($n = 40$) vs. deferred CEA ($n = 39$). There were no peri-operative deaths/strokes in either group.⁵⁹⁴ An observational study evaluated whether ACS

predisposed patients undergoing non-cardiac surgery to increased peri-operative stroke. Over a five year period 2 110 patients had DUS < 6 months of, or one month after, surgery (37% had ACS > 50%, 13% had > 70% ACS). Overall, 54 (3%) suffered a stroke. Neither of the ACS stenosis thresholds (> 50%; > 70%) were associated with increased rates of peri-operative stroke.⁵⁸⁶ It is, of course, possible that ACS patients with impaired CVR may be at higher risk of stroke after major non-cardiac surgery, but no association has been proven.⁵⁹⁵

The Society of Thoracic Surgeons and American College of Cardiology evaluated whether carotid disease increased stroke rates in 29 143 patients undergoing Transcatheter Aortic Valve Replacement, where 22% had a carotid stenosis > 50%. In hospital stroke was 2% in patients with no stenosis, 2.5% with moderate stenoses, 3% with severe stenosis and 2.6% with carotid occlusion. The Registry concluded there was no association between carotid disease and stroke after transcatheter aortic valve replacement.¹³⁹

Recommendation 116 (Unchanged)	Class	Level	References
For patients undergoing elective, non-cardiac surgery with a history of stroke or transient ischaemic attack within the preceding six months, carotid artery imaging is recommended.	I	B	585

Recommendation 117 (Unchanged)	Class	Level	References
For patients with a history of stroke or transient ischaemic attack in the preceding six months attributable to an ipsilateral 50-99% carotid stenosis and who are scheduled to undergo elective, non-cardiac surgery, it is recommended that carotid revascularisation be performed before the non-cardiac surgical procedure.	I	B	357,585

Recommendation 118 (Unchanged)	Class	Level	References
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For patients with a history of prior stroke and no significant carotid artery disease, it is recommended that, where possible, elective non-cardiac surgery should be delayed by 6 months. The decision to proceed with semi-urgent elective surgery will have to be individualised, based upon the underlying pathology	I	B	585
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Recommendation 119 (Unchanged)	Class	Level	References
For asymptomatic patients undergoing non-cardiac surgery procedures, routine carotid imaging is not recommended.	III	B	583,584

Recommendation 120 (Unchanged)	Class	Level	References
For patients undergoing major non-cardiac surgical procedures, it is recommended that they should undergo a comprehensive cardiovascular risk assessment to aid the consent process regarding the risk of peri-operative stroke	I	B	591,593

Recommendation 121 (Unchanged)	Class	Level	References
For patients with asymptomatic 50-99% carotid stenoses undergoing a major non-cardiac procedure, it is recommended not to stop statin therapy prior to surgery. Antithrombotic therapy withdrawal should be based on an assessment of thromboembolic and haemorrhagic risks	III	B	590,593

Recommendation 122 (Unchanged)	Class	Level	References
For patients with an asymptomatic 50-99% carotid stenosis undergoing a major non-cardiac surgical procedure, prophylactic carotid endarterectomy or carotid stenting is not recommended	III	B	586,594

The German-Austrian guidelines made no comment about managing patients with carotid stenoses scheduled to undergo major, non-cardiac procedures.³ The SVS guidelines simply

stated that patients with carotid disease undergoing non-cardiac surgery should have the same indications for intervention as the general population, without clarifying what this meant.⁴

Section 10: Disease of the common carotid and innominate arteries

10.1 Introduction

The incidence of stenosis or occlusion at the aortic arch branch vessel origins is 0.5 - 6.4%, with a higher frequency in the innominate (IA) and left subclavian arteries vs. left CCA.⁵⁹⁶ CCA occlusion occurs in 2 - 4% undergoing angiography for cerebrovascular disease.⁵⁹⁷ Patients with a symptomatic branch origin stenosis have a 2% annual risk of developing a stenosis in other arch vessels, while tandem disease of the carotid bifurcation occurs in 17%.⁵⁹⁶

10.2 Clinical presentation

Left CCA lesions cause left hemisphere and left retinal symptoms. Left subclavian lesions cause VB, or left arm symptoms, while IA lesions can affect the right carotid, VB, and right arm. Most are atherosclerotic, but arteritis and dissection are commoner in younger patients.

10.3 Indications for revascularisation

The natural history of isolated CCA and IA disease is unknown. In patients with neurological symptoms or upper limb ischaemia, indications for revascularisation are straightforward. There is no evidence supporting open or endovascular interventions in asymptomatic patients.

10.4 Endovascular vs. open surgical reconstruction

Historically, treatment of supra-aortic disease was mainly possible via open surgery, involving bypasses from the arch or subclavian artery, CCA transposition or CCA endarterectomy. CCA transposition to the subclavian artery provides direct autogenous revascularisation but may not

always be feasible. CCA endarterectomy can be performed via open or retrograde semi-closed endarterectomy. A meta-analysis of 77 observational studies ($n = 1\,969$) evaluated 30 day and midterm outcomes in patients with significant stenoses affecting the proximal CCA or IA who underwent isolated open surgery ($n = 686$) or an isolated endovascular approach ($n = 583$).⁹⁰ In the open surgery group (78% involving IA), the 30 day death/stroke was 7%, with a late ipsilateral stroke rate of 1% at a median 12 years follow up. Late re-stenosis within bypasses arising from the aortic arch was 2.6%. In the isolated endovascular group (52% IA), the majority (84%) were done percutaneously, with 30 day death/stroke rates of 1.5%. Late ipsilateral stroke was 1% at a median four years follow up with a 9% re-stenosis rate.⁹⁰ In a VSGNE audit of outcomes after a totally endovascular approach to treating tandem stenoses/occlusions of the innominate or proximal CCA and stenoses of the ipsilateral ICA in asymptomatic patients (not included in Robertson's meta-analysis), 30 day death/stroke was significantly higher compared with stenting isolated asymptomatic ICA stenoses (OR 1.85; 95% CI 1.03 - 3.33, $p = .039$).¹¹⁹

10.5 Open revascularisation: cervical vs. transthoracic

Options include bypass via a transthoracic route (median sternotomy or trapdoor incision), or an extra-thoracic (cervical) approach. Cervical reconstructions are less invasive with fewer risks. Patients with isolated subclavian or CCA lesions (with a patent ipsilateral carotid or subclavian artery) should undergo transposition or bypass via a cervical approach. Saphenous vein was previously the preferred conduit, but it is often small calibre and prone to kinking vs. prosthetic grafts which offer durable patency and low morbidity.⁵⁹⁸ At the other extreme is the patient with involvement of three arch branches, where graft outflow must arise from the aorta via a median sternotomy. Transthoracic reconstructions can be performed with acceptably low morbidity/mortality, and significantly better long term patency.^{90,599}

