

Carotid artery interventions - endarterectomy versus stenting



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KEYWORDS

- bare metal stent
- carotid
- drug-eluting stent
- stroke
- supra-aortic disease

Abstract

Current management of patients with carotid artery stenosis is based on well-established guidelines, including surgical procedures – carotid endarterectomy (CEA) and endovascular carotid artery stenting (CAS) – and optimal medical treatment alone. Outcomes in the postprocedural period after CAS and CEA are similar, suggesting strong clinical durability for both treatments. Recent advances, which include the emergence of novel endovascular treatment tools and techniques, combined with more recent randomised trial data shed new light on optimal patient selection and treatment in contemporary practice. Improved, modern technologies including enhanced embolic protection devices and dual-layered micromesh stents yield better outcomes and should result in further improvements in CAS. In centres of excellence, nowadays, the majority of patients with severe carotid artery stenosis can be successfully treated with either CEA or CAS.

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Abbreviations

ASR	average surgical risk
CABG	coronary artery bypass grafting
CAS	carotid artery stenting
CEA	carotid endarterectomy
CTA	computed tomography angiography
DAPT	dual antiplatelet therapy
DLMS	dual-layer micromesh stents
DUS	duplex ultrasonography
EPD	embolic protection device
HSR	high surgical risk
IEP	integrated embolic protection
MACE	major adverse cardiac events
MI	myocardial infarction
MRA	magnetic resonance angiography
MRI	magnetic resonance imaging
OMT	optimal medical therapy
PCI	percutaneous coronary intervention
RCT	randomised controlled trial
TCAR	transcarotid artery revascularisation
TIA	transient ischaemic attack

Introduction

Severely stenosed carotid arteries are predisposed to stroke, and carotid artery revascularisation, with either carotid artery stenting (CAS) or carotid endarterectomy (CEA), can restore patency and reduce the long-term risk of ischaemic stroke. Open carotid endarterectomy completely removes the atheromatous material, but CAS (introduced as an alternative to CEA in 1994) is a less invasive procedure. Carotid endarterectomy 30-day stroke and death rates have decreased over the last 50 years, and similarly, carotid artery stenting 30-day stroke and death rates have declined in a similar magnitude in the last 30 years. Outcomes in the postprocedural period after CAS and CEA are similar, suggesting robust clinical endurance for both treatments.

Several randomised clinical trials, related meta-analyses, and expert opinions have reshaped the present guidelines on the diagnosis and treatment of carotid artery stenosis^{1,2}. Although the indications for carotid revascularisation are well defined, there is less consensus on the preferred revascularisation technique (CEA or CAS). In contemporary clinical practice, many patients are equally suitable for both treatment options.

Currently, CAS is a standard procedure performed by operators of different specialities (cardiologists, neuroradiologists, angiologists, vascular surgeons, and neurosurgeons)¹. Regardless of the medical speciality, the high proficiency of operators and site experience remain paramount for reducing periprocedural adverse cerebral events³. However, the guidelines still seem to underestimate the great importance of operator and site experience, as well as the impact of healthcare providers' decisions on outcomes^{1,2,4}.

According to clinical presentation, patients with extracranial carotid artery stenosis may be asymptomatic or symptomatic. Patients classified as recently symptomatic include those with

symptoms in the past 6 months. All patients with carotid stenosis should undergo an appropriate, independent neurological evaluation followed by duplex ultrasonography (DUS) as a first-line imaging modality in everyday clinical practice^{1,2}. Before any decision for revascularisation is made, additional aspects, such as a patient's surgical risk profile, life expectancy, degree of stenosis, and symptomatic neurological status, should be considered. Further clinical and imaging evaluations may be conducted if justified^{1,2,4}. The degree of carotid artery stenosis identifies patients who would benefit from revascularisation, and the DUS consensus criteria are used to determine stenosis severity according to current guidelines^{1,5}.

DUS is frequently combined with additional imaging modalities, such as computed tomography angiography (CTA) and magnetic resonance angiography (MRA), for improved accuracy of stenosis assessment¹. CTA or MRA can simultaneously delineate the aortic arch, supra-aortic trunks, carotid bifurcation, distal internal carotid artery (ICA) and intracranial circulation, which is particularly useful if CAS is being considered. Contrast-enhanced MRA has higher accuracy than non-contrast MRA but necessitates paramagnetic contrast agents (gadolinium). A combination of 2 imaging modalities (DUS + CTA or DUS + MRA) further improves accuracy and is routinely practised in many centres. Furthermore, postprocedural CTA or brain magnetic resonance imaging (MRI) are usually recommended to characterise the strokes that can occur as periprocedural complications of carotid revascularisation.

SYMPTOMATIC CAROTID STENOSIS

In patients with severe carotid artery stenosis, CAS and CEA both carry procedural risks, which are about twice as great for symptomatic as for asymptomatic patients. The clinical benefit of revascularisation for stroke risk reduction in patients with symptomatic carotid artery stenosis $\geq 70\%$ is well established^{1,2,4}. The revascularisation of symptomatic lesions with 50–69% stenosis should also be performed, but, due to the lower absolute stroke risk in these patients, the treatment value should always be balanced against the possible procedural risks, taking into consideration the patient's clinical presentation, age, and sex^{1,2,4}. Exceptionally, in patients with recurrent symptoms despite best medical therapy and carotid stenosis $< 50\%$ or near occlusion with distal vessel collapse, upon multidisciplinary team review, revascularisation may also be considered^{1,4}. As recommended in current guidelines, revascularisation should be performed within 2 weeks of the index event⁶.

The ongoing uncertainty for prevention of future strokes in patients with symptomatic carotid stenosis stands in defining the optimal candidates for either CEA or CAS. The current multisocietal guideline recommendations agree that in symptomatic high surgical risk (HSR) patients who qualify for carotid revascularisation, CAS is indicated and preferred over CEA.

