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REVIEW

Carotid Artery Stenting: 2016 and Beyond

Siddharth Wayangankar, MD[1,*], Samir Kapadia, MD[1] and Christopher Bajzer, MD[1]

[1]*Department of Cardiovascular Medicine, Cleveland Clinic, 9500 Euclid Ave, Cleveland, OH 44195, USA*

Abstract

Surgical options developed to treat carotid artery stenosis have evolved in the last six decades, and studies have shown the superiority of carotid endarterectomy (CEA) compared to medical therapy. Similarly, as endovascular therapy has evolved over the last two decades, studies reflecting safety, feasibility, and equivalence of carotid artery stenting (CAS) to CEA have been replicated in several studies for intermediate to high surgical risk patients. However, since its inception, the field of CAS has been mired in several controversies and has been subject to intense scrutiny from multiple stakeholders within the field of medicine. This review discusses specific issues concerning CAS that are relevant in the current era.

Keywords: carotid artery stenting; carotid artery stenosis; carotid artery revascularization

Introduction

It has been over six decades since carotid stenosis was implicated in the pathophysiology of ischemic stroke [1]. Surgical options developed to treat carotid artery stenosis have evolved since then, and studies have shown superiority of carotid endarterectomy (CEA) compared to medical therapy [2]. Similarly, as endovascular therapy has evolved over the last two decades, studies reflecting safety, feasibility, and equivalence of carotid artery stenting (CAS) to CEA have been replicated in several studies for intermediate to high surgical risk patients [3, 4]. However, since its inception, the field of CAS has been mired in several controversies and has been subject to intense scrutiny from multiple stakeholders within the field of medicine. Despite this, CAS as a procedure continues to evolve. In this review, we discuss specific issues concerning CAS that are relevant in the current era.

*Present address: University of Florida, Division of Cardiovascular Medicine, Gainesville, FL, USA.
Correspondence: **Christopher Bajzer**, Department of Cardiovascular Medicine, Cleveland Clinic, 9500 Euclid Ave, Cleveland, OH 44195, USA, E-mail: bajzerc@ccf.org

Indications for Carotid Revascularization

Two aspects of traditional studies comparing surgical carotid revascularization and medical therapy have been flawed by the passage of time. First, medical therapy in most of these studies consisted only of aspirin. Current medical treatment consists of a potent cocktail of anti-platelet, anti-hypertensive and contemporary statin therapies. Hence, results from these traditional studies are difficult to extrapolate to the current era. Secondly, in retrospect, earlier studies were inadequate due to inaccurate post-procedural neurological assessments. In fact, a meta-analysis performed two decades ago showed that the choice of specialty evaluating the post-procedural neurological outcomes was the strongest predictor of 30-day adverse neurological outcomes [5]. It ranged from 7.7%, if evaluated by a neurologist, to 2.3% when evaluated by the operator surgeon. Despite the shortcomings of earlier studies, current guidelines recommend carotid revascularization if the risk of peri-procedural stroke and death is <6% in symptomatic patients and <3% in asymptomatic patients [6]. In general, CAS is preferred

Table 1 High Surgical Risk Medical and Surgical Conditions.

Medical conditions	Surgical considerations
Age >75–80 years	Lesion at or above C2
CHF with NYHA class III/IV	Lesion below the clavicle
Unstable angina – CCS III/IV	Prior neck radiation
CAD with >2 vessels with >70% stenosis	Spinal immobility of the neck
Recent myocardial infarction (<30 days)	Contralateral carotid artery occlusion
Planned open heart surgery (<30 days)	Laryngeal palsy
Ejection fraction <30%	Tracheostomy
Severe pulmonary disease (COPD)	Prior ipsilateral surgery
Renal disease	Prior ipsilateral CEA

CHF, congestive heart failure; NYHA, New York heart association; CAD, coronary artery disease; CCS, Canadian Cardiovascular Scale; CEA, carotid endarterectomy; COPD, chronic obstructive pulmonary disease.
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over CEA when patients have high surgical risks (Table 1).

Symptomatic High Surgical Risk Patients

One of the most important and well-designed studies to establish the equivalence of CAS with CEA was the Sapphire trial (Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy). In this study, both the operators (CAS and CEA) had comparable prior procedural experience. This study showed non-inferior 30-day (CAS, 2.1% vs. CEA, 9.3%, P=0.95) and 1-year (CAS, 16.3% vs. CEA, 20.0%, P=0.58) major adverse cardiac and cerebrovascular outcomes (MACCE) [4]. This equivalence was maintained at 3 years [8]. Currently, CAS coverage for reimbursement is limited to only those who have >70% stenosis and deemed to be high surgical risk patients, or if patients are enrolled in a US Food and Drug Administration (FDA) sanctioned clinical trial [7].