10.6 Tandem proximal inflow and internal carotid artery disease

Tandem disease refers to lesions affecting the IA or proximal CCA in the presence of significant disease of the ipsilateral ICA. Most now undergo a hybrid approach, where open retrograde angioplasty/stenting of the IA or proximal CCA is followed by CEA of the ipsilateral ICA. In a systematic review ($n = 700$), 30 day death/stroke was 3.3%, with a late ipsilateral stroke rate of 3.3% at a median six year follow up. Late re-stenosis was 10.5% for proximal CCA or IA and 4.1% in the ICA.⁹⁰ In symptomatic patients, data cautiously support an endovascular first strategy for isolated proximal CCA or IA lesions with a hybrid approach for tandem CCA or IA and ICA stenoses. ESVS recommendations regarding the management of patients with tandem IA or proximal CCA and bifurcation disease, are the same as 2021 SVS recommendations.⁴

Recommendation 123 (Unchanged)	Class	Level	References
For asymptomatic patients with proximal common carotid artery or innominate artery stenoses/occlusions, open or endovascular interventions are not recommended.	III	C	Expert Opinion

Recommendation 124 (Unchanged)	Class	Level	References
For symptomatic patients with proximal common carotid artery or innominate stenoses, open retrograde angioplasty and stenting should be considered.	IIa	C	90,596

Section 11. Management of asymptomatic vertebral artery disease

11.1 Optimal medical therapy

No RCTs have evaluated the effect of APRx, statin or antihypertensive therapy in patients with asymptomatic VA stenoses. Accordingly, it is reasonable to adopt the same BMT recommendations as for ACS patients (**section 3.1**).

11.2 Screening for asymptomatic VA disease

No RCTs have evaluated VA screening. Accordingly, it is reasonable to adopt the same strategy as for ACS (section 3.2).

11.3 Interventions for asymptomatic VA disease

Within a cohort of 3 717 patients with atherosclerotic disease in the SMART Registry, 7.6% had an asymptomatic VA stenosis > 50%, in whom the annual stroke risk was only 0.2%.⁶⁰⁰

Recommendation 125 (Unchanged)	Class	Level	References
For patients with asymptomatic vertebral artery atherosclerotic lesions, open or endovascular interventions are not recommended.	III	C	600

Section 12. Management of symptomatic vertebral artery disease

12.1 Aetiology of vertebrobasilar (VB) stroke

About 20% of ischaemic strokes are VB, mostly due to cardio-embolism, LAA and small vessel disease.⁶⁰¹ Atherosclerosis of VAs or basilar arteries (BA) accounts for 20 - 25% of VB strokes. Stenoses mainly occur at the VA origin but can affect distal or intracranial VAs and BAs. Intracranial stenoses are commoner with sub-Saharan or East-Asian ethnic origins. A haemodynamic aetiology was thought to be the commonest cause of VB symptoms. However, in a prospective registry, only 13/407 patients (3%) had symptoms due to haemodynamic ischaemia and this was most commonly seen in patients with bilateral intracranial VA disease.⁶⁰² Cardiac embolism (usually AF) accounted for 25% of strokes/TIAs, with 25% being due to disease of small penetrating arteries arising from the intracranial VA, BA and PCA arteries, causing lacunar stroke.⁶⁰² Thromboembolism was the main cause of symptoms with VA stenoses.

12.2 Symptoms attributable to VA disease

Bing recently symptomatic refers to VB symptoms in the preceding 6 months (**table 13, section 4.1**). In a series of VB strokes, common symptoms included dizziness (47%), unilateral limb weakness (41%), dysarthria (31%), headache (28%) and nausea/vomiting in (27%).⁶⁰³

12.3 Imaging strategies in VA disease

DSA has been replaced by CEMRA/CTA due to angiogram related stroke. CEMRA/CTA can image the entire VB system, enabling simultaneous detection of extra- and intracranial stenoses. In a systematic review and meta-analysis (11 observational studies) which measured VA stenoses as 50 - 99%, sensitivity was 100% for CTA (95% CI 15.8 - 100), 94% for CEMRA (95% CI 79.8 - 99.3) and 70% for DUS (95% CI 54.2 - 83.3). Specificities for CTA were 95% (95% CI 83.8 - 99.4), 95% for CEMRA (95% CI 91.1 - 97.3) and 98% for DUS (95% CI 95.2 - 99.1).⁶⁰⁴ The proximal VA can be visualised on DUS, but not the distal VA, so the likelihood of distal VA disease must be inferred from waveform abnormalities.⁶⁰⁵ DUS can estimate VA size and flow direction and may differentiate between hypoplasia, stenosis, occlusion and aplasia.^{605,606} It can also diagnose subclavian steal syndrome with pre-steal (transient midsystolic flow deceleration), partial steal (flow reversal during systole) and complete steal (retrograde flow throughout cardiac cycle). For detecting VB infarcts, MRI is more sensitive than CT,⁶⁰⁷ reflecting higher spatial resolution, especially with small infarcts in the brainstem. DWI-MRI is the most sensitive method for detecting acute ischaemia and may be positive for approximately two weeks after symptom onset.

Recommendation 126 (Unchanged)	Class	Level	References
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For patients with suspected vertebrobasilar ischaemia, computed tomographic angiography or contrast enhanced magnetic resonance angiography is recommended as the first line vascular imaging modality.

I

B

604,606

12.4 Optimal medical therapy

No RCTs have evaluated APRx, statin or antihypertensive therapy in symptomatic VA stenosis patients. It is reasonable to adopt the same recommendations as for SCS patients (**section 4.2**).