Factors in favour of CAS include younger age, specific anatomical features (such as very distal ICA stenosis or contralateral occlusion), lack of ICA tortuosity, absence of or only minimal plaque calcification, and local tissue scarring due to previous neck

radiotherapy or complex surgery. Furthermore, a medical history of congestive heart failure, myocardial ischaemia, or severe pulmonary disease makes CAS preferable over CEA. Patients receiving anticoagulation for indications such as atrial fibrillation might also be more suitable for CAS without increasing access site bleeding complications (particularly with transradial CAS). However, CAS is still associated with infrequent periprocedural embolic cerebral complications, resulting in a slightly higher rate of peri- and early postprocedural (up to 30 days) minor ipsilateral strokes, compared to CEA⁷. Although the frequency of such events has been significantly reduced over the past years, cerebral embolisms remain the main weakness of CAS⁸.

Certainly, advantages of CEA over CAS may be found in patients >70 years of age, those with lesion elongation, extreme calcification, visible thrombus presence, or those with challenging anatomies (aortic arch type III or arch calcification)⁴.

ASYMPTOMATIC CAROTID STENOSIS

An asymptomatic carotid artery stenosis (ACS) indicates a stenosis which is detected in patients without any clinical history of ischaemic stroke, transient ischaemic attack (TIA), or other neurological symptoms which might be related to the carotid arteries. Among asymptomatic patients with severe carotid artery stenosis but no recent stroke or TIA, either CAS or CEA can restore patency and reduce long-term stroke risks.

The procedural risks of CAS and CEA have decreased over the decades, but there is still about a 1% risk of disabling stroke or death. There is also some procedural risk of non-disabling stroke (particularly with CAS) or of non-fatal myocardial infarction or cranial nerve palsy (particularly with CEA). Optimal medical therapy (OMT) can likewise reduce stroke rates; however, patients with severe carotid stenosis still have a 1% annual risk of disabling stroke or death.

In contrast to symptomatic carotid patients, the benefit of revascularisation to prevent future strokes in asymptomatic carotid artery stenosis patients is still very much debated. Contrary to the previous belief based on randomised trials comparing medical therapy to revascularisation⁹⁻¹², Howard et al demonstrated a strong and unique relationship between the risk of stroke and the degree of asymptomatic carotid stenosis¹³. Data from a prospective population-based cohort study (OxVasc) screening 2,178 asymptomatic patients with carotid ultrasound between 2002 and 2017 were used, as well as a systematic review and meta-analysis performed of previously concluded cohort studies on this subject between 1980 and 2020.

The observed discrepancy in the evidence from the cohort studies compared with earlier randomised trials could result from a potential recruitment bias in relation to the severity of stenosis, which would undermine any expected risk association in trial cohorts¹³. The authors observed that, in asymptomatic patients, the risk of stroke or TIA strongly correlated with the degree of ipsilateral carotid artery stenosis. The 5-year ipsilateral stroke risk was 18.3% in those with 80-99% stenosis compared with 1.0% in

those with 50-79% stenosis ($p < 0.0001$). Therefore, the degree of asymptomatic carotid stenosis should be a primary consideration for patient selection for revascularisation.

Patients on OMT, featuring high-grade asymptomatic carotid stenosis (>70%), and particularly those with 80-99% artery narrowing, can greatly benefit from carotid revascularisation¹³. The importance of a prudent approach to asymptomatic patients is reflected in the most recent guideline updates. The German-Austrian S3 (2020), the European Stroke Organisation (2021) and the updated European Society for Vascular Surgery (ESVS; 2021) guidelines recommend the revascularisation of patients with asymptomatic high-grade stenoses, provided a meticulous pre-interventional assessment is done.^{4,14,15} The guidelines also recommend close monitoring of periprocedural stroke/death rate records to ensure that decision-making and clinical care are optimised and complications are kept to a minimum⁴.

Recent randomised clinical evidence reflecting real-world practice (the CREST, ACT-1, SPACE-2 and ACST-2 trials) demonstrates that CAS and CEA are both safe and effective in well-selected average surgical risk (ASR) asymptomatic patients¹⁶⁻¹⁹. All randomised controlled trials (RCT) have shown comparable outcomes for CAS and CEA for periprocedural complications (death, stroke, and myocardial infarction [MI]) as well as rates of ipsilateral stroke during follow-up.

The largest and most recently published trial, the ACST-2 trial, randomised 3,625 patients and compared contemporary CAS versus CEA in asymptomatic patients with carotid artery stenosis.¹⁹ The main finding from the ACST-2 trial is that the effects of CAS versus CEA on disabling or fatal events are approximately equal in terms of procedural hazards (1.0% vs 0.9%; $p = 0.77$). However, there was a slight excess of early non-disabling strokes after CAS and a slight excess of myocardial infarction after CEA. At 5 years, the risk of non-procedural fatal or disabling stroke was equivalent (2.5% vs 2.5%) and there was no significant difference for the incidence of any stroke (5.2% vs 4.5%) comparing CAS with CEA. The results were consistent across patient subgroups stratified by type of stroke, gender, age, and carotid artery diameter stenosis. The trial is scheduled to collect 10-year data which will provide additional evidence on the durability of their protective effects. Unfortunately, the ACST-2 study did not include an OMT arm, so the analysis of early procedural risk versus long-term benefit was not possible.

Furthermore, the investigators used the ACST-2 trial data to update a meta-analysis of long-term outcomes of RCTs comparing CAS versus CEA in patients with asymptomatic (ACST-2, CREST, SPACE-2, ACT-1) and symptomatic (ICSS, CREST, SPACE, EVA-3S) carotid artery stenosis. The meta-analysis confirmed that the protective effects of CAS and CEA are similar after the initial 30-day postprocedural period¹⁹.

One of the most important current questions regarding carotid revascularisation, whether OMT alone is as good as carotid revascularisation with OMT, still remains to be answered. The reports of a very low (~1%) annual stroke rate in asymptomatic carotid

stenosis patients²⁰ has led to 2 ongoing trials (the CREST-2 and ECST-2 trials) investigating the potential benefit of revascularisation compared to modern OMT alone^{21,22}.

In conclusion, properly selected asymptomatic patients can greatly benefit from carotid artery revascularisation, and CAS is a safe and efficient revascularisation alternative to CEA in subjects at high risk for stroke on best available medical therapy.

OPTIMAL MEDICAL THERAPY

In patients with carotid artery disease, adequate concomitant medication is of paramount importance. OMT including antiplatelet agents, statins, blood pressure and diabetes control, smoking cessation, and a healthy lifestyle are critical components of any revascularisation strategy for stroke prevention.

