99% ACS in the presence of one or more clinical or imaging features that make them higher risk for stroke on best medical therapy, 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).

NEW RECOMMENDATIONS IN THE 2023 GUIDELINES

New Class I recommendations

11. For patients with asymptomatic carotid stenosis who are undergoing carotid endarterectomy, lower dose aspirin (75–325 mg daily) rather than higher dose aspirin (> 325 mg daily) is recommended.
23. 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.
24. 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.
25. 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.
29. For symptomatic patients undergoing carotid endarterectomy on aspirin monotherapy, lower dose aspirin (75 – 325 mg daily) rather than higher doses (> 325 mg daily) is recommended.
30. In symptomatic carotid stenosis patients undergoing carotid endarterectomy who are intolerant of, or allergic to, aspirin and clopidogrel, dipyridamole modified release monotherapy (200 mg twice daily) is recommended.
35. For symptomatic carotid stenosis patients who do not reach their lipid targets on maximum doses or maximum tolerated doses of statins, ezetimibe (10 mg daily) is recommended.
58. For patients presenting with recent carotid territory symptoms and evidence of free floating thrombus within the carotid artery, therapeutic anticoagulation is recommended.
63. 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.
64. 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.
66. For patients undergoing carotid endarterectomy, it is recommended that the operation be performed by trained vascular surgeons, rather than by surgeons from other specialties.
91. For patients experiencing a peri-operative stroke, it is recommended to differentiate between an intra-operative and a post-operative stroke.
92. 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.
93. 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.

New Class IIa recommendations

10. For patients with >50% asymptomatic carotid stenosis who are intolerant or allergic to aspirin, clopidogrel 75 mg daily should be considered. If intolerant or allergic to both aspirin and clopidogrel, dipyridamole monotherapy (200 mg twice daily) should be considered.
14. 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.
27. 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.
28. 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 (300–325 mg daily for 14 days, followed by 75–162 mg daily) should be considered.
36. For symptomatic carotid stenosis patients who are intolerant of, or not achieving target low density lipoprotein levels on statins, with or without ezetimibe, additional or alternative treatment with PCSK9 inhibitors should be considered
49. 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.
54. 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.
62. 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.

77.	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.
79.	For patients undergoing carotid endarterectomy, selective wound drainage should be considered.
82.	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.
83.	For patients undergoing carotid artery stenting, decisions regarding stent design (open cell, closed cell) should be considered at the discretion of the operator.
85.	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.
88.	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.
New Class IIb recommendations	
51.	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.
57.	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.
59.	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.
61.	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.
84.	For patients undergoing elective carotid artery stenting, dual layer mesh covered stents may be considered.
90.	For patients undergoing transfemoral carotid stenting, at least twelve carotid stent procedures per year (per operator) may be considered an appropriate operator volume threshold to maintain optimal outcomes.
101.	In selected high risk for surgery patients or emergency patients with suspected prosthetic patch infection, insertion of a covered stent may be considered, as part of the three stage EndoVAC technique
New Class III recommendations	
60.	For patients presenting with recent carotid territory symptoms and evidence of free floating thrombus, intravenous thrombolysis is not recommended.
86.	For patients undergoing carotid artery stenting, post-dilation is not recommended when the residual stenosis is <30%, in order to reduce haemodynamic instability.
128.	For patients presenting with a vertebrobasilar territory transient ischaemic attack or stroke and a 50–99% vertebral artery stenosis, routine stenting is not recommended.

New recommendations included in the European Society for Vascular Surgery 2022 clinical practice guidelines on the management of atherosclerotic carotid and vertebral artery disease in comparison to the previous 2017 guidelines. Numbers correspond to the numbers of the recommendations in the guideline document.

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 of 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 at higher risk of stroke on BMT in patients 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 anti-platelet 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 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/TIA[167] (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 at '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 at '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 calcification,[172] 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 be considered only 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 RCTs[59] 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 question[174] (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.

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 (i.e., 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 guidelines[176] and a checklist is available (Appendix A). There was no formal evaluation of *Facilitators and Barriers* and the guidelines did not have the scope to go into detail regarding health economics, largely because individual countries have different processes for determining cost acceptability.

1.3. Guideline Writing Committee

Guideline Writing Committee (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 comprised 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 6 July 2020, at which topics and tasks were allocated. The GWC met monthly (by video conference) to review progress. Search strategies were undertaken for each of the 46 subsections, using Medline, Embase, and the Cardiosource Clinical Trials and Cochrane databases to 31 December 2020, plus reference checking of cited papers. Hand searches were undertaken of publications in 11 journals between 2017 and 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 and 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: (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 onset;[52] 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). The letters A, B, C denote evidence levels (Table 2), with A being the highest.

Table 1. Classes of recommendations according to the ESC (European Society of Cardiology)

Class of recommendation	Definition	Suggested wording
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful and effective	Is recommended
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure	
Class IIa	Weight of evidence/opinion is in favour of usefulness/efficacy	Should be considered
Class IIb	Usefulness/efficacy is less well established by evidence/opinion	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, should not be done

Table 2. Levels of evidence according to the ESC (European Society of Cardiology)

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 of 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 among 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, predefined 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 remains essentially unchanged (compared with 2017), grades of evidence have been revised and the relevant recommendation box is highlighted as having been "changed".

1.7. Review process

There were three rounds of external review, involving 25 reviewers (16 GC members plus nine external reviewers). Review comments were assessed by the co-chairs, who coordinated 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 6 April 2022.

1.8. Audit and update plan

These guidelines will be updated every four years. Vascular centres are encouraged to audit implementations made as a result of the guidelines. Audit cycles should be repeated and changes implemented. There are many ways to perform clinical audit and it is now a requirement for most centres to be registered with local audit committees.

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 hours, which is of a non-traumatic, vascular origin.[179] Crescendo TIAs refer to multiple TIAs in a short time period, defined by some as more than two TIAs in 24 hours,[180] or at least three events in seven days,[181] with full recovery between. Stroke is a sudden onset focal (rather than global) neurological dysfunction, with symptoms lasting $>$ 24 hours (or causing death in $<$ 24 hours), 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

In a European population of 715 million, 1.4 million strokes occur annually.[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] It is suggested that the number of Europeans living with stroke as a chronic condition may increase by 25% from 3.7 million (2015) to 4.6 million (2035), as a result of the 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 — 2016,[182] and are expected to increase to $ 129 billion (€ 114 billion) by 2035.[183]

2.3. Aetiology of stroke

Of strokes, 15—20% 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) cardioembolic; (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 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 cardioembolic stroke,[186] attributed to declines in total cholesterol, low density lipoprotein cholesterol (LDL-C), blood pressure (BP), increases in high density lipoprotein cholesterol,[187] and substantial increases in APRx, antihypertensive, and statin prescriptions.[186] Between 2002 and 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]