Carotid Artery Stenting: Review of Technique and Update of Recent Literature

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Semin Intervent Radiol 2013;30:288–296

Abstract

Keywords

- carotid stenosis
- carotid artery stenting
- stroke
- interventional radiology

Stroke is the fourth leading cause of death and the number one cause of long-term disability in the United States. Carotid stenosis is an important cause of ischemic strokes, accounting for 20 to 25%. Previous studies have established carotid endarterectomy as standard of care of symptomatic patients with > 50% stenosis and asymptomatic patients with > 60% stenosis; recently, carotid artery stenting has emerged as an alternative treatment for carotid stenosis. Several studies have been published comparing carotid artery stenting with endarterectomy with mixed results. In this article, the authors discuss carotid artery stenting technique, the results from the most recent trials, and future directions.

Objectives: Upon completion of this article, the reader will be able to describe carotid stenting, including indication, technique, perioperative patient care, and outcomes.

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Stroke is the fourth leading cause of death and the number one cause of long-term severe disability in the United States.¹ Carotid stenosis (CS) is an important cause of ischemic stroke accounting for 20 to 25%.² Previous studies have established the benefits of carotid endarterectomy (CEA) compared with best medical therapy (BMT).^{3–7} More recently, carotid artery stenting (CAS) has emerged as an alternative to CEA. This article aims to review CAS procedure with specific focus on technique, patient management, and a succinct evaluation of the latest available outcomes data.

Patient Selection

Appropriate patient selection is critical for success. Prior to any procedure, the interventional radiologist should perform a consultation including a tailored history and physical examination along with review of any available imaging and laboratory tests. Stroke risk stratification should be performed and will determine the appropriate treatment plan. Briefly, symptomatic patients (neurological event within the preceding 6 months) with > 50% CS and asymptomatic patients with > 60% CS are candidates for carotid revascularization. Choice between CEA and CAS will depend on patient factors, operator preference, and possibly third-party payer. At the time of writing this article, Medicare reimbursement is limited to high surgical risk symptomatic patients with > 70 to 99% stenosis, high surgical risk symptomatic patients with > 50 to 70% stenosis (in an approved trial), and high surgical risk asymptomatic patients with > 80% stenosis (in an approved trial). The Center of Medicare and Medicaid Services (CMS) defines high risk to include but not limited to the following comorbid conditions: congestive heart failure class III/IV, left ventricular ejection fraction < 30%, unstable angina, contralateral carotid occlusion, recent myocardial infarction, previous CEA with restenosis, prior radiation treatment to the neck, and other conditions enumerated by previous carotid stenting trials.⁸ Risk factor modifications

Issue Theme Neurointerventions for the Interventional Radiologist; Guest Editors, Gregory M. Soares, MD, FSIR and Sun Ho Ahn, MD

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Tel: +1(212) 584-4662.

DOI <http://dx.doi.org/10.1055/s-0033-1353482>.
ISSN 0739-9529.

(i.e., control of hypertension, diabetes, lipids, smoking cessation, and exercise) should be performed regardless of intent for revascularization.⁹

Patient Preparation

Once the decision to perform CAS has been made, a detailed informed consent should be obtained. Oral antiplatelet therapy with clopidogrel should be initiated 5 days prior to treatment date. If this is not practical, a loading dose of 300 mg of clopidogrel should be given 4 to 5 hours prior to the procedure. Routine prophylaxis for preexisting contrast allergy and/or renal insufficiency should be performed per protocol. Baseline neurological examination should be performed and documented. Bilateral inguinal regions should be sterilely prepared for access.

Diagnostic Arteriogram

The right common femoral artery (CFA) is the preferred access for CAS. The left CFA and the brachial artery are alternative accesses if the right CFA is not optimal. Once access is gained, a short 5-F vascular sheath should be placed and set to a continuous heparinized saline infusion. Cervical arch aortography obtained at approximately 35 degrees left anterior oblique projection should profile the origins of the great vessels. This step may be skipped if recent, high-quality, noninvasive imaging of the cervical aortic arch is available for reference. Catheter selection for common carotid artery (CCA) catheterization will depend on the aortic arch anatomy. The aortic arch may be classified based on the origins of the great vessels in reference to the convexity of the aortic arch: Type I—great vessel origins are level with upper convexity; Type II—great vessel origins are between the upper and lower convexity; and Type III—great vessel origins are caudal to lower convexity (►Fig. 1). Selection of great vessels in the setting of Type III arch can present a challenge and typically requires a reverse curve catheter (e.g., Simmons 2 or 3 [Cook Medical Inc., Bloomington, IN]).