12.5 Role of vertebral revascularisation in positional vertigo

A diagnosis of positional VB ischaemia is often assumed in patients with dizziness or vertigo during neck movement. However, the syndrome is over diagnosed, usually without further investigation. A systematic review reported no changes in VA or PCA flow in seven series, while 13 described varying changes (reversal, occlusion, reduced flow).⁶⁰⁸ In a study involving 46 patients with a TCD window who presented with dizziness or vertigo on head movement, none had changes in extracranial VA flow during head movement, none had reversal of VA flow and there were no changes in PCA flow (directionality or flow velocities) during head turning.⁶⁰⁹ Most symptoms relating to head/neck movement have other causes, including benign paroxysmal positional vertigo, vestibular neuritis and (occasionally) exacerbation of vertigo associated with migraine.⁶¹⁰ In a single centre experience, 74% were referred to a Balance Clinic, where 94% improved following a vestibular rehabilitation programme.⁶⁰⁹

Recommendation 127 (Unchanged)	Class	Level	References
For patients with vertigo or dizziness on head turning, it is recommended that a diagnosis of vertebrobasilar ischaemia (attributed to nipping of the vertebral arteries on head movement) should not be made, unless corroborated by vascular imaging showing clear disruption of blood flow during head turning.	III	C	608-610

12.6 Interventions in recently symptomatic patients

12.6.1 non-randomised studies

The 90 day risk of recurrent VB stroke was 7% in the absence of VA disease, 16% with extracranial VA stenoses and 33% with intracranial VA or BA stenoses.⁶¹¹ In a review of 600 patients with symptomatic VA stenoses treated by angioplasty/stenting, intracranial stenting incurred higher procedural stroke risks (10.6%) vs. extracranial VA stenoses (1.3%).⁶¹²

12.6.2 Randomised studies

12.6.2.1 meta-analysis of RCTs: VA stenting vs. BMT

Table 41 details an individual patient meta-analysis of data from 354 symptomatic patients with 50 - 99% VA stenoses who were randomised within VIST, VAST and SAMMPRIS.^{29,613,614}

Table 41: main findings of meta-analysis of three RCTs comparing VA stenting with BMT alone*

	30 day		HR (95% CI)	Cumulative		HR (95% CI)
	death or stroke		Stent vs. BMT	5 year stroke		stent vs. BMT
	Stenting	BMT		stenting	BMT	
All patients	11/185 (5.9%)	4/168 (2.4%)	2.20 (0.70-6.96)	23/186 (12%)	24/168 (14%)	0.81 (0.45-1.44)
EC VA stenosis	1/121 (1%)		0.33 (0.03-3.18)			0.63 (0.27-1.46)
IC VA stenosis	10/64 (16%)		7.46 (0.95-58.69)			1.06 (0.46-2.42)

* data derived from Markus et al⁷⁷. Stenting for symptomatic vertebral artery stenosis: a preplanned pooled individual patient data analysis. *The Lancet Neurology*. 2019;18:666-73. BMT = best medical therapy; HR (95% CI =

hazard ration (95% confidence intervals); yrs = years; EC = extracranial; VA = vertebral artery IC = intracranial stenosis.

There were no data from VISSIT (did not collaborate) or CAVATAS (VA angioplasty only).⁷⁷ Of 168 BMT patients, 46 had intracranial VA stenoses and 122 had extracranial VA stenoses. In the stented cohort, 64 had intracranial VA stenoses and 121 had extracranial VA stenoses. Mean age was 66 years and 80% were male. There were higher peri-operative rates of stroke/death after stenting (vs. BMT), with significant differences between extracranial and intracranial stenting (1% vs. 16%; $p < .0001$). At five years, there were no differences in stroke rates between stenting and BM.⁷⁷ In the carotid literature, interventions conferred maximum benefit if performed early (**section 4.5**). A subgroup analysis was undertaken in 161 patients randomised within 14 days of the most recent event. Stenting (vs. BMT) was associated with non-significant reductions in cumulative stroke (HR 0.65; 95% CI 0.31 - 1.39), including in patients with extracranial VA stenoses (HR 0.56; 95% CI 0.17 - 1.87) and intracranial VA stenoses (HR 0.72; 95% CI 0.27 - 1.90). The $p_{\text{interaction}}$ value .77).⁷⁷ There are, however, limitations regarding this meta-analysis. SAMMPRIS patients were randomised more quickly after symptom onset (10 days) than in VIST or VAST (36 days) and there were imbalances in prescribing combination APRx. Stent cohorts were more likely to receive DAPT than BMT patients. The current evidence indicates that stenting intracranial VA stenoses carries a significantly higher risk of death/stroke than stenting extracranial VA stenoses and that there is currently no evidence that stenting confers benefit over BMT.

Recommendation 128 (New)	Class	Level	References
			ToE

For patients presenting with a vertebrobasilar territory transient ischaemic attack or stroke and a 50-99% vertebral artery stenosis, routine stenting is not recommended.	III	A	77
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Recommendation 129 (Unchanged)	Class	Level	References
For patients with recurrent vertebrobasilar territory symptoms (despite best medical therapy) and a 50-99% extracranial vertebral artery stenosis, revascularisation may be considered.	IIb	B	29,77, 613,614

The SVS guidelines advise that in low risk symptomatic patients with proximal VA stenoses, open surgical revascularisation is recommended.⁴ However, no mention was made about managing a VA stenosis beyond its origin or on the role of VA stenting. The 2021 AHA guidelines advise there is no proven role for VA stenting in symptomatic patients.¹

12.6.3 Endovascular techniques

12.6.3.1 Adjuvant medical therapy

Protocols regarding APRx, statins and i.v. heparin are as for CAS (sections 4.2.2.3 and 4.3.7.4).

12.6.3.2 Access

Most are performed under LA via the CFA (93%), although transbrachial (3%) and TRA (5%) have been used.⁶¹⁵

12.6.3.3 Wires, catheters and stent design

A 5F or 6F guiding catheter or long access sheath (if working via CFA) is navigated to a stable position in the subclavian artery. The VA ostium is cannulated, and the lesion crossed with .014" or .018" guide wires and treated using small balloons and stents. Monorail and over the wire

systems are available. The former uses standard length wires, making catheter exchanges simpler. Dedicated VA stents are not available and coronary balloon expandable stents (BES) are used because of a low crossing profile, limited foreshortening, and easier navigation through tortuous vessels. One issue with VA stenting is optimal coverage of an ostial plaque. The use of a 'dual balloon' (allows flaring of the subclavian edge of the stent) is one option. Self expanding stents (SES) are more difficult to deploy as precisely as BES (especially in ostial lesions) and they tend to be used in large diameter VAs. Meta-analyses of non-randomised studies report no differences between drug eluting stents (DES) and bare metal stents (BMS) regarding technical success and procedural complications. However, BMS patients had more recurrent symptoms (11.3% vs. 2.8% (OR 3.3; 95% CI 1.3 - 8.3, $p = .01$) and re-interventions (19.2% vs. 4.8% (OR 4.1; 95% CI 2.0 - 8.2, $p = .001$) than with DES.⁶¹⁶

12.6.3.4 Cerebral protection devices

The use of CPDs in VA interventions has not been adequately investigated.⁶¹⁵

12.6.3.5 Pre-dilation

Risks associated with pre-dilation in extracranial VA stenting have not been evaluated. Pre-dilation is indicated if the stent cannot pass through the VA stenosis.