Since atherosclerosis is a generalised condition, patients with carotid artery stenosis would benefit from optimal medical therapy, including antiplatelet and lipid-lowering drugs, irrespective of the revascularisation method^{1,2}.

After CAS, dual antiplatelet therapy (DAPT) with aspirin and clopidogrel is recommended for at least 3 weeks to 3 months after the procedure, followed by lifelong antiplatelet monotherapy thereafter^{1,2,4}. There are limited data on the value of novel P2Y₁₂ inhibitors (ticagrelor, prasugrel) after CAS. Some benefits from prolonged DAPT treatment, up to 12 months, may be expected in selected low bleeding risk CAS patients after recent myocardial infarction, as part of the secondary cardiovascular preventive strategy². The type and duration of antithrombotic treatment during and after CAS should be patient-tailored, always balancing the risk of cerebral ischaemic events against the bleeding risks, especially in patients on oral anticoagulation therapy¹. More dedicated clinical trials are needed to elucidate the optimal duration and type of antithrombotic regimen during and post-CAS to standardise current practice. Patients with severe carotid stenosis may further benefit from more aggressive preventive treatments and more frequent follow-up.

Arterial hypertension remains the most important, modifiable stroke risk factor and blood pressure control is among the most effective strategies for preventing both ischaemic and haemorrhagic stroke. Hypertension as a primary risk factor for stroke is also a risk factor for atrial fibrillation and MI, which both increase the likelihood of stroke. Statins, with ezetimibe as needed, should target low-density lipoprotein cholesterol (LDL-C) <70 mg/dL (<1.8 mmol/L) if not achieved with intensive statin therapy alone. Glycaemic control should target a glycosylated haemoglobin <7% if feasible.

NOVEL CAS TOOLS AND TECHNIQUES

CAS practices have evolved with better patient selection, further refinement of technique, and advanced technology to avoid periprocedural complications. Recently, several technical improvements and new tools have been introduced into CAS practice to further improve the treatment outcomes by providing better cerebral protection and optimal plaque scaffolding. However,

anatomical difficulties, including aortic arch complexity, severe calcification and target vessel tortuosity, need to be considered before endovascular carotid artery revascularisation⁸. Selecting optimal treatment tools and approaches for a smooth and uneventful device delivery is of paramount importance for overall treatment success and favourable mid- to long-term outcomes.

EMBOLIC PROTECTION DEVICES

Primary stenting with self-expanding stents using embolic cerebral protection is a default strategy of endovascular carotid stenosis treatment¹. According to the latest recommendations for patients undergoing CAS, decisions regarding the choice of cerebral protection (filter, proximal flow reversal) should be at the discretion of the operator¹. Of note, technical performance based on embolic protection device (EPD) dwell time has been shown to be a significant predictor for 30-day outcome (death, stroke, MI)²³. The selection of EPD should be based on operator experience, lesion characteristics, anatomical factors and current availability of devices. Using different types of embolic protection devices in a more appropriate and individually tailored way may further improve CAS outcomes.

The embolic risk during CAS is highest during the post-dilation after stent deployment^{24,25}.

The majority of embolic particles are under 100 µm in size and may reach the cerebral circulation, despite the use of conventional distal filters, due to malapposition or through the filter pores (larger than 100 µm in most filters) and may contribute to the higher risk of procedural minor stroke seen with CAS²⁶. Recently, double filtration during CAS using a novel post-dilation balloon with an integrated embolic protection (IEP) filter with 40 µm pores showed a low 30-day death, stroke, or MI rate of 1%²⁶.

Another innovative approach in CAS is illustrated by the Neuroguard IEP (Contego Medical, Inc.), a 3-in-1 system comprising a carotid stent (with a closed-cell design), a post-dilation balloon and an IEP 40 µm filter, designed to reduce the number of CAS steps while maintaining macro- and microembolic cerebral protection²⁷. Results from the preliminary study demonstrated that the Neuroguard IEP system is safe and feasible for CAS of clinically significant carotid artery stenosis with a stroke/death rate of 0% at 30 days²⁷. A large pivotal study is currently underway.

TRANSRADIAL CAS

The transradial approach (TRA) has become the standard of care for cardiac catheterisation and coronary interventions. Its benefits are also well documented in peripheral interventions, including CAS, leading to a reduced risk of bleeding and access site complications, early ambulation and discharge and, ultimately, cost saving²⁸.

The technical failure of CAS through the femoral approach in most of the cases is due to a complex aortic arch. Features that increase the risk of complications during CAS procedures are some type 2 & 3 arches, bovine arch and plongeant innominate arteries²⁸.

TRA has been a subject of interest in CAS as part of the strategy to tackle some anatomical variants of the aortic arch and supra-aortic vessels more safely. This alternative approach may reduce the time for catheter manipulation in the aortic arch and supra-aortic vessels, thus directly limiting the CAS-associated stroke risk²⁹. Devices featuring low crossing-profile delivery systems are facilitating the TRA and yielding excellent results²⁸. However, large-bore devices can be used only selectively in patients with larger-size radial arteries. Furthermore, TRA CAS can be performed safely while the patient is taking anticoagulants plus antiplatelet therapy during the periprocedural period, without increasing access site bleeding complications.

While the adoption of transradial access has been increasing in CAS in recent years, more training initiatives and sharing of best practices are needed to bring its full potential to everyday clinical practice. Notably, the growing importance of alternative approaches (i.e., transradial and transcervical access) in modern CAS practice has recently been recognised in the latest ESVS guidelines update, with a recommendation that the 2 methods should be considered for cases in which the transfemoral (TF) route may confer a higher risk of complications¹.

TRANSCAROTID ARTERY REVASCULARISATION

Transcarotid artery revascularisation (TCAR) combines carotid artery stent placement with cerebral protection by clamping the proximal common carotid artery and reversing cerebral arterial flow. The major advantage of TCAR compared with TF CAS is avoiding catheter manipulation in the aortic arch with direct carotid artery access. Some relative contraindications include proximal lesions that are <5 cm cranial to the clavicle, severe target vessel tortuosity, a small or significantly diseased common carotid artery (CCA) or depth of the CCA, which makes access difficult. There are no randomised trials directly comparing TCAR with any other method of carotid revascularisation.

