

EDITORIAL

The ESVS 2023 guidelines on the management of atherosclerotic carotid and vertebral artery disease. What is new and what remains to be answered

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The European Society for Vascular Surgery (ESVS) has recently published updated guidelines on the management of atherosclerotic carotid and vertebral artery disease,¹ revising the previously published 2017² and 2009³ guidelines. The rationale for writing the ESVS 2023 carotid guidelines is that several studies have been published since 2017, including 39 primary or secondary analyses from randomised controlled trials (RCTs), 71 systematic reviews and/or meta-analyses, and data from 50 vascular registries or quality initiative programmes.¹ Consequently, 133 recommendations were issued, of which 84 were unchanged, 11 were "regraded" since 2017 and 38 are new. Five new sections were added, including the management of free floating thrombus (FFT), the management of carotid webs (CaW), the management of symptomatic patients with an ipsilateral 50-99% carotid stenosis and atrial fibrillation, the planning of carotid interventions in anticoagulated patients, and the timing of carotid interventions in patients with acute ischaemic stroke undergoing thrombolysis.

For patients presenting with recent carotid territory symptoms and evidence of FFT within the carotid artery, therapeutic anticoagulation is recommended (Class I, Level C). For patients who develop recurrent symptoms whilst receiving anticoagulation therapy, surgical or endovascular removal of the thrombus may be considered (IIb, C). Intravenous thrombolysis is not recommended (III, C), since it is associated with a 15-fold increased risk of silent ischaemia, TIA, or stroke/death.⁴ In any case, factors that should be taken into account in the decision making include the presumed aetiology, the recurrence of symptoms during anticoagulation, the interval since TIA/stroke onset, the size of infarct and the accessibility of the FFT.¹

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doi: 10.59037/hjves.v5i2.44

ISSN 2732-7175 / 2023 Hellenic Society of Vascular and Endovascular Surgery Published by Rotonda Publications
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A CaW is a ridge like filling defect, possibly a variant of fibromuscular dysplasia, that may act as a pocket for thrombus accumulation and cerebral embolisation.¹ According to the ESVS 2023 carotid guidelines, for symptomatic patients with a carotid web in whom no other cause for stroke can be identified after detailed neurovascular work up, carotid endarterectomy (CEA) or carotid artery stenting (CAS) may be considered to prevent recurrent stroke (IIb, C).

For patients with a transient ischaemic attack or minor ischaemic stroke in the presence of atrial fibrillation and an ipsilateral 50-99% carotid stenosis, multidisciplinary team review is recommended to determine whether urgent carotid revascularisation or anticoagulation alone is indicated (I, C). For patients who report recurrent event(s) in the territory ipsilateral to a 50-99% carotid stenosis whilst on therapeutic levels of anticoagulation, CEA or CAS is recommended (I, C). Factors that should be taken into account in the decision making include the presence of infarctions in other vascular territories, the evidence of emboli on transcranial doppler and the presence of left atrial appendage thrombus.

The optimal timing of carotid interventions after thrombolytic therapy (TT) remains controversial. A recent systematic review and meta-analysis has shown an inverse relationship between timing to CEA and peri-procedural stroke/death: peri-operative stroke/death rate was 13% when CEA was performed three days after TT completion and 10.6% after four days.⁵ The risk was predicted to reduce to below the 6% threshold after six days. Consequently, the ESVS 2023 carotid guidelines recommend that, for patients with acute ischaemic stroke due to a symptomatic 50-99% carotid stenosis who have received intravenous thrombolysis, delaying CEA or CAS by six days following completion of thrombolysis should be considered (IIa, B).