Symptomatic Average Surgical Risk Patient

Table 2 shows the serious shortcomings associated with early studies comparing CAS with CEA. Studies like EVA-3S, SPACE and ICSS had operators with almost negligible prior experience with CAS, and the use of an embolic protection device (EPD) was not mandatory. The latter being a standard of care in clinical practice in the US [13]. As noted in the table, some of the earlier studies had trainees perform CAS to accelerate enrollment. In light of the poor experience, rates of EPD deployment were low, leading to compromised procedural safety within the CAS cohort.

On the other hand, the CREST trial enrolled 1321 symptomatic patients and found no difference in 4-year composite cardiovascular and cerebrovascular outcomes. It was one of the best designed (comparable operator experience) and largest clinical trials comparing CAS and CEA (Table 2). Stroke rates remained similar between groups at 4 years [3]. Unlike the European trials, low volume operators within the CREST trial had a "vetted in" phase where they performed around 10–30 CAS. Based on the lead in phase, operators were selected to be part of the randomized clinical trial. Therefore, the trial compared operators (for CAS and CEA) with similar experience in each of the modalities, thereby bolstering the validity of trial results. Multi-societal guidelines recommend CAS over CEA for average surgical risk patients with the estimated peri-procedural stroke risk being <6% (Table 3).

Should Asymptomatic Patients be Treated?

Studies supporting carotid revascularization like ACAS (Asymptomatic Carotid Atherosclerosis Study) and ACST (Asymptomatic Carotid Sur-

Table 2 Randomized Control Trials Suggesting the Existence of a Procedure-Related Learning Curve with CAS.

Study name	Study period	Population	EPD	N	30-Day event rate	Operator experience
EVA-3S [9]	2000–2005	Sx	78–98%	527	D/S • CEA – 3.9% • CAS – 9.6% (P<0.01)	CAS – 12* or 5* if experience with 30 non-carotid supra-aortic stenting CEA – 25
SPACE [10]	2001–2006	Sx	27%	1200	D/S • CEA – 6.3% • CAS – 6.8% P value for non-inferiority – 0.09	CAS – 10* (perform or assist) CEA – ≥25
ICSS [11]	2001–2008	Sx	72%	1710	D/S • CEA – 4.0% • CAS – 7.4% (P<0.01)	CAS – 10* CEA – 50
CREST [3]	2000–2008	Asx+Sx	96%	2502	MACCE • CEA – 4.5% • CAS – 5.2% (P=0.38)	CAS – 20† CEA – 50

EPD, embolic protection device; Asx, asymptomatic; Sx, symptomatic; MACCE, major adverse cardiac and cerebrovascular events; CAS, carotid artery stenting; CEA, carotid endarterectomy; D, death; S, stroke; ICSS, International Carotid Stenting Study; EVA-3S, endarterectomy versus angioplasty in patients with symptomatic severe carotid stenosis; SPACE, stent-supported percutaneous angioplasty of the carotid artery versus endarterectomy; SAPPHIRE, stenting and angioplasty with protection in patients at high risk for endarterectomy; CREST, carotid revascularization endarterectomy vs. stenting trial.
*Tutoring for CAS was allowed; †Those with more experience (≥30 cases) performed 5–10 procedures in the lead-in phase, and those with less experience (<30 cases) performed 10–20 procedures in the lead-in phase. Operators were selected by the Interventional Management Committee to participate in the randomized portion of the trial based upon experience, training and lead-in results.
Modified from Wayangankar et al. [12].

gery Trial) were performed in the pre-statin era. Given improvement in medical therapy since those studies were performed, the applicability of these study results is questionable. There are some observations that raise the question whether or not asymptomatic lesions need to be revascularized. Firstly, the 30-day MACCE for CAS (5.2%) and CEA (4.5%) within the CREST trial were historically low across all centers; and more importantly, improvements were seen both in CAS and CEA [3]. Secondly, two consecutive studies dealing with supra-aortic atherosclerotic disease have shown good outcomes with intensification of medical therapy (Table 4). The earlier WASID trial [16] compared warfarin to aspirin in symptomatic patients with intra-cranial disease. The 30-day and 1-year death/stroke outcomes are shown in Table 4. The subsequent SAMPRISS trial [17] compared stenting with intensive medical therapy (IMT) and IMT alone; again in patients with intra-cranial disease. When data from the patients in the IMT alone group were analyzed, they had outcomes at half the rate of those in the WASID trial, thereby underscoring the possible benefit afforded by IMT alone.

Thus, the medical community currently needs more definitive and contemporary evidence to determine if revascularization has added benefit in asymptomatic carotid artery stenosis in addition to intensive medical therapy. The CREST 2 trial (Figure 1) will randomize 2480 patients (1240 in each limb) to revascularization (CAS or CEA) with IMT vs. IMT alone in a parallel study design and will probably shed more light on this topic.