The CCA is selected and anterior-posterior and lateral projections of the cervical carotid artery should be obtained.

Oblique projections may be necessary to optimally visualize the stenosis. In some instances, a reference marker (e.g., 1-cm metallic sphere) may be placed on the patient to allow accurate calibration for stenosis grading. Meticulous attention to flushing technique is recommended to minimize the risk of embolus. For stenosis analysis, North American Symptomatic Carotid Endarterectomy Trial (NASCET) technique is recommended; that is, the narrowest portion of the stenosis is referenced to the most normal diameter immediately cephalad to the stenosis and not below. If the stenosis fails to meet criteria, then the procedure is terminated and the patient should be followed clinically and managed with BMT. If the stenosis is confirmed, baseline ipsilateral cerebral angiography is performed.

Carotid Artery Stenting

An exchange length guide-wire is placed with the tip in the distal CCA or in the external carotid artery. Attention is needed to avoid inadvertent wire contact with the stenosis. A sheath with sufficient length and diameter is placed (most commonly a 90-cm 6F sheath). The authors prefer the 6F Shuttle (Cook Medical Inc.). When using the Shuttle sheath, extra attention should be paid once the tip has reached the CCA. As the leading dilator portion is lengthy and rather non-radio-opaque, the sheath should be carefully advanced with the dilator portion fixed once the combination has securely reached the CCA, to avoid inadvertent advancement of the dilator into the stenosis. The Shuttle is equipped with a Tuohy-Borst (Y-adapter) (Cook Medical Inc.), which is adequate, but can lead to much back bleeding during exchanges and stent deployment. The authors prefer to replace the Tuohy-Borst sidearm with a Check-Flo Performer Assembly (Cook Medical Inc.) to reduce blood loss (►Fig. 2).

Intravenous anticoagulation is required and most operators prefer unfractionated heparin. A bolus dose of 100 unit/kg is administered and titrated to reach an activated clotting time (ACT) of 250 to 300 seconds. Bivalirudin, a direct thrombin inhibitor, is an effective alternative to heparin and favored by some due to its short half-life of 25 minutes. The dosage of bivalirudin is 1 mg/kg bolus followed by a 0.2

Figure 1 Cervical arch classification. (A) Type 1—The origins of the great vessels (solid line) are level to the upper convexity of the aortic arch. (B) Type 2—The origins of the great vessels (solid line) occur between the levels of the upper and lower convexities of the aortic arch (dashed line). (C) Type 3—The origins of the great vessels (solid line) occur below the lower convexity of the aortic arch (dashed line).

Figure 2 Shuttle sheath with pre-packaged Y-adaptor (top). Check-Flo Performer Assembly (Cook Medical Inc., Bloomington, IN) connected to the 6F shuttle sheath to minimize back bleeding (bottom).

mg/kg infusion. Routine administration of glycoprotein IIb/IIIa inhibitors is not recommended.

Once the sheath is in place and the desired ACT level is reached, anticipated equipment should be prepped and readied for use on the sterile field, including the embolic protection device (EPD), stent, angioplasty balloon, and recapture catheter. Having the equipment ready will help to minimize the time duration of the deployed EPD.

Embolic Protection Device Placement

There are three general types of EPD: distal occlusion balloon, distal filter device, and proximal flow diversion. All these three types have advantages and disadvantages. The authors prefer the distal filter type and as a result will limit the discussion to it; techniques for proximal flow diversion devices have been published elsewhere.^{10,11} Using the reference marker, an appropriately sized EPD (slightly larger than internal carotid diameter) should be selected and placed. Irrespective of the type, the EPD should be upsized approximately 1 mm to provide optimal embolic protection. The EPD should be deployed in the straight terminal segment of the cervical carotid artery with enough distance from the stenosis to allow sufficient space to deliver the stent. Once deployed, adequate apposition to the carotid arterial wall needs to be ensured by angiography. If the device is too small, emboli may not be captured, and if too large the EPD may cause arterial injury or induce vasospasm. Special attention should be given to minimize cranial-caudal motion of the EPD once deployed, as excess motion may also lead to dissection or, more commonly, vasospasm (—Fig. 3). The major disadvantage of