Another interesting, new recommendation is that, for patients undergoing CEA, intra-operative completion imaging with angiography, duplex ultrasound or angioscopy should be considered in order to reduce the risk of peri-operative stroke (IIa, B). The recommendation is based on a meta-analysis of 34 observational studies, which showed that perioperative stroke is reduced by 17% when completion angiography is performed, whereas completion angioscopy is associated with a 52% reduction.⁶

Although these guidelines cover some gaps in our everyday practice, several questions remain to be answered. One of these questions is whether the 3% (asymptomatic) and 6% (symptomatic) 30-day risk thresholds for performing CEA or CAS should be reduced, since many vascular surgeons would claim that we can do better than that. A meta-analysis, however, of four large RCTs comparing CEA with CAS in patients with asymptomatic carotid stenosis (n=6,659) showed that the 30-day death/stroke rate was 2.2% (CEA) vs. 3.1% (CAS). In a meta-analysis of 10 RCTs comparing CEA with CAS in patients with symptomatic carotid stenosis (n=5,797), the respective rates were 5.1% and 9.3%. Therefore, it seems that the 3% and 6% thresholds should not be reduced at present.

Another debatable issue is whether the time threshold for a patient being defined as recently symptomatic (currently six months) should be reduced. Since 2004, when an analysis of pooled data from ECST and NASCET was published, it is known that the highest-risk period for stroke recurrence is the first 2 weeks and that the benefit of carotid endarterectomy is maximal in the first 2 weeks, whereas, after 3 months there is no statistically significant benefit.⁷ Consequently, the 6-month threshold, apart from arbitrary, is probably obsolete and should be reduced to 3 months.⁸

Are 80-99% asymptomatic carotid stenoses (ACS) associated with higher rates of late ipsilateral stroke compared with 60-79% stenoses? A linear association between stroke risk and the degree of carotid stenosis was found in the ACSRS study⁹ as well as in a meta-analysis of 12 cohort studies.¹⁰ Nevertheless, this association was not reproduced in a meta-analysis of the medical treatment group of three RCTs.¹⁰

Does severe ACS cause cognitive impairment and can carotid interventions either reverse or prevent cognitive decline? It seems that whether ACS causes cognitive impairment depends on whether it causes impairment of the cerebrovascular reserve (CVR), since it has been shown that an abnormal breath holding index, which is a measure of CVR, is a statistically significant predictor of a decrease in the Mini-Mental State Examination score. Whether this cognitive decline can be reversed or prevented by carotid interventions remains questionable, with mixed results in the literature. Patients with ACS and objective ipsilateral ischemia would be the best candidates for neurocognitive function improvement after carotid revascularization.

What is the effectiveness of low dose rivaroxaban plus aspirin (vs. aspirin alone) in ACS patients? The COPMASS trial enrolled 7,470 patients, 1,919 of whom had carotid disease.¹¹ In this particular group of patients, after a mean follow-up of 21 months, there was a non-statistically significant reduction in the endpoints of efficacy and a non-significant increase in major bleeding with low dose rivaroxaban plus aspirin vs. aspirin alone. The subgroup analysis was underpowered, so further trials are required and there is no guideline from any scientific society currently recommending low dose rivaroxaban plus aspirin in ACS patients.

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

analysis of ECST and NASCET concluded that CEA conferred no notable reduction in stroke at five and eight years in patients with symptomatic carotid near occlusion (CNO), largely because of low rates of ipsilateral stroke in patients who were treated medically.¹² A meta-analysis, however, of 32 observational studies including 703 patients with CNO showed that the 1-year stroke/death rate was 4% following CEA, 6% after CAS, and 19% with BMT.¹³ Similarly, a subsequent meta-analysis of 26 studies including 1,506 patients reported that the late risk of ipsilateral stroke, neurological/cardiac death, or MI was 4.26/100 patient years in CNO patients treated by CEA or CAS, and 13.3/100 patient years (95% CI 5.54 e 31.95) in patients treated medically. The guideline that CEA and CAS are not recommended in patients with CNO (III, B) was not changed, but the debate has grown.¹⁴

In conclusion, the ESVS 2023 guidelines on the management of atherosclerotic carotid and vertebral artery disease have addressed some questions but, due to the lack of available data, have left several others unanswered. These unanswered questions highlight the existing gaps in the literature and offer opportunities for future research. One of the problems faced by research on carotid stenosis is that, fortunately for the patients - unfortunately for the studies, the outcomes, such as strokes and deaths, are relatively rare, so large number of patients are required to draw firm conclusions. This problem calls for multicenter studies and research coordination among vascular centers dealing with carotid disease and, fortunately enough, there are several of those in Greece.

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