12.6.4 Open surgical management

Options with VA origin lesions include transposition to ipsilateral CCA, VA re-implantation, vein bypass from subclavian artery and trans-subclavian VA endarterectomy. Distal VA reconstruction can treat lesions within V2 or V3 segments, but worldwide experience is limited. Techniques for reconstructing the V3 segment (C2 to where the VA perforates the dura) include transposition and bypass. Transposition using the ECA, or occipital artery are options if there is no suitable graft available.⁶¹⁷

12.6.5 Complications after vertebral interventions

12.6.5.1 open surgery

Table 42 details outcomes after open VA reconstructions, mostly single centre series. While 30 day death/stroke rates after proximal and/or distal VA reconstructions were relatively low (2 - 7%), there was evidence that risks were higher if VA reconstructions were combined with carotid procedures (30 day death/stroke 8 - 33%). Paralysis of the spinal accessory nerve complicated 1 - 13% of procedures (average 7%), while Horner's syndrome (temporary or permanent) complicated 2 - 21% of procedures.

Table 42. 30 day morbidity and mortality rates after vertebral artery reconstructions

Author	Operation	<i>n</i>	% Symp	Death	Any stroke	Carotid stroke	VB stroke	Death/ stroke
Habozi ⁶¹⁸	all VA ops	109	100%	1.8%	2.8%	0.9%	1.8%	4.6%
	VA ops only	73		0.0%	1.4%			1.4%
	VA + carotid	36		5.5%	5.5%			11%
Berguer ⁶¹⁹	all VA ops	369	94%	2.2%	3.2%	2.2%	1.1%	3.8%
	prox VA ops	252		1.6%	2.8%	2.8%	0.0%	
	distal VA ops	117		3.4%	4.3%	0.9%	3.4%	
	VA ops only	286			2.4%			
	VA + carotid	83			6.0%			
Kieffer ⁶¹⁷	distal VA	352	94%	2.0%	3.4%	2.0%	1.4%	3.4%
	VA ops only	264		0.4%	2.3%	1.1%	1.1%	2.3%
	VA + carotid	88		6.8%	6.8%	3.4%	3.4%	6.8%

Hanel ⁶²⁰	proximal VA	29		0.0%	0.0%	0.0%	0.0%	0.0%
Ramirez ⁶²¹	all VA ops	74	82%	4.1%	4.1%			6.8%
	VA ops only	39			2.6%	0.0%	2.6%	5.1%
	VA + carotid	35			5.7%			8.5%
Coleman ⁶²²	distal VA ops	41	91%	0.0%	2.4%			2.4%
	VA ops only	35		0.0%	0.0%			0.0%
	VA + carotid	6		0.0%	33%			33%
Mert ⁶²³	Proximal VA	43	100%	2.3%	4.7%	4.7%	0%	7%
	VA + carotid	11			18%	18%		18%

VB = vertebralis; VA = vertebral artery.

Recommendation 130 (Unchanged)	Class	Level	References
For patients with combined carotid and vertebral artery disease, synchronous carotid and vertebral artery revascularisations are not recommended.	III	C	617,619, 621,622

12.6.5.2 Endovascular Interventions

Peri-operative events

In a systematic review of 20 non-randomised studies (1 767 VA stented patients), only five peri-operative strokes (0.3%) were reported, access complications occurred in 0.7%, while 0.5% were complicated by dissection.⁶²⁴ In the absence of specific studies on treating procedural stroke after VA stenting, no recommendations can be made other than advising they should be treated in the same way as after CAS (section 7.1.2).

In stent re-stenosis (ISR) after VA stenting

Table 43 summarises four systematic reviews on ISR after VA stenting.

Table 43: Meta-analyses on in stent re-stenosis after VA stenting

Author	Years	<i>n</i>	BMS <i>n</i>	DES <i>n</i>	Mean follow up	Mean ISR %	ISR BMS	ISR DES
Eberhardt ⁶¹²	1966-2005	313			12mth	25.7%		
Stayman ⁶²⁵		980	340	196	24mth		30%	11.2%
Antoniou ⁶¹⁵	1981-2011	1 010	801	209		23%		12%
Langwieser ⁶²⁶	up to 2013	457	287	170			23.7%	8.2%
Tank ⁶¹⁶	2006-2012	304	148	156	14mth DES 20mth BMS	24.4%	33.6%	15.5%

BMS = bare metal stent; DES = drug eluting stent; ISR = in stent re-stenosis

Risk factors for ISR include intracranial stenosis, ostial stenosis, stenosis > 10 mm, smaller stent size, BMS vs. DES, higher residual stenosis, VA tortuosity, contralateral VA occlusion, DM, and smoking. A multicentre study (420 patients undergoing VA stenting with BMS ($n = 204$) or DES ($n = 216$), reported a mean ISR rate of 26% at 12 months. ISR was significantly lower with DES vs. BMS (OR 0.38; 95% CI 0.19 - 0.75, $p = .01$),⁶²⁷ a finding corroborated in another study, where DES were associated with significantly lower ISR rates (18% at one year) vs. 31% with BMS (OR 2.6; $p = .02$).⁶²⁸ In a single centre series, stent fracture rates were 5%, 15% and 30% at one, three and five years respectively, but the majority were asymptomatic.⁶²⁷

There are no RCT data to guide management of ISR following VA stenting. In a multicentre, retrospective registry involving 72 patients with ISR $\geq 70\%$ (83% asymptomatic), 48 (67%) underwent treatment by redo stenting ($n = 26$) or balloon angioplasty ($n = 22$), without complications.¹⁷⁴ However, the one year rate of stroke/TIA was not significantly different in

patients undergoing repeat interventions vs. BMT, with recurrent re-stenoses developing in 33%. The rate of recurrent ISR was higher (50%) in patients undergoing balloon angioplasty alone vs. 22% with redo stenting ($p = .009$).¹⁷⁴ Patients with recurrent VB symptoms after stenting should probably be considered for re-do stenting (having ensured all were on optimal BMT). However, there are no data to guide practice in patients who with an asymptomatic > 70% re-stenosis after VA stenting.