Figure 3 Vasospasm caused by EPD. The left image shows EPD in place. The right image shows mild vasospasm (arrow) at the site of EPD deployment on completion angiogram. This degree of vasospasm typically will resolve with time without any consequence. Occurrence of EPD-induced vasospasm can be reduced by appropriately sized EPD and minimization of motion of EPD during the carotid artery stenting. EPD, embolic protection device.

the distal protection devices is the lack of protection during the initial engagement of the stenosis with the EPD delivery system prior to EPD deployment. As mentioned above, at the authors' institution, the distal filter-type EPD is favored—that is, Angioguard RX Emboli Capture Guidewire System (Cordis Corporation, Bridgewater, NJ). The authors tend to use road-map technique during positioning of the EPD, as it avoids blind probing of the stenosis. In complex or severe stenosis, the leading wire portion of the EPD may not be sufficiently selective to atraumatically traverse the stenosis, usually due to lack of steerability of the wire tip. In such instance, a 0.014-inch guide-wire, e.g., Synchro (Stryker, Kalamazoo, MI) and a microcatheter may be necessary to successfully and atraumatically cross the stenosis. Once the wire has successfully crossed the stenosis, a distal filter type such as SpiderFx Embolic Protection Device (Covidien, Mansfield, MA) can be deployed. Briefly, the SpiderFx is housed in the “garage,” which is distal (closer to the CFA access) to the monorail wire exit port. Thus, once the micro-wire and microcatheter are used to successfully negotiate the stenosis, the delivery system is advanced beyond the stenosis over the micro-wire. Then the micro-wire is removed via the monorail exit, and the EPD is advanced from the garage to the delivery catheter tip, uncovered, and deployed. The distal occlusion type, in comparison with the distal filter type, has additional disadvantages aside from lack of protection during delivery. A small number of patients may develop neurological symptoms during distal balloon occlusion, precluding its use. The advantage of the proximal protection device such as the Gore Flow Reversal (Gore & Associates, Flagstaff, AZ) or Mo.Ma Ultra Proximal Cerebral Protection Device (Medtronic, Inc., Minneapolis, MN) is that the stenosis is not crossed with any device until protection is engaged; thus, the entire procedure is protected. However, a larger 9F sheath and venous access are also required. Additionally, as with the distal occlusion

type, a minority of patients may not tolerate the occlusion due to insufficient collateral circulation.

Predilation

Predilation of the stenosis after the placement of the EPD and before stent deployment is controversial. The theoretical benefits include less traumatic stent delivery and reduced need for postdelivery dilation. The potential disadvantages include the risk of distal embolization, potential for plaque rupture without stent protection, and additional time requirements. The authors do not favor predilation but will perform it for cases when the stent cannot be safely advanced. If predilation is desired, a 2.5- or 3-mm diameter balloon should suffice. In a native carotid artery (i.e., no previous CEA), prior to predilation 0.5 to 1 mg of atropine may be given prophylactically or be ready for administration if bradycardia ensues.

Stent Placement

Nitinol or Elgiloy-based self-expanding stents are used for CAS. The stent length has to be sufficiently long enough to completely cover the stenosis, which in most cases necessitates extending from it from the CCA to the ICA. To achieve optimal wall apposition in all carotid segments, the stent diameter needs to match that of the CCA. The stent should be advanced slightly beyond the desired location distal to the stenosis and retracted prior to deployment to reduce any slack or redundancy that may cause the stent to jump forward. If there is incomplete coverage of the stenosis, a second stent may need to be placed. Atropine should be given or be ready to give immediately in the event of bradycardia.

Postdilation

After the stent is placed, postdilation may be required if the stent is not expanded adequately. However, it is generally advised to avoid the temptation to over-dilate the stent or to make it look "perfect." Successful outcomes of CAS have been reported with intentional avoidance of routine postdilation as stents have been observed to expand spontaneously over time.^{12,13} Avoiding routine postdilation of the stent may help to reduce undesired embolic events. Judicious use of balloon dilation may be required in recalcitrant or heavily calcified stenoses, in which the luminal diameter is inadequate after initial stent deployment. The authors prefer not to post-dilate unless the post-CAS carotid diameter is < 5 mm. If postdilation is required, a 5-mm balloon is used to gently dilate the stenosis. Again, atropine may be necessary.