Two recent systematic reviews and meta-analyses reported on 4,852 patients from 10 prospective registries and 8 retrospective studies³⁰, and the second also included 2,110 patients in 18 reports of outcomes with TCAR³¹. Both reviews highlight low rates of periprocedural complications with TCAR; in symptomatic patients, the periprocedural risk of stroke or TIA was 2.5% compared with 1.2% in asymptomatic patients. Further comparative studies are warranted to overcome the potential for selection bias and ascertainment bias in these reports.

CONVENTIONAL CAROTID STENT DESIGN

Regarding the different conventional stent types, devices with open- and closed-cell designs are currently available. It has been shown that, during CAS, the new ipsilateral changes in diffusion-weighted brain MRI are reduced with the use of closed-cell versus open-cell stents (51% vs 31%; $p < 0.01$)³². Consistently, the more recent meta-analysis confirmed that open-cell stents are associated with a 25% higher risk ($p = 0.03$) of developing postprocedural new ischaemic lesions than closed-cell stents³³. No difference,

however, in the short- and intermediate-term risk of stroke or death was observed in patients during CAS with either open-cell or closed-cell stents.

Simplified categorisation into open-cell and closed-cell stent design might conceal true differences, since both stent types may feature different free cell areas and strut connections. The risk for postprocedural adverse cerebral events has been related to the size of the carotid stent free cell area, indicating a significant impact of carotid stent design on CAS outcome. Consistently, open-cell stents with a free cell area $> 7.5 \text{ mm}^2$ have been associated with an increased 30-day stroke risk³⁴.

Importantly, based on the CREST trial, around 40% of strokes in the CAS treatment arm occurred 24 hours post-procedure (median 3.5 days)³⁵. Significant incidence of serious cerebral ischaemic complications after removing embolic protection further highlights the importance of good plaque coverage for optimal CAS results.

DUAL-LAYER MICROMESH STENTS

Dual-layer micromesh stents (DLMS) are the next generation of carotid stents with an additional built-in protective micromesh which were specifically designed to provide sustained embolic protection after the stent implantation period. The feasibility and good clinical performance of DLMS have been confirmed in several CAS clinical studies³⁶⁻³⁸. Currently, there are two DLMS available, Roadsaver (Terumo) and CGuard (InspireMD).

The CLEAR-ROAD study of the Roadsaver carotid stent reported a 2.1% rate of major adverse events at 30 days in 100 treated patients, with only 1 patient suffering a minor ipsilateral stroke due to atrial fibrillation with inadequate anticoagulation³⁹. An Italian multicentre registry reported excellent clinical performance with no cerebrovascular events within 30 days after CAS using the Roadsaver DLMS in 150 patients⁴⁰. Another multicentre Italian study including 200 patients implanted with the CGuard carotid stent resulted in 2 TIAs, 5 periprocedural minor strokes (2.5%), including 1 thrombosis – solved by surgery – up to 30 days post-procedure⁴¹.

Of note, results of studies reporting mid- to long-term outcomes (up to 6 years) of different DLMS support the efficacy and durability of this novel device class by showing relatively low ipsilateral stroke, in-stent restenosis, and target lesion revascularisation rates^{28,42-48}. Importantly, the latest German-Austrian S3 (2020) recommendations for management of carotid stenosis revascularisation updated the acceptable periprocedural (in-hospital) death/stroke incidence (as monitored by expert neurologists) to $< 2\%$ for asymptomatic and $< 4\%$ in symptomatic patients⁴. This is stricter than the most recent ESVS guideline update, which recommends 30-day death/stroke incidence thresholds of $< 3\%$ and $< 6\%$ for the two patient populations, respectively¹.

In this regard, it is important that an individual patient-level meta-analysis of 4 DLMS studies, including 556 asymptomatic or symptomatic patients treated either with the Roadsaver or CGuard carotid stents, showed very favourable 30-day safety results, with periprocedural stroke noted in 1.07% (0 major strokes), 30-day

stroke in 1.25%, and death in 0.17% of patients⁴⁹. Furthermore, no independent predictors of peri- or postprocedural adverse events, including symptomatic status, were identified. The investigators concluded that the low rate of adverse events, independent of clinical, anatomical and procedural characteristics, suggests that DLMS as a device class are safe for usage in guideline-based CAS and that they may have a possible clinical benefit over the conventional single-layer stents⁴⁹.

Comparably, a meta-analysis of 10 studies (combining the data on 635 asymptomatic or symptomatic patients) confirmed a low 30-day stroke and death rate of 2% ($p < 0.0001$) with DLMS, without a major difference in the clinical performance of the 2 types of DLMS (CGuard vs Roadsaver)⁵⁰. Recently, other real-world studies have also confirmed the excellent safety and performance of DLMS during CAS in non-selected patient populations^{28,45,48,51,52}. Finally, the ROADS AVER study, the largest real-world DLMS study to date, with close to 2,000 elective patients enrolled, further complements the available clinical evidence on DLMS use in current CAS⁵³.

In this all-comers patient cohort, reflecting pan-European contemporary CAS practice, the Roadsaver DLMS results in 30-day death/stroke rates well below the strictest German-Austrian S3 recommendations⁴, 1.6% versus 2.0% in asymptomatic and 2.8% versus 4.0% in symptomatic patients (data not published).

While the current guidelines do not explicitly support the use of a particular stent type, stent designs providing better plaque coverage, including closed-cell stents and particularly DLMS, may actually limit plaque protrusion through the stent struts, thus lowering the incidence of cerebral embolisation during and after device implantation¹.

FUTURE PERSPECTIVES

A quality assurance program adopting competency in practice-based training and improvement, credentialing, and monitoring of procedural technique and outcomes can ensure high-quality CAS or CEA.

A multidisciplinary team review (neurologists or stroke physicians, vascular surgeons and interventional cardiologists or radiologists) is recommended to reach consensus decisions regarding the indications and treatment of patients with carotid stenosis regarding CEA, CAS or OMT alone. Shared decision-making, including patient preferences after thoughtful informed consent, is vital in selecting the more appropriate procedure for individual patients. A thorough pre-revascularisation multidisciplinary assessment, using multimodality imaging, with particular emphasis on the degree of stenosis as one of the main factors determining the benefits of revascularisation, may be the most appropriate approach in eligible patients.