Current Data on Treating Asymptomatic Patients

A. High surgical risk patients – Though 30-day MACCE was similar between CEA and CAS within the SAPPHIRE trial [4] (CAS, 5.4% vs.

Table 3 Multidisciplinary Carotid Stent Guidelines.

Neurological H/O	Co-morbid conditions	Surgical risk	Recommendation	LOE	Guideline society
Symptomatic*	• Stenosis difficult to access surgically • Medical conditions increasing surgical risks • Radiation induced • Post CEA stenosis	High	Class II a	B	AHA and American Stroke Association [14]
Symptomatic OR asymptomatic	Neck anatomy unfavorable to carotid artery surgery	High/average/low	Class II a	B	Multi-society Guideline [15]
Symptomatic	Periprocedural stroke and death rate <6%	Average	Class I	B	Multi-society Guideline [15]
Symptomatic	N/A	Average	Class I	B	AHA and American Stroke Association [14]
Asymptomatic	• Medical condition • Life expectancy • Patient preferences	High	Class II a	C	Multi-society Guideline [15]
Asymptomatic	• 60% by angiography and 70% by duplex • Prophylactic • Effectiveness against OMT alone not yet validated	Average	Class II b	B	Multi-society Guideline [15]

*All symptomatic stenoses are defined as >50% by angiography and >70% by duplex.
AHA, American heart association; OMT, optimal medical therapy; CEA, carotid endarterectomy; LOE, level of evidence.
Adapted from White et al. [7].

Table 4 Studies on Medical Therapy in Intra-Cranial Atherosclerotic Disease.

	WASID trial	SAMPRISS trial
Year	1999–2003	2008–2011
Sample size	567	451
Patients	Symptomatic high grade intracranial atherosclerotic stenosis	Symptomatic high grade intracranial atherosclerotic stenosis
Study design	ASA+RF Mx vs. Warfarin+RF Mx	Stenting+IMT vs. IMT
30 day DS	10.7%	5.8% in IMT arm
1 Year composite	25.7%	12.2% in IMT arm

CEA, 10.2%; P=0.20); CAS proved to have a significant edge over CEA with regards to 1-year (9.9% vs. 21.5%, P=0.02) MACCE outcomes. At 3 years, though the absolute number of MACCE events were lower in the CAS group, the differences were not statistically significant (CAS – 24.6% vs. CEA – 26.9%, P>0.05) [8]. Refer to Table 3 for current multi-societal recommendations on treating such patients.

B. Average surgical risk patients – The CREST trial showed that in these patient groups, CAS was comparable to CEA with respect to a composite endpoint of MACCE (CAS, 5.6±1.0% vs. CEA, 4.9±1.0%; P=0.56 and rates of stroke up to 4 years (CAS, 4.5±0.9% vs. CEA, 2.7±0.8%; P=0.07) [3]. Refer to Table 3 for current multi-societal recommendations on treating such patients.

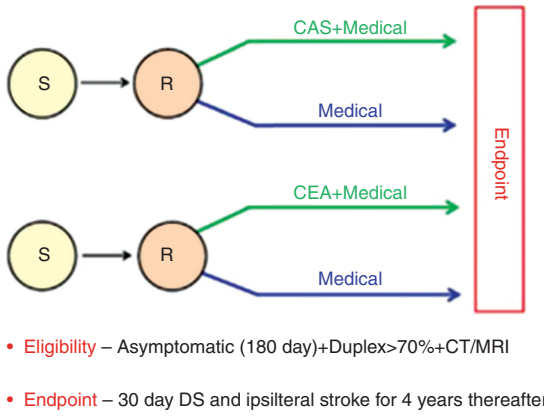

Figure 1 CREST-2 Parallel Study Design.
S, Screening; R, randomization, CAS, carotid artery stenting; CEA, carotid end-arterectomy.
Adapted from Brott et al. [18].

Procedural Risk Assessment

While the CREST trial showed a composite clinical equivalence of CAS and CEA with regards to the MACCE outcomes, the individual risks associated with each revascularization modality were slightly different. The CAS cohort had slightly higher minor strokes, while the CEA cohort had higher cranial nerve palsies and myocardial infarction [3]. Hence, risk stratification for CAS would help individualize carotid revascularization options and hopefully translate to best outcomes.

Table 5 shows the medical, anatomic, and procedural related variables contributing to procedural risk.