EPD Removal and Completion Angiogram

After the stent placement and postdilation (if needed) are completed, then the EPD must be evaluated for trapped embolic material before it can be recaptured. In cases where a significant embolic load is detected, an aspiration catheter should be used to clear any trapped debris. In the vast

majority of cases, the embolic load will be minimal and the EPD can be collapsed safely with the appropriate catheter. Once the EPD is recaptured, removal under fluoroscopic observation is recommended as the EPD may engage the stent margin because it is withdrawn through the stent. Turning the patient's head or asking the patient to cough or perform the Valsalva maneuver may aid with removal. In the rare instance that typical maneuvers are not successful, increased steerability of the EPD is required. Replacing the recapture catheter with an angled 5F catheter will allow the EPD to be negotiated through stent in most cases. If the EPD is on a monorail system, then a 5F catheter will need to be converted to a monorail from over the wire system by creating a hole near the leading end of the catheter.¹⁴ At the authors' institution, this technique has been performed successfully with a 5F Davis (Cook Medical Inc.) catheter (►Fig. 4). The SpiderFx (Covidien) is an exception as it has enough length for an over-the-wire exchange, as long as the wire has not been intentionally separated. After the EPD is successfully removed, a completion angiogram to include both the cervical ICA and the intracranial circulation is performed to evaluate for residual stenosis, exclude vasospasm or dissection, and evaluate intracranial blood flow. This should be compared with the preprocedure angiogram, as distal emboli can be subtle. The patient may be asked to answer simple questions or perform simple tasks as a basic neurological evaluation prior to access discontinuation. Hemostasis may be obtained with manual compression or a closure device. ►Figure 5 demonstrates the typical steps for routine CAS procedure.

Postprocedural Care

After CAS is completed, the patient should be recovered from anesthesia and admitted for observation. Serial neurological examinations should be performed and documented. Routine evaluation of the access site is appropriate. Serial hemodynamic monitoring is recommended; if postprocedural hypotension is noted, volume resuscitation is typically adequate. Rarely, pharmacological pressure support and critical care monitoring are required. If hypertension is present, it is advised to lower the blood pressure to below 150 mm Hg systolic. At the authors' institution, most patients are admitted to a neurology unit on the interventional radiology admission service after brief recovery in the postprocedure unit. Most patients are discharged the next day with longitudinal follow-up. Clopidogrel should be continued for 30 to 45 days, after which aspirin should be taken for life. Ultrasound follow-up is recommended at 3 months, 6 months, and then yearly.

Outcomes

Several randomized controlled trials have compared CAS with CEA in the recent literature. Because of the heterogeneity of patient populations, study endpoints, operator experience levels, treatment technique, etc., consensus has been difficult to reach and more questions have been raised than

Figure 4 Removal of EPD with a 5F Davis catheter. Recaptured EPD could not be removed as it engaged the top margin of the stent despite typical maneuvers including turning of the head and Valsalva maneuver (not shown). (A) 5F Davis catheter (black arrow) was converted into a monorail recapture device and advanced through the stent. (B) Once the EPD was captured into the 5F Davis catheter, it was easily removed. EPD, embolic protection device.

answered. However, several trends have been observed, and the authors of the article will attempt to highlight these in a practical manner.

Overall, the data for CAS are encouraging. Over the past 10 to 15 years, the CAS data have shown progressive improvements in terms of 30-day mortality and stroke rates, as illustrated by Silver et al.¹⁵ Wallstent (2001, published only in abstract form), which enrolled symptomatic patients with > 60% stenosis and was terminated early, and Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS, in 2001), a trial of average risk and mostly symptomatic patients, produced combined 30-day stroke and death rates of 12.1 and 10%, respectively.^{16,17} Subsequently, Stent-Protected Angioplasty versus Carotid Endarterectomy (SPACE, in 2006), Endarterectomy versus Angioplasty in Patients with Severe Symptomatic Carotid Stenosis (EVA-3S, in 2006), International Carotid Stent Study (ICSS, in 2009), and Carotid Revascularization Endarterectomy versus Stenting Trial (CREST, in 2010) have shown 7.7, 9.6, 7.4, and 6% combined 30-day stroke and death rates, respectively, for symptomatic and average risk patients.^{18–21} Please note that CREST included asymptomatic patients in its study population. This is an encouraging trend and not unlike what has been seen with CEA publications. It stands within reason that with better understanding of natural history of carotid occlusive disease and advances in technology, CAS data will continue to improve.

Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) investigators compared CAS with CEA in symptomatic and asymptomatic patients with high surgical risk, that is, those excluded in the prior surgical trial comparing CEA with BMT. Using a composite of stroke, myocardial infarction, and death as the primary endpoint, CAS was shown not to be inferior to CEA.²² The SAPPHIRE trial findings ultimately contributed to CMS and Medicare coverage decision for CAS in high surgical risk patients with symptomatic CS between 51 and 99% and high

surgical risk patients with asymptomatic CS > 80%. Within the eligible group, symptomatic patients with 51 to 70% and asymptomatic patients with > 80% CS are eligible for CAS Medicare coverage only if enrolled in an approved research trial. Stenting must be performed with EPD in all patients to qualify for reimbursement.

Following SAPPHIRE, several studies have compared CAS with CEA for average surgical risk patients. The results have been mixed. No significant difference between CAS and CEA was shown in the most recent randomized trial, CREST. This was a study of 2,502 patients with symptomatic or asymptomatic CS with average surgical risk randomized to either CAS or CEA. The combined rates of stroke, myocardial infarction, or death were not significantly different between CAS and CEA (7.2 vs. 6.8%, respectively).²⁰ In contrast, EVA-3S, a randomized study of $\geq 60\%$ symptomatic stenosis, was terminated early due to excessively higher rate of death and stroke in the CAS treatment arm at 30 days (9.6 vs. 3.9%; $p = 0.01$).¹⁹ In the SPACE trial, another comparison of CAS versus CEA, similar results to CREST, was reported in 1,200 symptomatic patients. The primary endpoints (ipsilateral stroke and death) were not significantly different between CAS (6.8%) and CEA (6.3%). However, due to the design of the study, the investigators concluded that CAS had failed to demonstrate noninferiority, as CAS did not meet the prespecified 2.5% margin difference.¹⁸ CAS compared with endarterectomy in patients with symptomatic CS (International Carotid Stenting Study) randomized 1,713 patients; at 120 days, the rates of disabling strokes and death were 4.0 versus 3.2% for CAS and CEA, respectively; and combined stroke, death, and myocardial infarction rates were higher for CAS compared with CEA (8.5 vs. 5.2%, respectively).²¹

A more detailed evaluation of these studies reveals limitations that may hinder the validity of their results. As CAS is a relatively newer procedure compared with CEA, which has matured over several decades, operator inexperience may be

Figure 5 Step-by-step approach to carotid stenting. (A) Anterior-posterior and lateral projections of the cervical carotid artery show restenosis of the left internal carotid artery (arrow) after previous CEA. (B) Lateral image of the neck shows the EPD deployed, confirmed by visibility of the four separate radio-opaque dots (arrow). (C) Lateral projection shows the appropriately sized EPD deployed (arrow). (D) Post-stent carotid angiogram shows no emboli in the EPD allowing for safe removal. (E) Completion carotid angiogram shows technically successful stent placement (arrow). CEA, carotid endarterectomy; EPD, embolic protection device.

a factor contributing to higher complication rates. In a review of Medicare beneficiaries treated with CAS, a correlation between lower annual case volumes and early experience with increased 30-day mortality rates was observed.²³ The investigators of SPACE also found that centers with higher

numbers of study enrollees had lower complication rates in CAS, but this was not observed in the CEA group, attesting to the maturity of CEA.²⁴ Both SPACE and EVA-3S have been criticized for inclusion of inexperienced operators. On the contrary, CREST applied much more rigorous criteria to select

its CAS operators, which may partially explain the improved outcomes of this study.