Based on current expertise, and considering recently published data, contemporary CAS and CEA can be considered as complementary methods for treating asymptomatic patients with 70-99% stenosis and symptomatic patients with 50-99% artery stenosis. Considering anatomical and medical factors, it is particularly important to identify patients who would benefit mostly from one approach or the other (**Table 1**).

A recent analysis suggested that high operator volume was associated with a lower risk of death or stroke following CAS⁵⁴. Consequently, the importance of the centre's and operator's experience, particularly the annual operator volume (a better predictor of 30-day death or stroke rate after CAS than lifetime operator volume), in performing CAS should always be emphasised^{3,55}. Among appropriately trained, high-volume operators, satisfactory short- and long-term CAS outcomes can be achieved regardless of their specialisation⁵⁶. Continuous training of operators while maintaining a high procedural volume at both the centre and operator level are crucial for successful carotid revascularisation practice. In addition, quality assurance programs and continuous monitoring of complications are required to maintain high-quality management. Decisively, a collaboration between interventionalists, surgeons, and neurologists is essential to ensure proper patient selection and choose the optimal treatment approach.

Table 1. Revascularisation risks and benefits of CAS and CEA.

CAS preferred		CEA preferred	
Clinical history	Anatomical factors	Clinical history	Anatomical factors
<ul style="list-style-type: none"> • Congestive heart failure (NYHA Functional Class III/IV) • Left ventricular ejection fraction $\leq 30\%$ 	<ul style="list-style-type: none"> • Surgically inaccessible lesions: above C2 or below the clavicle • Previous ipsilateral neck irradiation or complex neck surgery 	<ul style="list-style-type: none"> • Elderly (>75 y) 	<ul style="list-style-type: none"> • Extreme access challenges
<ul style="list-style-type: none"> • Unstable angina • Recent myocardial infarction (≤ 30 days) • CAD with left main or multivessel CAD • Planned open heart surgery (≤ 30 days) 	<ul style="list-style-type: none"> • Contralateral carotid artery occlusion • Restenosis after CEA or CAS 	<ul style="list-style-type: none"> • Bleeding disorder, contraindication for DAPT 	<ul style="list-style-type: none"> • Complex and high-grade aortic arch atheroma • Circumferential target lesion calcification • Fresh thrombotic lesion
<ul style="list-style-type: none"> • Advanced COPD 	<ul style="list-style-type: none"> • Spinal neck immobility 		<ul style="list-style-type: none"> • Extreme ICA tortuosity
<ul style="list-style-type: none"> • Contralateral laryngeal palsy 	<ul style="list-style-type: none"> • Tracheostoma 		<ul style="list-style-type: none"> • Aneurismatic ICA morphology

C2: second cervical spine vertebral body; CAD: coronary artery disease; CAS: carotid artery stenting; CEA: carotid endarterectomy; COPD: chronic obstructive pulmonary disease; DAPT: dual antiplatelet therapy; ICA: internal carotid artery; NYHA: New York Heart Association

Conclusions

The recent trials of CAS versus CEA have provided better evidence that both procedures carry similar risks and provide comparable long-term benefits. Comparisons between the two modalities often represent a false choice because the two therapies are better viewed as complementary approaches rather than competitive procedures. In centres of excellence, nowadays, the majority of patients with severe carotid artery stenosis can be successfully treated with either CEA or CAS. A multidisciplinary assessment with a careful patient and lesion analysis based on inclusion and exclusion criteria for both treatment options in high-volume centres of excellence in both strategies, are essential for selecting an optimal treatment approach. Finally, the evaluation should be done individually, tailoring the procedure to a specific patient in order to achieve the best risk-to-benefit balance.

Conflict of interest statement

The author has no conflicts of interest to declare.

References

- Naylor R, Rantner B, Ancetti S, Gert J, de Borst GJ, De Carlo M, Halliday A, Kakkos SK, Markus HS, McCabe DJH, Sillesen H, van den Berg JC, Vega de Ceniga M, Venermo MA, Vermassen FEG, Esvs Guidelines Committee, Antoniou GA, Bastos Goncalves F, Björck M, Chakfe N, Coscas R, Dias NV, Dick F, Hinchliffe RJ, Kolh P, Koncar IB, Lindholt, Mees BME, Resch TA, Trimarchi S, Tulamo R, Twine CP, Wanhainen A, Document Reviewers, Bellmunt-Montoya S, Bulbulia R, Darling 3rd, RC, Eckstein HH, Giannoukas A, Koelemay MJW, Lindström D, Schermerhorn M, Stone DH. Editor's Choice - European Society for Vascular Surgery (ESVS) 2023 Clinical Practice Guidelines on the Management of Atherosclerotic Carotid and Vertebral Artery Disease. *Eur J Vasc Endovasc Surg.* 2023;65:7-111.
- Aboyans V, Ricco JB, Bartelink MEL, Björck M, Brodmann M, Cohnert T, Collet JP, Czerny M, De Carlo M, Debus S, Espinola-Klein C, Kahan T, Kownator S, Mazzola L, Naylor AR, Roffi M, Röther J, Sprynger M, Tendera M, Tepe G, Venermo M, Vlachopoulos C, Desormais I; ESC Scientific Document Group. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS): Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries. Endorsed by: the European Stroke Organization (ESO) The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). *Eur Heart J.* 2018;39:763-816.
- Stabile E, Esposito G. Operator's experience is the most efficient embolic protection device for carotid artery stenting. *Circ Cardiovasc Interv.* 2013;6:496-7.
- Eckstein H-H, Kühnl A, Berkefeld J, Lawall H, Storck M, Sander D. Diagnosis, Treatment and Follow-up in Extracranial Carotid Stenosis. *Dtsch Arztebl Int.* 2020;117:801-7.
- Arning C, Widder B, von Reutern G, Stiegler H, Görtler M. Ultraschallkriterien zur Graduierung von Stenosen der A. carotis interna - Revision der DEGUM-Kriterien und Transfer in NASCET-Stenosierungsgrade. [Revision of DEGUM ultrasound criteria for grading internal carotid artery stenoses and transfer to NASCET measurement]. *Ultraschall Med.* 2010;31:251-7.
- Kleindorfer DO, Towfighi A, Chaturvedi S, Cockroft KM, Gutierrez J, Lombardi-Hill D, Kamel H, Kernan WN, Kittner SJ, Leira EC, Lennon O, Meschia JF, Nguyen TN, Pollak PM, Santangeli P, Sharrief AZ, Smith SC Jr, Turan TN, Williams LS. 2021 Guideline for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack: A Guideline From the American Heart Association/American Stroke Association. *Stroke.* 2021;52:e364-467.
- Müller MD, Lyrer PA, Brown MM, Bonati LH. Carotid artery stenting versus endarterectomy for treatment of carotid artery stenosis. *Stroke.* 2021;52:e3-5
- White CJ, Brott TG, Gray WA, Heck D, Jovin T, Lyden SP, Metzger DC, Rosenfield K, Roubin G, Sachar R, Siddiqui A. Carotid Artery Stenting: JACC State-of-the-Art Review. *J Am Coll Cardiol.* 2022;80:155-70.
- Hobson RW 2nd, Weiss DG, Fields WS, Goldstone J, Moore WS, Towne JB, Wright CB. Efficacy of carotid endarterectomy for asymptomatic carotid stenosis. The Veterans Affairs Cooperative Study Group. *N Engl J Med.* 1993;328:221-7.