Recent publications provide risk models to assess procedural risk for mortality or stroke [19–21]. These models encompass multiple variables known to increase risk of CAS-associated adverse outcomes and provide a summary risk score of death or stroke. Similar risk scores have been used effectively in various fields of medicine (e.g., CHADS2 score), and the development of an effective CAS score may help physicians with shared decision making with respect to the best modality of carotid revascularization. The NCDR CAS score [19] is a recently published score that assesses risk of periprocedural death and stroke from pre-procedural variables (before angiography). This score, developed by Hawkins et al., utilized the NCDR CARE registry database of 11,122 CAS procedures, asymptomatic and symptomatic, with low, average and high surgical risks. Figure 2 demonstrates the use of the CAS score for estimation of in-hospital stroke or death following carotid artery stenting.

Finally, despite development of risk models and predictors, clinicians should keep in mind that any anatomic or technical feature that prolongs instrumentation within the supra-aortic vasculature, or makes delivery of embolic protection device difficult, would be best reserved for the surgical mode of revascularization. Other issues such as vascular access, chronic kidney dysfunction or contrast allergy should also be considered before deciding on a plan of care [7].

CAS – The Procedure

A. Patient selection is the most important foundation on which a new CAS program should develop. A recently published executive consensus document (ECD) on CAS training and Credentialing [13] highlights the tenets on which a program needs to be designed and executed. In general, operators and institutions should self-

Table 5 Features Suggesting Increased Risk of Carotid Stent Procedures.

Medical comorbidity	Anatomic criteria	Procedural factor
Elderly (>75/80 years)	Type III aortic arch	Inexperienced operator/center
Symptom status	Vessel tortuosity	EPD not used
Bleeding risk/hypercoagulable state	Heavy calcification	Lack of femoral access
Severe aortic stenosis	Lesion related thrombus	Time delay to perform procedure from onset of symptoms
Chronic kidney disease	Echolucent plaque	
Decreased cerebral reserve	Aortic arch atheroma	

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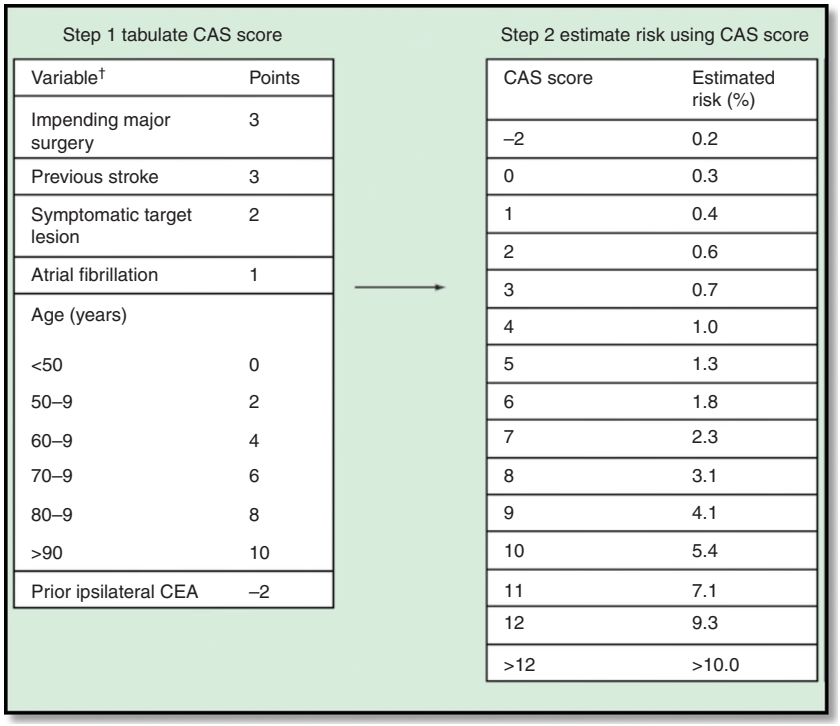

Step 1 tabulate CAS score

Variable†	Points
Impending major surgery	3
Previous stroke	3
Symptomatic target lesion	2
Atrial fibrillation	1
Age (years)	
<50	0
50–9	2
60–9	4
70–9	6
80–9	8
>90	10
Prior ipsilateral CEA	–2

Step 2 estimate risk using CAS score

CAS score	Estimated risk (%)
–2	0.2
0	0.3
1	0.4
2	0.6
3	0.7
4	1.0
5	1.3
6	1.8
7	2.3
8	3.1
9	4.1
10	5.4
11	7.1
12	9.3
>12	>10.0

Figure 2 The NCDR CAS Score.
Reproduced with permission from Hawkins et al. [22].

evaluate themselves on the spectrum of annual CAS volume. This will help them select appropriate patients for their CAS program. Low volume operators and institutions should start with low risk CAS procedures and keep the complicated ones for proctoring. Also, patients inherently at high surgical risk and/or symptomatic may be the target candidates that a new program should enroll initially [7].