EPD utilizations may also have contributed to mixed outcomes. While no conclusive data exist on the absolute benefits of EPD, its use is widely adopted. While CREST had near universal application of EPD, EVA-3S adopted EPD use late in the trial and only 27 and 72% of patients in SPACE and ICSS, respectively, used EPD, which may have contributed to higher stroke rates. Moreover, similar to CAS, there is likely a learning curve for EPD use. In addition, future refinements will hopefully lead to reductions in perioperative stroke rates.

A Cochrane database meta-analysis of 16 trials, totaling 7,572 patients, has provided several insights regarding the efficacy of CAS. For non-high-risk patients with symptomatic CS in the perioperative period (randomization to 30 days): (1) CAS and CEA did not show significant difference in death and disabling stroke rates, (2) CAS had higher total stroke rate, and (3) CAS had lower myocardial infarction, cranial nerve palsy, and access site hematoma rates compared with CEA.²⁵ In the follow-up period after 30 days from the procedure, CAS and CEA had no significant difference in stroke rates.²⁵ CREST, which was included in the meta-analysis, showed that, in the periprocedural period, CAS had a higher death rate (0.7 vs. 0.3%, respectively; not significant (ns), CAS had a higher overall stroke rate (4.1 vs. 2.3%, respectively; $p = 0.01$), and CEA had a higher myocardial infarction rate (2.3 vs. 1.1%, respectively; $p = 0.03$). From 30 days after the procedure to 4 years of follow-up, the stroke rates were low for both groups (2.0% for CAS and 2.4% for CEA).²⁰ It is clear that if CAS is to make further gains, reduction in perioperative stroke rate may hold the key.

Investigators have performed secondary analyses in an attempt to identify factors that may have potential effects on CAS outcomes. Advanced patient age appears to have a negative effect on CAS outcomes. Despite the exclusion of > 80-year-old patients in the earlier CEA trials as high risk, recent comparative studies have indicated that CAS had worse outcomes than CEA in older patients.^{18–20} Meta-analysis of EVA-3S, SPACE, ICSS, and Cochrane meta-analysis have shown that patients older than 70 years have higher incidence of negative events with CAS compared with CEA.^{25,26} Conversely, patients younger than 70 years tended to do slightly better with CAS.²⁰ The negative CAS outcome correlation with advanced age is likely due to difficult anatomy more commonly found in the elderly who may pose a technical challenge, especially for the less experienced operators. With experience and proper patient selection, researchers have shown that CAS can be performed with low complication rates in the elderly. Grant et al²⁷ and Setacci et al²⁸ have published their experience of CAS in octogenarians with low complication rates; not surprisingly, difficult anatomies including aortic and great vessel calcification and tortuosity, as well as Type III aortic arch configuration, were statistically more common in the elderly.²⁸ The true effect of age on CAS and CEA outcomes is critical²⁹ as the proportion of the elderly population increases. Moreover, in general practice, the majority (59%) of carotid revascularization is performed on patients older than 70 years.³⁰

The effect of operator experience has been proposed to influence CAS outcomes. It makes sense that lack of experience and expertise in any procedure may lead to higher complication rates during the learning curve. The comparison of study centers in SPACE showed that the complications rates were directly correlated with lower numbers of study patients.²⁴ Nallamothu et al stratified Medicaid beneficiaries who had CAS from 2005 to 2007 by operator case volume levels, and early and late results during new operators' experience. The study showed statistically significant relationship between 30-day mortality rates and low operator volume and early experience.²³ Analysis of the Carotid AC-CULINK/ACCUNET Post Approval Trial to Uncover Rare Events (CAPTURE 2) revealed that to achieve a combined death and stroke rate below 3%, a minimum of 72 cases was necessary, a strikingly high number. In another study, more adverse events were also found in hospitals with low patient volumes and for individual operators with low volumes.³¹ Despite these reports, large meta-analyses have not shown significant differences in outcomes related to CAS operator experience.^{25,32}

Outcomes based on patient gender, symptomatic/asymptomatic status, and EPD use are less compelling and did not show a significant difference.^{15,20,25,32,33} In CREST, gender had no significant effect on primary endpoints; however, women tended to have higher perioperative event rates (mostly stroke) with CAS than with CEA.^{20,33} SPACE and meta-analyses have failed to show any gender predilection for differences in outcomes.^{18,25,32} The current data for EPD use is also inconclusive. Kastrup et al reported a significantly lower perioperative stroke rate with EPD utilization (1.8 vs. 5.5%; $p < 0.001$),³⁴ but recent analyses have not supported this finding.^{25,32}