- No authors listed. Endarterectomy for asymptomatic carotid artery stenosis. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. *JAMA.* 1995;273:1421-8.
- Halliday A, Mansfield A, Marro J, Peto C, Peto R, Potter J, Thomas D; MRC Asymptomatic Carotid Surgery Trial (ACST) Collaborative Group. Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomised controlled trial. *Lancet.* 2004;363:1491-502.
- Halliday A, Harrison M, Hayter E, Kong X, Mansfield A, Marro J, Pan H, Peto R, Potter J, Rahimi K, Rau A, Robertson S, Streifler J, Thomas D; Asymptomatic Carotid Surgery Trial (ACST) Collaborative Group. 10-year stroke prevention after successful carotid endarterectomy for asymptomatic stenosis (ACST-1): a multicentre randomised trial. *Lancet.* 2010;376:1074-84.
- Howard DPJ, Gaziano L, Rothwell PM; Oxford Vascular Study. Risk of stroke in relation to degree of asymptomatic carotid stenosis: a population-based cohort study, systematic review, and meta-analysis. *Lancet Neurol.* 2021;20:193-202.
- Bonati LH, Kakkos S, Berkefeld J, de Borst GJ, Bulbulia R, Halliday A, van Herzele I, Koncar I, McCabe DJ, Lal A, Ricco JB, Ringleb P, Taylor-Rowan M, Eckstein HH. European Stroke Organisation guideline on endarterectomy and stenting for carotid artery stenosis. *Eur Stroke J.* 2021;6:1-XXVII.
- AbuRahma AF, Avgerinos ED, Chang RW, Darling RC 3rd, Duncan AA, Forbes TL, Malas MB, Perler BA, Powell RJ, Rockman CB, Zhou W. The Society for Vascular Surgery implementation document for management of extracranial cerebrovascular disease. *J Vasc Surg.* 2022;75:26S-98S.
- Brott TG, Hobson RW, Howard G, Roubin GS, Clark WM, Brooks W, Mackey A, Hill MD, Leimgruber PP, Sheffet AJ, Howard VJ, Moore WS, Voeks JH, Hopkins LN, Cutlip DE, Cohen DJ, Popma JJ, Ferguson RD, Cohen SN, Blackshear JL, Silver FL, Mohr JP, Lal BK, Meschia JF; CREST Investigators. Stenting versus endarterectomy for treatment of carotid-artery stenosis. *N Engl J Med.* 2010;363:11-23.
- Rosenfield K, Matsumura JS, Chaturvedi S, Riles T, Ansel GM, Metzger DC, Wechsler L, Jaff MR, Gray W; ACT I Investigators. Randomized Trial of Stent versus Surgery for Asymptomatic Carotid Stenosis. *N Engl J Med.* 2016;374:1011-20.
- Reiff T, Eckstein HH, Mansmann U, Jansen O, Fraedrich G, Mudra H, Böckler D, Böhm M, Brückmann H, Debus ES, Fiehler J, Lang W, Mathias K, Ringelstein EB, Schmidli J, Stinglele R, Zahn R, Zeller T, Hetzel A, Bodechtel U, Binder A, Glahn J, Hacke W, Ringleb PA. Angioplasty in asymptomatic carotid artery stenosis vs. endarterectomy compared to best medical treatment: one-year interim results of SPACE-2. *Int J Stroke.* 2020;15:638-49.
- Halliday A, Bulbulia R, Bonati LH, Chester J, Craddock-Bamford A, Peto R, Pan H; ACST-2 Collaborative Group. Second asymptomatic carotid surgery trial (ACST-2): a randomised comparison of carotid artery stenting versus carotid endarterectomy. *Lancet.* 2021;398:1065-73.
- Jaillant N, Thibouw F, Loucou JD, Pouhin A, Kazandjian C, Steinmetz E. A Prospective Survey of The Incidence of Cranial and Cervical Nerve Injuries After Carotid Surgery. *Ann Vasc Surg.* 2022;87:380-7.
- Lal BK, Meschia JF, Brott TG. Clinical need, design, and goals for the Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis trial. *Semin Vasc Surg.* 2017;30:2-7.
- Featherstone R, Brown M. The Second European Carotid Surgery Trial. *Endovasc Today.* 2012;10:75-77. <https://evtoday.com/articles/2012-oct/the-second-european-carotid-surgery-trial>. Last accessed 14 June 23.
- Shishebor MH, Venkatachalam S, Gray WA, Metzger C, Lal BK, Peng L, Omran HL, Blackstone EH. Experience and Outcomes With Carotid Artery Stenting: An Analysis of the CHOICE (Carotid Stenting for High Surgical-Risk Patients; Evaluating Outcomes Through the Collection of Clinical Evidence) Study. *JACC Cardiovasc Interv.* 2014;7:1307-17.
- Hellings WE, Ackerstaff RG, Pasterkamp G, De Vries JP, Moll FL. The carotid atherosclerotic plaque and microembolisation during carotid stenting. *J Cardiovasc Surg (Torino).* 2006;47:115-26.
- Obeid T, Arnaoutakis DJ, Arhuidese I, Qazi U, Abularrage CJ, Black J, Perler B, Malas M. Poststent ballooning is associated with increased peri-procedural stroke and death rate in carotid artery stenting. *J Vasc Surg.* 2015;62:616-23.
- Langhoff R, Schofer J, Scheinert D, Schmidt A, Sedgewick G, Saylor E, Sachar R, Sievert H, Zeller T. Double filtration during carotid artery stenting using a novel post-dilatation balloon with integrated embolic protection. *JACC Cardiovasc Interv.* 2019;12:395-403.
- Langhoff R, Petrov I, Kedev S, Milosevic Z, Schmidt A, Scheinert D, Schofer J, Sievert H, Sedgewick G, Saylor E, Sachar R, Cremonesi A, Micari A. PERFORMANCE 1 study: Novel carotid stent system with integrated post-dilatation balloon and embolic protection device. *Catheter Cardiovasc Interv.* 2022;100:1090-9.
- Petkoska D, Zafirovska B, Vasilev I, Novotni G, Bertrand OF, Kedev S. Radial and ulnar approach for carotid artery stenting with Roadsaver™ double layer micromesh stent: Early and long-term follow-up. *Catheter Cardiovasc Interv.* 2023;101:154-63.