B. Access – Though performed via the trans-femoral route traditionally, the newer generation of interventional operators have adopted to radial access for CAS. A recent randomized controlled trial comparing the two access sites showed no difference in MACCE or access related complications [23]. This study established the safety and feasibility of performing CAS via the trans-radial route, albeit with some shortcomings of higher access turn-over rates and higher radiation compared to femoral access routes. On the other hand, the trans-radial approach provided the benefit of a shorter hospital stay [23]. In general, radial access provides greater and prompt post-procedural ambulation which may sometimes be important to circumvent post-procedural hemodynamic issues. Also trans-radial can make some anatomical variants (Right carotid intervention via right radial artery in type III arch, Bovine left carotid artery via right radial artery etc.) more amenable to intervention compared to the trans-femoral route.

Despite technological advancement, technique refinement and contemporary studies showing equivalence of CAS and CEA with regards to MACCE, the trans-femoral CAS (TF-CAS) is associated with a higher number of peri-procedural cerebrovascular events, especially within the 24 hour post-procedure period [24, 25]. This has been attributed to unprotected catheterization (Pre-EPD) of carotid arteries through diseased and difficult aortic arches [26]. Consequently, the concept of CAS via direct carotid access has gained some leverage. The safety and feasibility of this approach was demonstrated in the ROADSTER trial [24]. This was a prospective, single-arm, multicenter clinical trial that evaluated the use of the ENROUTE Transcarotid neuroprotection system (NPS; Silk Road Medical Inc., Sunnyvale, CA, USA) during CAS pro-

cedures performed in patients considered high risk for complications from carotid endarterectomy. Essentially this entailed a hybrid approach where the common carotid artery (CCA) is occluded proximally via surgical means, and the NPS is delivered distal to the surgical occlusion. This equipment allows flow reversal (CCA to femoral vein) while also allowing CAS via carotid access distal to the occlusion. This trial showed an excellent 30-day stroke rate of 1.4%, the lowest observed in any kind of prospective studies. This technique may also have significant advantages over traditional CEA in light of its lower cranial nerve injury and oro-pharyngeal dysfunction rates.

C. Procedural anti-coagulation – As an extension to the hemorrhagic benefit observed with bivalirudin in the coronary era, several operators had started using bivalirudin based on limited single-center retrospective feasibility studies [27–29]. However, large scale real world data were limited until the study by Wayangankar et al. [30] which used the national registry of CAS (NCDR-CARE Registry) to compare CAS procedures with bivalirudin (n=3555) with unfractionated heparin (UFH, n=3555) in a propensity matched fashion. This study showed that bivalirudin was associated with lower rates of hemorrhagic outcomes compared with UFH during the index hospitalization for carotid artery stenting. In-hospital and 30-day ischemic events were similar between the two groups (Table 6). Until the results of ENDOMAX trial (ENDOvascular interventions with angioMAX, n=4000) are published, this is the largest real world study we have to draw inferences from. However, operators should keep in mind that variables other than bleeding (cost, presence of heparin induced thrombocytopenia, and lack of antidote with bivalirudin) may be instrumental in choosing the type of anticoagulant.

Table 6 Clinical Outcomes by Treatment Group Among Propensity-Matched Cohort.

Clinical outcomes	CAS with UFH (n=3555)	CAS with bival (n=3555)	P value	OR (95% CI)
In-hospital clinical outcomes				
Bleeding or hematoma requiring red blood tell transfusion	54 (1.5%)	31 (0.9%)	0.01	0.57 (0.36–0.89)
Intracerebral hemorrtiage	8 (0.2%)	5 (0.1%)	0.41	0.62 (0.20–1.91)
Composite mortality+stroke+MI	97 (2.73%)	76 (2.14%)	0.11	0.78 (0.58–1.06)
Composite mortality+MI	27 (0.76%)	21 (0.59%)	0.38	0.78 (0.44–1.38)
Composite mortalrty+stroke	88 (2.5%)	66 (1.9%)	0.07	0.75 (0.54–1.04)
All-cause mortality	15 (0.4%)	11 (0.3%)	0.43	0.73 (0.34–1.60)
Ml	12 (0.34%)	12 (0.34%)	0.99	1.0 (0.45–2.23)
Stroke	80 (2.3%)	59 (1.7%)	0.07	0.73 (0.52–1.03)
TIA	40 (1.1%)	46 (1.3%)	0.52	1.15 (0.75–1.76)
Composite stroke+TIA	120 (3.4%)	105 (3.0%)	0.31	0.87 (0.67–1.14)
Vascular complications	19 (0.5%)	23 (0.6%)	0.54	1.21 (0.66–2.23)
30-Day clinical outcomes				
Patient follow-up available, n (%)	2802 (78.8%)	2767 (77.8%)	0.31	
Composite mortality/stroke/MI	139 (4.9%)	120 (4.3%)	0.29	0.87 (0.68–1.12)
Composite mortality/MI	37 (1.3%)	37 (1.3%)	0.94	1.02 (0.64–1.61)
Composite mortality/stroke	114 (4.0%)	95 (3.4%)	0.23	0.84 (0.64–1.11)
All-cause mortality	22 (0.8%)	20 (0.7%)	0.80	0.93 (0.50–1.70)
Ml	25 (0.9%)	25 (0.9%)	0.95	1.02 (0.58–1.78)
Stroke	102 (3.6%)	83 (3.0%)	0.20	0.82 (0.61–1.11)