Recommendation 131 (Unchanged)	Class	Level	References
For patients undergoing vertebral artery stenting, drug eluting stents should be considered in preference to bare metal stents	IIa	C	615,616, 626-628

12.6.7 Surveillance after VA revascularisation

Open reconstructions for proximal VA lesions are associated with high rates of symptomatic improvement and low rates of re-stenosis. In 29 patients undergoing proximal VA reconstruction, only two developed recurrent VB symptoms, while only one developed a recurrent stenosis.⁶²⁰ In another series of 36 patients, no re-stenoses or recurrent strokes occurred during a mean follow up of 54 months after VA to subclavian artery transposition.⁶²⁹ VA stenting is associated with higher rates of ISR. While DUS can identify proximal VA stenoses, it is suboptimal for diagnosing re-stenoses within stented vessels. Accordingly, while a diagnosis of recurrent stenosis after CEA/CAS is more straightforward, surveillance after VA stenting is challenging. DSA was the gold standard, but its use in surveillance cannot be justified (angiographic stroke), especially as recurrent VB events are low. Accordingly, for those advocating surveillance after interventions in the V1 segment of the VA, DUS may be performed at six and 12 months and yearly thereafter. Suspected lesions should be corroborated by

CTA/MRA (unless contraindicated) before considering DSA.^{256,612} Anyone experiencing a recurrent VB stroke/TIA after VA revascularisations should be investigated as in **section 12.3**.

Recommendation 132 (Unchanged)	Class	Level	References
For patients undergoing vertebral artery interventions, serial surveillance with catheter angiography is not recommended.	III	B	615,625

Recommendation 133 (Unchanged)	Class	Level	References
For patients who have undergone an open or endovascular vertebral artery intervention, serial non-invasive imaging surveillance may be considered.	IIb	C	256,612

Section 13. Unanswered questions from 2023 ESVS guidelines.

During preparation of the 2023 guidelines, unanswered questions were identified by the GWC as being research priorities for the future. These involve situations where there was either no data, or conflicting evidence that did not allow recommendations to be made.

Should the 3% (asymptomatic) and 6% (symptomatic) 30 day risk thresholds for performing CEA or CAS be reduced?

Should the time threshold for a patient being defined as recently symptomatic (currently 6 months) be reduced?

The need for a validated algorithm for identifying high risk of stroke on BM' asymptomatic patients in whom to target CEA and CAS.

Is stroke risk on modern BMT in ACS patients lower than when ACAS and ACST-1 were recruiting?

Are 80 - 99% ACS associated with higher rates of late ipsilateral stroke compared with 60 - 79% stenoses?

Does measurement of plasma biomarkers (to evaluate excessive endothelial and coagulation system activation) have the potential to aid risk stratification in patients with asymptomatic or symptomatic carotid stenosis?

Does severe ACS cause cognitive impairment and can carotid interventions either reverse or prevent cognitive decline?

What is the effectiveness of low dose rivaroxaban plus aspirin (vs. aspirin alone) in ACS patients?

In patients undergoing mechanical thrombectomy after acute ischaemic stroke, who should undergo synchronous CAS to treat tandem extracranial ICA stenoses and when should CAS (or CEA) be deferred?

For symptomatic patients with a 50 - 99% stenosis who have undergone thrombolysis, with no evidence of acute cerebral infarction on CT/MRI, should they still wait six days before undergoing a carotid intervention?

Should patients with NIBLs after carotid interventions receive more intense BMT (eg. combination APRx)?

Are new ischaemic brain lesions after CEA or CAS associated with long term cognitive impairment?

Is carotid artery near occlusion as benign as previously thought in patients presenting with stroke/TIA?

Does intravenous heparin confer additional benefit over dual antiplatelet therapy in patients presenting with crescendo TIAs associated with an ipsilateral 50 - 99% carotid stenosis?

What is the effectiveness of long term low dose rivaroxaban plus aspirin (vs. aspirin alone) in patients presenting with a recently symptomatic carotid stenosis?

Can transcarotid artery revascularisation be performed safely in the first 7 - 14 days after symptom onset with procedural risks similar to CEA?

Is CEA under locoregional anaesthesia safer than CAS in symptomatic high risk of CEA patients with significant cardiac or chronic pulmonary disease?

Should locoregional anaesthesia be preferred over general anaesthesia in CEA patients?

Does carotid revascularisation improve visual acuity in patients with established, neovascularisation related glaucoma?

Is there a role for routine pre- and post-operative troponin measurement in CEA or CAS patients?

What is the annual hospital or individual surgeon CEA volume needed to maintain competence and safety?

Is there a role for stenting within two weeks of TIA/stroke onset in patients with extracranial VA stenoses?

Is there a role for routine testing of antiplatelet high on-treatment platelet reactivity (HTPR) (previously termed antiplatelet resistance) to guide adjustment of the regimen or dose of antiplatelet therapy?

How best to manage patients with > 70% asymptomatic re-stenoses after VA stenting?

Journal Pre-proof

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Section 14. Information for the patient.

The ESVS gratefully acknowledge the assistance of Mr Chris Macey (*Irish Heart Foundation and the Stroke Alliance for Europe*) in preparing this section and to Dr Antonino Logiacco (Alma Mater Studiorum, University of Bologna) for designing the illustrations.

The ESVS has commissioned guidelines for Healthcare Professionals involved in treating patients with carotid or vertebral artery disease. They were prepared by experts in the field representing vascular surgery, vascular neurology, stroke medicine, interventional radiology, and interventional cardiology.

The carotid arteries are the main arteries supplying blood to the eyes and front of the brain, while the vertebral arteries are the main blood supply to the back of the brain (**Figure 1**). One of the aims of the guideline is to optimise *shared decision making*, where you (the patient) have choice and control over how you want to be treated and that you are supported in how your care is delivered. This requires doctors to provide you with as much information as possible, which should include discussion of all available treatment options, together with their risks, benefits, and potential consequences in a manner that you can easily understand.

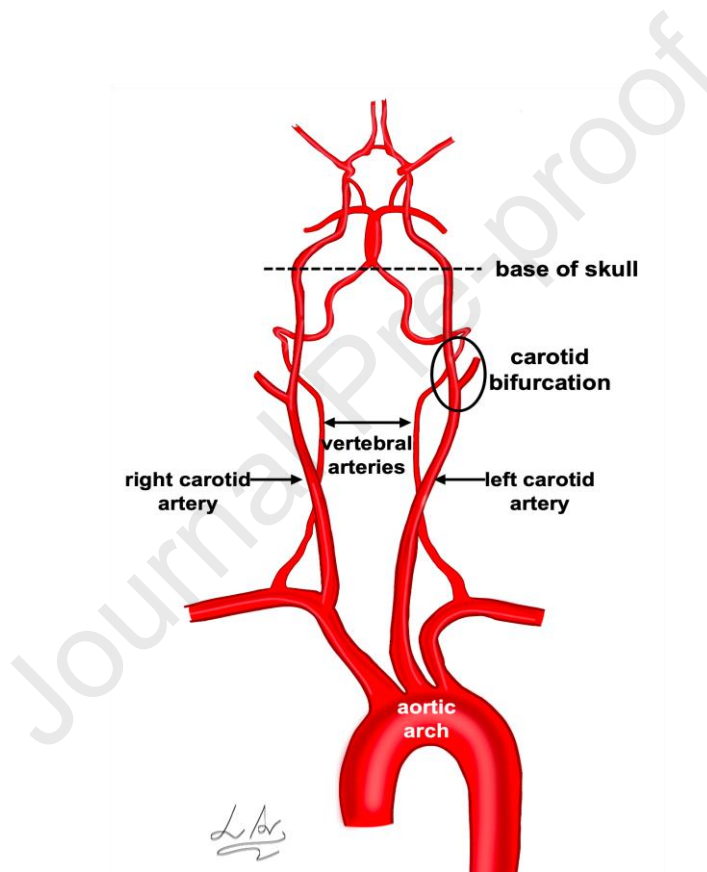


Figure 1: main blood supply to the brain comes from the carotid and vertebral arteries.