29. Maciejewski DR, Tekieli L, Trystula M, Tomaszewski T, Machnik R, Legutko J, Kazibudzki M, Musiał R, Misztal M, Pieniążek P. Clinical situations requiring radial or brachial access during carotid artery stenting. *Postępy Kardiologii Interwencyjnej*. 2020;16:410-7.
30. Galyfos GC, Tsoutsas I, Konstantopoulos T, Galanopoulos G, Sigala F, Filis K, Papavassiliou V. Editor's Choice - Early and Late Outcomes after Transcarotid Revascularisation for Internal Carotid Artery Stenosis: A Systematic Review and Meta-Analysis. *Eur J Vasc Endovasc Surg*. 2021;61:725-38.
31. Paraskevas KI, Antonopoulos CN, Kakisis JD, Geroulakos G. An updated systematic review and meta-analysis of results of transcervical carotid artery stenting with flow reversal. *J Vasc Surg*. 2020;72:1489-98.e1.
32. Schnaudigel S, Gröschel K, Pilgram SM, Kastrop A. New brain lesions after carotid stenting versus carotid endarterectomy: a systematic review of the literature. *Stroke*. 2008;39:1911-9.
33. de Vries EE, Meershoek AJA, Vonken EJ, den Ruijter HM, van den Berg JC, de Borst GJ. A meta-analysis of the effect of stent design on clinical and radiologic outcomes of carotid artery stenting. *J Vasc Surg*. 2019;69:1952-61 e1.
34. Stabile E, Giugliano G, Cremonesi A, Bosiers M, Reimers B, Setacci C, Cao P, Schmidt A, Sievert H, Peeters P, Nikas D, Sannino A, de Donato G, Parlani G, Castriota F, Hornung M, Rubino P, Esposito G, Tesorio T. Impact on outcome of different types of carotid stent: results from the European Registry of Carotid Artery Stenting. *EuroIntervention*. 2016;12:e265-70.
35. Hill MD, Brooks W, Mackey A, Clark WM, Meschia JF, Morrish WF, Mohr JP, Rhodes JD, Popma JJ, Lal BK, Longbottom ME, Voeks JH, Howard G, Brott TG; CREST Investigators. Stroke after carotid stenting and endarterectomy in the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST). *Circulation*. 2012;126:3054-61.
36. Musialek P, Mazurek A, Trystula M, Borratynska A, Lesniak-Sobelga A, Urbanczyk M, Barys P, Brzywczy A, Zajdel W, Partyka L, Zmudka K, Podolec P. Novel PARADIGM in carotid revascularisation: Prospective evaluation of All-come peRcutaneous cAroTiD revascularisation in symptomatic and Increased-risk asymptomatic carotid artery stenosis using CGuard MicroNet-covered embolic prevention stent system. *EuroIntervention*. 2016;12:e658-70.
37. Schofer J, Musialek P, Bijuklic K, Kolvenbach R, Trystula M, Siudak Z, Sievert H. A Prospective, Multicenter Study of a Novel Mesh-Covered Carotid Stent: The CGuard CARENET Trial (Carotid Embolic Protection Using MicroNet). *JACC Cardiovasc Interv*. 2015;8:1229-34.
38. Hopf-Jensen S, Marques L, Preiss M, Müller-Hülsbeck S. Initial clinical experience with the micromesh Roadsaver carotid artery stent for the treatment of patients with symptomatic carotid artery disease. *J Endovasc Ther*. 2015;22:220-5.
39. Bosiers M, Deloose K, Torsello G, Scheinert D, Maene L, Peeters P, Müller-Hülsbeck S, Sievert H, Langhoff R, Bosiers M, Setacci C. The CLEAR-ROAD study: evaluation of a new dual layer micromesh stent system for the carotid artery. *EuroIntervention*. 2016;12:e671-6.
40. Nerla R, Castriota F, Micari A, Sbarzaglia P, Secco GG, Ruffino MA, de Donato G, Setacci C, Cremonesi A. Carotid artery stenting with a new-generation double-mesh stent in three high-volume Italian centres: clinical results of a multidisciplinary approach. *EuroIntervention*. 2016;12:e677-83.
41. Speziale F, Capoccia L, Sirignano P, Mansour W, Pranteda C, Casana R, Setacci C, Accrocca F, Alberti D, de Donato G, Ferri M, Gaggiano A, Galzerano G, Ippoliti A, Mangialardi N, Pratesi G, Ronchey S, Ruffino MA, Siani A, Spinazzola A, Sponza M. Thirty-day results from prospective multi-specialty evaluation of carotid artery stenting using the CGuard MicroNet-covered Embolic Prevention System in real-world multicentre clinical practice: the IRON-Guard study. *EuroIntervention*. 2018;13:1714-20.
42. Bosiers M, Deloose K, Torsello G, Scheinert D, Maene L, Peeters P, Müller-Hülsbeck S, Sievert H, Langhoff R, Callaert J, Setacci C, Wauters J. Evaluation of a new dual-layer micromesh stent system for the carotid artery: 12-month results from the CLEAR-ROAD study. *EuroIntervention*. 2018;14:1144-6.
43. Nerla R, Micari A, Castriota F, Miccichè E, Ruffino MA, de Donato G, Setacci C, Cremonesi A. Carotid artery stenting with a new-generation double-mesh stent in three high-volume Italian centres: 12-month follow-up results. *EuroIntervention*. 2018;14:1147-9.