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Embolic Protection Device

Data on neuro-protection relies on summary data in the form of meta-analysis or systematic reviews. This is because the rates of clinical cerebrovascular events are small and designing a randomized control trial would be technically and financially difficult. One such study was by Garg et al. [31] that reviewed data from procedures done between 1995 and 2007 and assessed the association of 30-day peri-procedural stroke. Using pooled analysis of 134 articles (n>23,000), the authors showed that compared to procedures without embolic protection devices, patients with neuro-protection did better with respect to post-procedural stroke at 30 days (RR – 0.62, 95% CI – 0.54–0.72, P<0.01) [31]. A similar benefit was observed in a pooled analysis by Touze et al. which showed a stroke and death benefit in favor of neuro-protection (RR – 0.57, 95% CI – 0.43–0.76, P<0.01) [32].

Embolic protection can be of the following three types

- **Distal non-occlusive system** – Distal embolic protection filters. This preserves blood flow but prevents distal embolization. Table 7 shows the current available distal EPD filters in practice.
- **Distal Occlusive system** – GuardWire Protection System (PercuSurge, Sunnyvale, CA, USA) occludes distally, and an aspiration catheter Export (Medtronic) provides suction. This technique relies on prevention of distal embolization by preventing both blood flow and embolic debris.
- **Proximal protection devices** rely on flow reversal after occluding CCA and ECA flow either by direct aspiration (Mo.Ma; Medtronic, Minneapolis, MN, USA) or via a filter into the venous system (GORE Flow reversal system, WL Gore and Associates, Flagstaff, AZ, USA). The biggest advantage of this concept is that the EPD does not cross the lesion and hence decreases the chance of manipulation induced distal embolization. The MICHI neuro-protection system (Silk Road Medical Inc., Sunnyvale, CA, USA) is similar to the GORE system with the difference that it is used with direct carotid access – obviating the need to deal with hostile arches [33].

One of the first randomized control trials comparing the two strategies (proximal vs. distal protection) showed that new ipsilateral cerebral lesions with diffusion weighted imaging lesions were lesser with proximal protection device MoMa (Invatec/Medtronic Vascular Inc., Santa Rosa, CA, USA) compared to distal protection device – Angioguard (Cordis Corporation, Bridgewater, NJ, USA) [34]. Another single center study (n=140 patients) showed no difference in 30-day clinical outcomes when the two strategies were compared [35]. A recent publication from the NCDRs CARE registry (n=10,246) also showed no clinical differences within the two strategies [36]. Since large scale randomized studies would not be feasible to answer this question, with the current base of evidence, it can be safely concluded that either type of neuro-protection would be equally beneficial as long as it is used consistently and precisely.

D. Intra-cerebral angiography – These should be performed before and after carotid intervention. A pre-stenting intra-cerebral angiography

Table 7 Currently Available Embolic Protection Devices.

Device	Manufacturer	Pore size (μm)	Vessel size (mm)	Fixed wire
Gore embolic filter	Gore (Newark, DE, USA)	100	2.5–5.5	Y
Emboshield	Abbott (Chicago, IL, USA)	120	2.5–7	N
Spider	Covidien (Irvine, CA, USA)	50–300	3.0–7.0	N
Accunet	Abbott	125	3.2–5	Y
FilterWire EZ	Boston Scientific(Natick, MA, USA)	110	3.5–5.5	Y
FiberNet	Medtronic (Minneapolis, MN, USA)	>40	3.5–7	Y
Angioguard	Cordis (Bridge water, NJ, USA)	100	4.5–7.5	Y

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provides good information about vascular anatomy (patency, presence of collaterals, Circle of Willis, dominance, isolated hemisphere) that not only helps with patient selection but also helps to maintain a template of pre-intervention status should complications occur [7]. Likewise, intra-cerebral angiography post-stenting helps to detect any kind of distal embolization in the form of intra-cerebral vascular "cut off." Ideally two orthogonal views (AP and lateral) are recommended.