A carotid or vertebral artery narrowing (otherwise known as a stenosis) may develop because of a condition called atherosclerosis (hardening of the arteries), where deposits of fat and calcium develop in the artery walls. In the carotid artery, most narrowings develop at the point where the carotid artery divides in two. This area is known as the carotid bifurcation (**Figure 1**).

Carotid and vertebral artery stenoses can cause a stroke or a transient ischaemic attack (TIA), which is otherwise known as a warning or mini stroke. The ESVS Guidelines Writing Committee was asked to review the available evidence about the management of carotid and vertebral artery narrowings (which mainly deals with prevention of TIA and stroke), and to make recommendations about how patients like you should be managed.

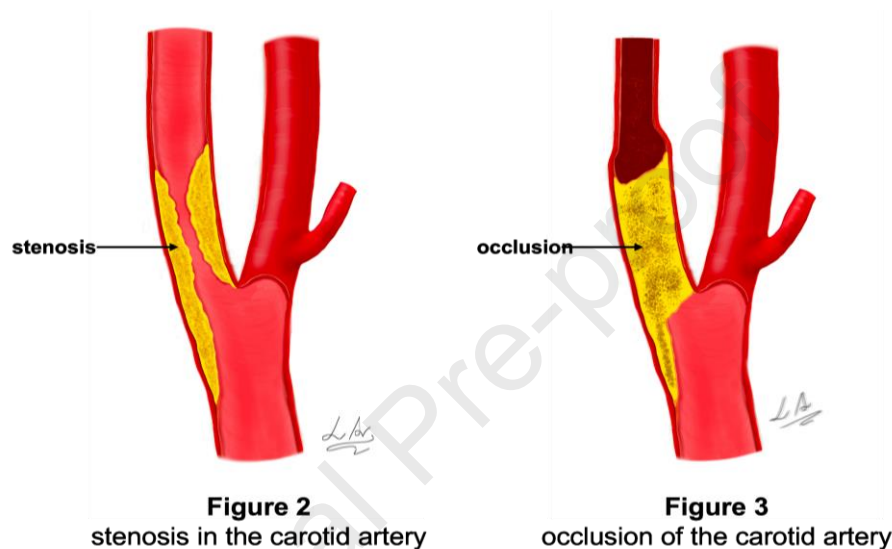
During the guideline process, all pieces of evidence are considered. A decision is then made about whether the evidence is strong enough to make a firm recommendation which all doctors should follow, or whether the evidence is not strong enough to make a recommendation. In some areas of practice, there is surprisingly little evidence to make a recommendation. The committee then decides whether a particular treatment is one that 'Experts' would agree was best. For each recommendation, the committee awards a '**level of evidence**' from 'A' (best quality evidence) to 'C' (no real evidence or expert opinion). The committee also awards a '**class of recommendation**' from class I (strong recommendation and general agreement amongst experts that the treatment is beneficial, useful, or effective) to III (agreement that the treatment is not effective or may be harmful).

The following is a summary of the advice and recommendations in a format suitable for non-experts. It has been prepared by the ESVS Guidelines Committee in collaboration with patient organisations working to combat stroke.

How are carotid and vertebral artery narrowings classified, and can their appearance predict an individual patient's stroke risk?

Narrowings in the artery may stay small and localised (termed a plaque). Their extent and severity can be imaged and measured by ultrasound or other imaging techniques (eg. computed

tomographic (CT) scans or magnetic resonance imaging (MRI) scans). Over time, a plaque may become larger and cause the artery to become more furred up (or stenosed), which may lead to reduced blood flow beyond the narrowing (**figure 2**). If a plaque causes narrowing of an artery to half its original diameter, this is called a 50% stenosis. If three quarters of the artery is narrowed, this is called a 75% stenosis. If the whole artery is blocked off, this is called an occlusion (**Figure 3**).



Is screening for carotid artery stenosis worthwhile?

At present, screening is not recommended for everyone to see if they have carotid disease, even though this might seem like a sensible thing to do. This is because the chances of identifying someone with an important narrowing of the carotid artery (70% stenosed or more) at the age of 65 years is very small (about one in every 100 people screened).

In addition, even if asymptomatic narrowings are detected (these are stenoses that have never caused a TIA or stroke), in most cases, we would not normally recommend operating on or stenting the stenosis in question. The ESVS (and other national guidelines) sometimes recommend ultrasound screening in a subgroup of usually older patients who have several risk

factors for vascular disease (eg. heart disease, smokers, people with high blood pressure, vascular disease affecting the legs or those with high cholesterol).

It is important to remember that most people with an asymptomatic narrowing in their carotid artery will not experience a stroke (and therefore do not need an operation or intervention), but all will benefit from lifestyle modification and control of vascular risk factors.

What problems can carotid and vertebral artery disease cause and what warning signs should members of the public look out for?

Carotid and vertebral artery stenoses often cause no problems at all (termed asymptomatic stenoses which are picked up incidentally during other investigations), or they can be directly responsible for causing a TIA or stroke (where stenoses are termed symptomatic).

For every 100 TIAs or strokes, about 15 are due to narrowings of the carotid or vertebral arteries. The most common way in which narrowings cause a TIA or stroke is by small blood clots forming on the surface of the narrowed arteries. These blood clots can then break off and go into the eye or brain where they can block off the eye or brain blood vessels. These small circulating blood clots are called emboli (**Figure 4**).



Figure 4: Emboli (made up of plaque debris and small blood clots) break off the narrowing and go up into the brain.