44. Mazurek A, Borratynska A, Malinowski KP, Brozda M, Gancarczyk U, Dłużniewska N, Czyż L, Duplicka M, Sobieraj E, Trystula M, Drazkiewicz T, Podolec P, Musialek P. MicroNET-covered stents for embolic prevention in patients undergoing carotid revascularisation: twelve-month outcomes from the PARADIGM study. *EuroIntervention*. 2020;16:e950-2.
45. Machnik RA, Pieniążek P, Misztal M, Plens K, Kazibudzki M, Tomaszewski T, Brzywczy A, Musiał R, Trystula M, Tekieli LM. Carotid artery stenting with Roadsaver stent. Early and four-year results from a single-center registry. *Postępy Kardiologii Interwencyjnej*. 2020;16:444-51.
46. Gray WA, Levy E, Bacharach JM, Metzger DC, Randall B, Siddiqui A, Schonholz C, Alani F, Schneider PA. Evaluation of a novel mesh-covered stent for treatment of carotid stenosis in patients at high risk for endarterectomy: 1-year results of the SCAFFOLD trial. *Catheter Cardiovasc Interv*. 2020;96:121-7.
47. Capoccia L, Sirignano P, Mansour W, Sbarigia E, Speziale F. Twelve-month results of the Italian registry on protected CAS with the mesh-covered CGuard stent: the IRON-Guard study. *EuroIntervention*. 2018;14:1150-2.
48. Sirignano P, Stabile E, Mansour W, Capoccia L, Faccenna F, Intrieri F, Ferri M, Saccà S, Sponza M, Mortola P, Ronchey S, Praquin B, Grillo P, Chiappa R, Losa S, Setacci F, Pirrelli S, Taurino M, Ruffino MA, Udini M, Palombo D, Ippoliti A, Montelione N, Setacci C, de Donato G, Ruggeri M, Speziale F. 1-Year Results From a Prospective Experience on CAS Using the CGuard Stent System: The IRONGUARD 2 Study. *JACC Cardiovasc Interv*. 2021;14:1917-23.
49. Stabile E, de Donato G, Musialek P, De Loose K, Nerla R, Sirignano P, Chianese S, Mazurek A, Tesorio T, Bosiers M, Setacci C, Speziale F, Micari A, Esposito G. Use of Dual-Layered Stents in Endovascular Treatment of Extracranial Stenosis of the Internal Carotid Artery: Results of a Patient-Based Meta-Analysis of 4 Clinical Studies. *JACC Cardiovasc Interv*. 2018;11:2405-11.
50. Sannino A, Giugliano G, Toscano E, Schiattarella GG, Franzone A, Tesorio T, Trimarco B, Esposito G, Stabile E. Double layered stents for carotid angioplasty: A meta-analysis of available clinical data. *Catheter Cardiovasc Interv*. 2018;91:751-7.
51. Sirignano P, Stabile E, Mansour W, Capoccia L, Faccenna F, Intrieri F, Ferri M, Saccà S, Sponza M, Mortola P, Ronchey S, Grillo P, Chiappa R, Losa S, Setacci F, Pirrelli S, Taurino M, Ruffino MA, Udini M, Palombo D, Ippoliti A, Montelione N, Setacci C, de Donato G, Ruggeri M, Speziale F. 1-Month Results From a Prospective Experience on CAS Using CGuard Stent System: The IRONGUARD 2 Study. *JACC Cardiovasc Interv*. 2020;13:2170-7.
52. Kahlberg A, Bilman V, Ardita V, Mascia D, Bertoglio L, Rinaldi E, Melissano G, Chiesa R. Contemporary Results of Carotid Artery Stenting Using Low-Profile Dual-Metal Layer Nitinol Micromesh Stents in Relation to Single-Layer Carotid Stents. *J Endovasc Ther*. 2021;28:726-36.
53. Kedev S, Müller-Hülsbeck S, Langhoff R. "Real-World Study of a Dual-Layer Micromesh Stent in Elective Treatment of Symptomatic and Asymptomatic Carotid Artery Stenosis (ROADSAVER)". *Cardiovasc Intervent Radiol*. 2022;45:277-82.
54. Kallmayer MA, Salvermoser M, Knappich C, Trenner M, Karlas A, Wein F, Eckstein HH, Kuehl A. Quality appraisal of systematic reviews, and meta-analysis of the hospital/surgeon-linked volume-outcome relationship of carotid revascularization procedures. *J Cardiovasc Surg (Torino)*. 2019;60:354-63.
55. Calvet D, Mas JL, Algra A, Becquemin JP, Bonati LH, Dobson J, Fraedrich G, Jansen O, Mali WP, Ringleb PA, Chatellier G, Brown MM, Calvet D, Mas JL, Algra A, Becquemin JP, Bonati LH, Dobson J, Fraedrich G, Jansen O, Mali WP, Ringleb PA, Chatellier G, Brown MM, Algra A, Becquemin JP, Chatellier G, Mas JL, Fraedrich G, Ringleb PA, Jansen O, Brown MM; Carotid Stenting Trialists' Collaboration. Carotid stenting: is there an operator effect? A pooled analysis from the carotid stenting trialists' collaboration. *Stroke*. 2014;45:527-32.
56. Timaran CH, Mantese VA, Malas M, Brown OW, Lal BK, Moore WS, Voeks JH, Brott TG; CREST Investigators. Differential outcomes of carotid stenting and endarterectomy performed exclusively by vascular surgeons in the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST). *J Vasc Surg*. 2013;57:303-8.