E. Balloon dilatations – Traditionally, the CAS procedure consisted of an embolic protection device placement, pre-stent balloon dilatation with a <4 mm balloon at nominal pressures, followed by placement of a self-expanding stent, and eventually ending with a post-stent balloon inflation (≤5 mm balloon). While the pre-stent balloon inflation helps to allow the stent to pass, more importantly it provides a glimpse of hemodynamic response the patient may have with stent and post-dilatation. This step helps re-adjust medications and fluids before proceeding and stenting in a more controlled manner. Alternatively, some studies have alluded to the drawbacks of routine post-dilatations, mainly stemming from increased microscopic emboli (Doppler signals in intra-cranial imaging). The practice of post-dilatation doesn't improve restenosis rates, and self-expanding stents eventually expand to their nominal diameters post stenting.

F. Carotid stent – Contemporary carotid stents are self-expanding by design, self-tapering or with a manufactured taper to deal with the discordant sizes of the internal carotid artery and common carotid artery. Though studies [37] have found no difference between closed and open cell types, operators are inclined to use the more conformable open cell type stents in more angulated lesions, whereas a higher surface area afforded by closed cell stents may be best suited for straighter lesions. Table 8 shows current available stents.

G. Treatment of ostial common carotid artery – Most trials comparing CAS and CEA evaluate the two modalities with respect to internal carotid artery interventions. A special subset of patient to consider is the ostial common carotid artery. Surgical treatment for such lesions is usually a carotid-subclavian bypass which is often limited by higher than average peri-procedural stroke outcomes [38, 39]. There exists limited data on how to treat such patients via CAS since these lesions are rare, and when present pose technical challenge to engage, cross, deliver and deploy interventional equipment [40]. Cam et al. report a single center experience with 17 such patients who underwent CAS from 2005 to 2011 [40]. Most of the lesions involved the left CCA. Though various techniques have been described by the authors, the one that stands out is the one that they used in all the latter cases. This involved using a modified AL-1 catheter to deliver long 300 cm 014 wires (one of them being the filter wire) across the lesion, pre-dilatation followed by delivery of the stent mounted on both wires to provide good support for delivery and deployment of the stent. The authors report excellent short and long-term outcomes with this technique [40]. EPD is removed first followed by the buddy wire.

H. Patients with significant coronary artery disease – Around 10% of patients undergoing open heart surgery (OHS) have severe carotid artery disease (stenosis >80%) [41]. Due to lack of randomized data, clinical practice revolves around three strategies based on local practice patterns – staged CEA-OHS; combine CEA-OHS; and staged CAS-CEA. Shishehbor et al. evaluated 350 such patients from 1997 to 2009 at the Cleveland Clinic. The authors found that despite CAS-OHS group being a higher risk group (higher pre-procedural stroke rates) and undergoing more complex OHS, they ended up with similar peri-procedural composite outcomes (1 year death, stroke, MI) compared to combined CEA-OHS and significantly better outcomes when compared to staged CEA-OHS [42]. When outcomes were evaluated after one year, the staged CAS-OHS strategy outscored both combined CEA-OHS and staged CEA-OHS. While the staged strategies were associated with higher inter-stage myocardial infarctions, the combined strategy was asso-

Table 8 Characteristics of Commonly Used Stents.

Stent	Manufacturer	Cell type	Free cell area (mm^2)	Nontaper option	Taper option
Wallstent	Boston Scientific (Natick, MA, USA)	Closed	1.08	Y	N
Xact	Abbott Vascular (Abbott Park, IL, USA)	Closed	2.74	Y	Y
NexStent	Boston Scientific	Closed	4.70	N	Y
Precise	Cordis (Bridgewater, NJ, USA)	Open	5.89	Y	N
Exponent	Medtronic (Minneapolis, MN, USA)	Open	6.51	Y	Y
Protégé	Covidien (Irvine, CA, USA)	Open	10.71	Y	Y
Acculink	Abbott Vascular	Open	11.48	Y	Y
Zilver 518® RX	Cook Medical (Bloomington, IN, USA)	Open	12.76	Y	N
Cristallo Idenle	Medtronic	Hybrid: closed-cell center; open-cell ends		Y	
Sinus-Carotid-Rx	Optimed (Ettlingen, Germany)	Hybrid: open-cell center; closed-cell ends		Y	

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ciated with more peri-procedural stroke [42]. The lower late composite outcomes associated with staged CAS-OHS were driven by lower mortality; underscoring the importance of this strategy in this high risk group of patients. Until prospective randomized data becomes available, this study may provide some guidance to clinicians to provide best individualized treatment to this high risk sub-group of patients. Finally, hybrid approaches of combined CAS-OHS still needs to be explored and evaluated.