About 20% of strokes due to reduced blood supply to the eye or brain (called ischaemic stroke) are preceded by a TIA. A TIA is caused by a shorter, temporary reduction in blood supply to the brain. A TIA causes exactly the same symptoms as a stroke, but the symptoms usually resolve within minutes but definitely within 24 hours, which is the time based definition for TIA. This provides patients and doctors with an extremely important window of opportunity for urgent stroke prevention. This is why drugs (eg. aspirin, clopidogrel, dipyridamole) are prescribed to reduce the risk of blood clot formation and so prevent further TIAs or stroke in people with carotid or vertebral narrowings, regardless of whether they need an operation or stent.

An easy way to remember the symptoms of a TIA or stroke is to remember that they can cause the “S” symptoms, involving Sudden problems with:

Sight	blurring or loss of vision or double vision
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Speech	impaired expression, understanding or slurring
Swallowing	Problems swallowing liquids or solids (more common with stroke than TIA)
Strength	weakness of the face, arm and/or leg
Sensation	usually numbness / reduced feeling and less commonly pins and needles in the face, arm and/or leg.
Stability	sudden unsteadiness or a sense that you are moving or the environment around you is moving or spinning, called vertigo

If you experience any of these symptoms, you should seek immediate medical assessment by your family doctor that day or attend your local hospital Emergency Department (if your family doctor is not available). If you have symptoms of a stroke which are not immediately resolving, you or your relative must call an ambulance to arrange urgent transfer to your local Emergency Department for immediate investigations and stroke care.

Can doctors predict which people with carotid disease are most at risk of suffering a stroke?

There has been a lot of debate about whether patients with asymptomatic narrowings should undergo an operation to remove the narrowing, in order to prevent a stroke from happening. In fact, about 80% of people who have a severe asymptomatic narrowing will not have a stroke over a 10 year period, provided they follow lifestyle advice and take their prescribed medicines.

This means that only a relatively small number of people are at high risk of experiencing a stroke if the stenosis remains in place. Therefore, if they do not have higher risk features which predict an increased risk of TIA/stroke, most patients with asymptomatic carotid narrowings are advised to follow healthy lifestyle advice and to take appropriate medications alone.

In the past, it was difficult to predict who was more likely to have a stroke. The 2023 ESVS guidelines for managing patients with asymptomatic carotid stenosis recommend that several investigations should be performed before any decision is made about the need for an operation or stent. These tests look at the severity of the narrowing in the carotid artery and whether it has become more severe since the last scan (using ultrasound). Brain scans (CT/MRI) are used to see if there is evidence of old areas of reduced blood supply (called infarction), which can occur in some patients even if there have been no obvious symptoms.

Ultrasound scans can look directly at the narrowing to see whether there are any features that make a TIA or stroke more likely (e.g. very large or very soft plaques). It is also possible to detect if little blood clots (emboli) are silently breaking off the surface of the carotid narrowing and going up to the brain without your knowledge. If any of these tests show higher risk features, your doctor may recommend that you have an operation to remove the narrowing.

However, if you present with a TIA or minor stroke and are found to have at least a 50% narrowing of your carotid artery, then your risk of stroke in the next few weeks is increased. In this situation, most people (but not those with an occlusion) will be considered for an operation to remove the narrowing (carotid endarterectomy), or to insert a stent via an arterial puncture in the groin, arm or neck, to open up the diseased artery (carotid artery stenting). This is especially true in patients with at least a 70% narrowing of the carotid artery.

Does carotid artery disease cause dementia?

Stroke can also cause problems with memory, language and paying attention (known as cognitive impairment). Sometimes, stroke can cause dementia, particularly if patients have had multiple strokes. Therefore, it may be possible that a carotid stenosis can increase the risk of

dementia. However, many people with carotid stenosis also have vascular disease affecting the small arteries deep inside the brain (especially if they have poorly treated high blood pressure, or have a history of smoking or diabetes), which can also increase the risk of cognitive impairment and dementia.

In patients who have never had any symptoms from their carotid stenosis, research has suggested a possible association with cognitive impairment. However, there is no definite evidence that this type of narrowing is directly responsible for causing dementia. It is possible that in a few patients, the combination of a very severe stenosis, together with markedly reduced brain blood flow, can make cognitive impairment more likely.

Are chronic kidney disease and carotid artery disease connected?

Not directly. However, if a patient has risk factors for vascular disease (conditions that make a patient more likely to develop narrowings in their arteries), then one or both conditions may co-exist. These risk factors might include untreated or poorly treated high blood pressure and diabetes (which over time, is associated with worsening kidney function, furring up of small arteries inside the brain and carotid artery narrowings), or smoking (which increases the likelihood of narrowings developing in both carotid and kidney arteries).

What is meant by best medical therapy?

Everyone with a narrowing in their carotid or vertebral arteries (whether they have symptoms or not) will benefit from lifestyle advice (stopping smoking, losing weight, reducing alcohol intake, better diet, taking more exercise). These lifestyle changes will reduce the risk of having a TIA or stroke in the future.

It is also likely your doctor will advise you to take certain medications. The 2023 ESVS guidelines have greatly expanded its advice for doctors to enable them to prescribe the best possible combinations of medicines to reduce your long term risk of TIA, stroke, or other vascular events (such as heart attacks). These are detailed separately in the guidelines for asymptomatic patients and for symptomatic patients. They include 'antiplatelet' tablets (eg. aspirin, clopidogrel, dipyridamole), which thin the blood and reduce the chances of blood clots passing into the eye or brain and causing a TIA or stroke.

A small number of patients need stronger blood thinning drugs (anticoagulants), especially those with an irregular heartbeat called atrial fibrillation. But this aspect of TIA and stroke prevention and treatment is outside the remit of the current guidelines. If your blood pressure is elevated, you will be advised to take medicines, because treatment of high blood pressure greatly reduces your risk of TIA/stroke or other vascular events.

Patients need to know their own blood pressure readings, lipid profiles and blood sugar readings (if diabetic) to empower them to work closely with their doctors to reach their treatment targets We advise aiming for the following targets in relation to blood pressure and cholesterol:

Blood Pressure	
Non-diabetic patients	Under 65 years = <130/80mmHg
	65 years and over = systolic 130-139mmHg and diastolic <80mmHg
Diabetic patients	Under 65 years = systolic 120-129mmHg)

	= diastolic 70-79mmHg) 65 years and over = systolic 120-139mmHg = diastolic 70-79mmHg)
Cholesterol	
Total cholesterol	<3.5mmol/L (<135mg/dL)
LDL 'bad' cholesterol	<1.8mmol/L (<70mg/dL)
LDL 'bad' cholesterol in higher risk patients	<1.4mmol/L (<54mg/dL)

Slightly different blood pressure targets are advised for patients with diabetes, as outlined in the table above. In addition, it is likely that your doctor will advise you to take a 'statin' tablet (or something similar) to reduce levels of cholesterol and other harmful fats in your blood to further reduce your risk of TIA/stroke or other vascular events. If you have diabetes, your doctor will advise you regarding control of your blood sugar levels.