The literature suggests that both CAS and CEA can provide durable treatments for CS. In the CREST trial, CAS had a slightly lower restenosis rate, which was not statistically significant. Female gender, diabetes, and dyslipidemia significantly increased the risk of restenosis for both CAS and CEA groups in CREST, while smoking was correlated to restenosis for the CAS group only.³⁵ Similarly, EVA-3S did not show a significant difference in restenosis rates between CAS and CEA.¹⁹ In contrast, SPACE showed a significantly higher rate of restenosis for CAS compared with CEA (11.1 vs. 4.6% at 2 years; $p = 0.0007$).¹⁸ Although trying to decipher these conflicting reports is challenging, CREST data may be the most reliable due to more uniform and updated ultrasound criteria for restenosis as well as core ultrasound reading laboratory.

Future Directions

Asymptomatic Patients

In previous studies, CEA has been shown to be superior to BMT for asymptomatic patients with CS > 60%.^{4,6,7} While these trials provided favorable data for CEA, high surgical risk patients were not included. Moreover, the comparison may not be applicable today, as significant improvements in BMT have been made in terms of antiplatelet and antilipid agents. As a result, the optimal treatment for asymptomatic patients

with CS has been the subject of debate.^{36,37} Recent epidemiological studies have shown that with BMT advances, the annual risk of stroke has been reduced to approximately 0.5%^{37–39} compared with 2 to 3% described in aforementioned older studies. Given the low annual risk of stroke, CAS would have to be performed with an extremely low rate of negative outcomes. The current data, including CREST, is underpowered and insufficient to provide any conclusions for the asymptomatic patient population. Going forward, CREST-2 (proposed to compare BMT, CEA, and CAS in asymptomatic patients) and Against Carotid Artery Disease I (ACT1) trial may add additional information regarding the best therapy for asymptomatic patients.

Improvements in Perioperative Stroke

CAS outcomes continue to improve as worldwide operator experience grows and refinements/innovations in equipment occur. This evolution is not dissimilar to the maturation process of CEA. To further improve the safety of the procedure and gain wider acceptance, CAS must be reliably performed with a lower perioperative stroke rate. Improvements in operator experience, identification of the “high risk” CAS patient, and better EPD design may help to decrease CAS perioperative stroke rates. Proximal EPDs appear promising as they allow embolic protection throughout the entire CAS procedure. Distal EPDs, in contrast, offer protection only after the stenosis has been traversed. In a meta-analysis of 2,397 patients treated with two proximal occlusion devices (Gore Flow Reversal System [W. L. Gore & Associates, Inc., Newark, DE] and Mo.Ma Proximal Cerebral Protection Device [Medtronic]), the 30-day stroke, myocardial infarction, and death rates were 1.71, 0.02, and 0.40%, respectively, to yield a composite primary endpoint of 2.25%.⁴⁰ In a recent small study of 62 patients randomized to distal filter device (Emboshield Protection System [Abbott Vascular, Abbott, IL]) or proximal balloon occlusion (PBO) (MO.MA [Invatec, Roncadelle, Italy]), the PBO group had significantly fewer new ischemic lesions on MR imaging. The 30-day rate of major adverse cardiovascular and cerebral events for the PBO was 0% compared with 3.2% for filter protection group.¹⁰

Conclusions

CAS has undergone tremendous evolution over the past 20 years; however, it continues to be the subject of much debate and scrutiny. Large studies performed over the past decade have shown that CAS, when performed by skilled operators, can provide a safe and durable option for revascularization of CS. In certain high-risk patients, some might argue that CAS is already the standard of care. While overall CAS outcomes are similar to those of CEA, further improvements, especially in the reduction of perioperative stroke rate, are likely needed to allow the treatment to become the equivalent or standard of care for all patients. Furthermore, more data, including comparison to BMT particularly in the asymptomatic population, are needed in the future. This work should help to fully define the role of CAS in light of the many

advances that have been made in BMT over the past few decades.

Conflict of Interest

The authors have no conflict of interest.

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