Learning Curve

Carotid artery stenting is a technically demanding procedure with a significant learning curve associated. Importantly, this learning curve is associated with technical success and peri-procedural outcomes [43]. There are two components of the learning curve – operator and institutional. Multiple studies have shown that as the operator gained more CAS volume, rates of peri-procedural complications declined [28, 44–46]. Similarly, institutions with higher volume fared better than lower

Table 9 Data on Learning Curve Thresholds for Individual Operators.

Study	Period	Sample size	Learning-curve thresholds
Ahmadi et al.	1997–2000	320	30-Day neurologic event and death rate 5% vs. 15% (P=0.03) comparing >80 vs. <80 CAS procedures
Siena Score Study	2000–2009	2124	OR for 30-d stroke 0.81 (95% CI 0.67–0.95) comparing >100 vs. <100 CAS procedures
Lin et al.	2002–2005	200	30-Day stroke 2% vs. 8% (P<0.05) for >50 vs. <50 CAS procedures
CAPTURE 2	2006–2009	3388	To attain target 30-d D/S rate <3%: >72 CAS procedures
Vogel et al.	2005–2006	18,599	Postprocedure stroke rates 1.5% vs. 2.2%. (P=0.02) comparing >30 CAS per 2 year vs. <30 CAS per 2 year
Nallamothu et al.	2005–2007	24,701	30-Day mortality 1.4% vs. 2.5% (P<0.001) comparing >24 vs. <6 CAS per year

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Table 10 Data on Learning Curve Thresholds for Institutions.

Study	Period	Sample size	Learning-curve thresholds
Wholey and Al-Mubarek	1988–2002	53 Centers 12,392 Cases	30-d D/S 1.3% vs. 4.0% comparing >100 CAS cases per center vs. <100 cases per center
Pro-CAS Study	1999–2005	25 Centers 5341 Cases	OR for periprocedural death and stroke 1.77 (CI 1.1–2.8, P=0.02) comparing ≤50 CAS cases per center vs. >150 CAS cases per center OR for periprocedural death and stroke 1.48 (CI 1.0–2.1, P=0.03) comparing 50–150 CAS cases per center vs. >150 CAS cases per center
Vogel et al.	2005–2006	18,599 Patients from NIS	Postprocedure stroke rates 1.8% vs. 2.4%. (P=0.02) comparing >60 CAS per center per 2 year vs. <60 CAS per center per 2 year
Verzini et al.	2001–2006	627 Patients	To attain D/S rates <2% to >195 CAS cases

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volume ones [43, 46–49]. Availability of technical mentoring, peer-to-peer feedback on patient and device selection provides an ideal milieu to ensure patient safety even with novices. Wayangankar et al. [43] summarized operator and learning curve thresholds to attain acceptable per-procedural death/stroke outcomes (Tables 9 and 10). Prior consensus statements by various societies on credentialing and training operators for CAS have been non-uniform and probably unrealistic in the contemporary setting. While the Italian SPREAD joint committee consensus document [50] recommends >75 cases (at least 50 as primary operator) to achieve competency and 50 per year to maintain, the prior 2007 US document (SCAI/SVM/SVS) was a bit liberal and stated that 25 supervised operators (half as primary operator) need to be performed to achieve competency. It did not provide thresholds for maintaining competency. The recently published 2015 SCAI/SVM CAS training and credentialing document [12] underscores the importance of annual CAS volume. "Maintenance" volume is important since studies have shown that increased time interval between consecutive CAS procedures is associated with greater risk of death, MI or stroke at 30 days [51]. With declining volumes, multiple competing sub-specialties, and issues with re-imbursement within the US, applicability of aggressive European CAS guidelines (on operator thresholds) would be difficult and prohibitive. The newer 2015 SCAI/SVM competency statement [12] recognizes this dilemma, and for the first time, has recommended a more realistic maintenance volume of 10–15 cases/year (threshold for achieving competency being 25 cases). Additionally, the document recommends double scrubbing, proctoring, and simulation as tools to complement clinical exposure for low volume operators.

Challenges for Budding Operators

- The role of carotid revascularization is recently being challenged in asymptomatic patients. The CREST2 trial may offer some insights on the best strategy to manage such patients, and may have future implications on CAS procedural volume.
- In the US, the Centers for Medicare Services (CMS) has not yet revised the current national coverage determination (NCD) to correspond with the FDA approval of CAS devices with indications. Moreover there is a marked disconnect between CMS coverage and current guidelines. Current NCD limit a patient's access to CAS who could have possible benefit. Hence, uncertainties in reimbursements will further worsen the CAS volume.
- Such an atmosphere may force patients and physicians into poor patient selection that may ultimately lead to worse clinical outcomes.
- Finally, this decline in CAS volume and the complexity of decision-making would magnify the current challenges in training and in maintaining competent CAS operators.

Conflict of Interest

The authors declare no conflict of interest.

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