Which interventions are currently available?

Some patients with moderate to severe carotid narrowings will be advised to undergo an intervention, with the decision and urgency based on whether you have had recent symptoms or not. There are currently two options. ***Carotid endarterectomy*** is an operation which removes the stenosis from the carotid artery via an incision in your neck. ***Carotid artery stenting*** is a less-invasive intervention. It involves passing a fine wire and tube (catheter) through the skin in the groin, arm or neck, then into the narrowed artery in the neck in order to place a stent (a metallic meshlike cylinder) inside the carotid artery to open up the narrowing.

The highest risk period for having a stroke after presenting with a TIA or minor stroke is the first 7 - 14 days, which is why ESVS guidelines advise that carotid endarterectomy or stenting be performed as soon as possible after symptom onset. At present, the available evidence suggests that carotid endarterectomy is preferred to carotid artery stenting during this early time period. However, once you have recovered from your operation or stent insertion, there is good evidence that the long term results of both techniques are identical in terms of preventing further strokes from happening. The risks of developing a recurrent narrowing (re-stenosis) may be slightly higher after stenting than after surgery.

When it comes to planning which intervention is best for you, your doctor will consider a lot of factors (your age, blood vessel appearance, timing of symptoms and your own preference) before advising which might be the best option for you.

What does carotid endarterectomy involve?

Carotid endarterectomy is an operation to remove the stenosis inside the carotid artery. It is performed under either local or general anaesthesia and involves an incision on the side of your neck. The carotid artery is identified (**Figure 5**), and a medicine called heparin is given to prevent blood clots forming during the procedure. The carotid artery is then clamped and opened (**Figure 6**).



Figure 5
site of incision in the
carotid artery (dotted line)



Figure 6
carotid artery is opened
to reveal the narrowing

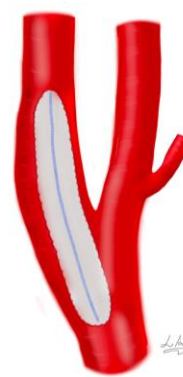


Figure 7
the narrowing is removed and
the artery closed with a patch

Sometimes, a piece of plastic tubing (a shunt) is temporarily inserted to maintain blood flow to the brain during the operation, but this is not always necessary. The stenosis is then carefully removed, and a patch is usually inserted to close the incision in the artery (**Figure 7**) in order to make it a little wider and so reduce the chance of further narrowings developing in the future. The operation takes about 1 - 2 hours. When it is finished, you will be kept in the recovery area of theatre for about three hours, during which time you will be carefully monitored.

Most patients go back to the vascular ward or stroke unit, and most are discharged on the second post-operative day. The commonest reason for delayed discharge is the need to control high blood pressure, which can sometimes increase after carotid surgery and stenting. Thereafter, you will need to continue taking the antiplatelet medications, lipid lowering medications and any other medications which are prescribed by your doctor in the long term.

What does carotid artery stenting involve?

Carotid artery stenting is usually performed under local anaesthesia, but some are done under general anaesthesia. The procedure starts by having a small wire and tube (catheter) inserted

into an artery in your groin, or arm or low down in your neck. Through this catheter, the stent delivery system is passed up into the carotid artery and then across the stenosis (**Figure 8**). As with carotid endarterectomy, you will be given heparin to reduce the chance of blood clots forming on the surface of the stent.



Figure 8
a catheter containing the stent is positioned within the stenosis and is then slowly opened out



Figure 9
once the stent has opened, the wires and catheters are removed

Patients undergoing carotid stenting also receive medicines to prevent the heart rate from slowing down, because stretching up a narrowed carotid can sometimes cause this to occur. Most operators insert a brain protection device, which is designed to prevent blood clots (emboli) passing to the brain during the stent procedure.

The stent is then carefully positioned within the narrowed artery and released, which causes it to open within the artery (**Figure 9**). The operator will take lots of Xray pictures to make sure that the stent is positioned correctly. As with carotid endarterectomy, your blood pressure will be monitored for about three hours after the procedure before you return to the ward. Most patients undergoing stenting go home on day one or day two after the intervention.

Your doctor will arrange for you to have two antiplatelet drugs (usually aspirin and clopidogrel), which will have been started before stenting and which are then continued for at least a month after stent insertion. Thereafter, you usually only need to continue taking one of the antiplatelet medications, along with the rest of the medications which are prescribed by your doctor.

Following surgery or stenting, is scanning to detect a recurrent narrowing necessary?

Weeks to months after endarterectomy or stenting, it is usual to do a scan of the operation site, using an ultrasound scan. After carotid endarterectomy or carotid artery stenting, about 5 - 10% will develop an asymptomatic recurrent narrowing within the treated artery. This is called a re-stenosis. However, this very rarely causes patients to experience another TIA or stroke.

Health systems across Europe adopt varying approaches to surveillance (imaging arteries after treatment). Some keep everyone under surveillance (using ultrasound), some only keep a small subgroup under surveillance, whereas others do no surveillance at all. The 2023 ESVS guidelines advise post-operative surveillance in a subgroup of patients who either have a > 50% narrowing of the non-operated carotid artery (on the other side of your neck), or who might be at higher risk of having a TIA/stroke should their operated artery block off sometime after your operation. Your doctor will explain the reasons why surveillance may or may not be necessary when your operation or stent procedure is discussed with you, and again after it has been performed.

How can patients prevent recurrent symptoms or recurrent narrowings?

Evidence suggests that people who are at higher risk of developing a recurrent narrowing (re-stenosis) include: women, patients with diabetes, high cholesterol, chronic kidney disease, poorly treated high blood pressure, and (very importantly) those who smoke after their

operation or stenting procedure. Accordingly, it is vital that you remember just how important it is to make any lifestyle changes permanent, as well as taking all the medications prescribed by your doctor to actively treat any vascular risk factors which are under your control.

Do patients who have a stroke due to narrowings in their vertebral arteries need an operation or stent, in addition to medical treatment?

All patients who have a stroke or TIA due to narrowings in their vertebral arteries will benefit from the same lifestyle advice, risk factor control and medications (antiplatelet agents, medicines to lower blood pressure, statins to reduce cholesterol and careful control of diabetes) as described for patients with symptoms due to carotid disease.

Open operations are very rarely performed in symptomatic patients with narrowings in their vertebral arteries and most are treated by medicines alone. The 2023 ESVS guidelines do, however, advise that stenting of vertebral artery narrowings may be considered in patients who have recurrent TIA/stroke despite taking their medications.

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