

A systematic review of carotid stent design and selection: strategies to optimize procedural outcomes

Carotid artery stenting is an alternative to carotid endarterectomy in select patients. The stroke and death rate following carotid artery stenting must be reduced to allow more general use of this technology. Online databases were utilized to review the impact of stent design. Results specifically for symptomatic patients were reported by four investigators and these data were pooled. A total of 4352 symptomatic patients were pooled (1892 closed cell and 2460 open cell). The odds ratio when comparing open-cell stents with closed-cell stents was 1.35 (95% CI: 0.99–1.83; $p = 0.057$) for the end point of a 30-day transient ischemic attack, stroke or death. Symptomatic patients with favorable anatomy may have a reduced 30-day risk of transient ischemic attack, stroke or death when closed-cell stents are utilized.

KEYWORDS: carotid ■ carotid stenosis ■ carotid stenting ■ closed cell ■ embolic ■ endovascular ■ open cell ■ stent design ■ stenting

Carotid artery stenting (CAS) is gaining popularity as an alternative to carotid endarterectomy (CEA) in select high-risk patients with internal carotid artery (ICA) stenoses [1,2]. At present, CEA is the gold standard intervention in most patients with moderate-to-severe ICA stenosis in both asymptomatic and symptomatic populations [3–6]. CAS has not achieved equipoise when compared with CEA due to a higher stroke and death rate in most studies [1,7–11]. Of all the studies, the best results were achieved when experienced operators were used as part of the study inclusion criteria [1]. Comparable stroke and death rates were demonstrated in the SPACE trial results at 2 years [12]. However, in the original analysis of the SPACE trial, CAS did not meet its objective of noninferiority at 30 days.

Emboli can be generated during multiple phases of a CAS procedure, and therefore, the potential for cerebrovascular sequelae is high. Bonati *et al.*, in a study using pre- and post-procedure diffusion-weighted MRI to assess for new cerebral ischemic lesions following CAS and CEA, clearly demonstrated more distal embolization following carotid stenting [13]. These findings are further supported by a number of randomized control studies demonstrating a higher stroke and death rate in patients undergoing CAS [1,7–11]. In particular, patients older than 70 years of age appear to have an increased stroke risk after CAS [1]. This increased risk most likely relates to the anatomic challenges observed more frequently in the elderly. Specifically, arch elongation and calcification, common carotid artery (CCA) and innominate artery occlusive disease, CCA and

ICA tortuosity, and higher grade carotid stenoses are seen more commonly in older populations [14,15]. Lam *et al.* clearly demonstrated increased anatomical challenges in patients older than 80 years of age undergoing CAS [14]. However, due to a small sample size, differences in outcomes were not observed.

Identifying subgroups of high-risk CEA patients may make the performance of CAS preferable in select scenarios [2,16]. Furthermore, adopting strategies aimed at minimizing the embolic risk during CAS through appropriate patient selection, embolic protection and device selection will likely reduce cerebrovascular complications. Ultimately, as CAS technology becomes more refined, CAS may supersede CEA as the intervention of choice in patients with extracranial carotid disease.

Procedural steps & the potential for embolization

Cerebral emboli can be generated at varying points during CAS. In a study of 84 symptomatic patients undergoing CAS, Blasel *et al.* studied the impact of various technical details on neurologic sequelae by obtaining pre- and post-CAS diffusion-weighted MRIs [17]. Although the number of new lesions found on MRI did not vary between the groups compared, new ischemic lesions were seen. To better understand the embolic risk during CAS, a review of the procedural steps is necessary [18].

After obtaining transfemoral access and placing a short vascular sheath in the common femoral artery, a guide wire is advanced into the aortic arch. Imprudent wire advancement can

Rami O Tadros^{*1},
Rajesh K Malik¹,
Ageliki G Vouyouka¹,
Sharif H Ellozy¹,
Michael L Marin¹
& Peter L Faries¹

¹Mount Sinai Medical Center, Division of Vascular Surgery, 5 East 98th Street, 4th Floor, New York, NY 10029, USA

^{*}Author for correspondence:
Tel.: +1 212 241 6500
rami.tadros@mountsinai.org

traumatize the aortic arch and its arterial branches, resulting in the release of debris. Similarly, once the wire is in position, a flush catheter, commonly a pigtail, is advanced into the aortic arch. This step results in further manipulation of an atherosclerotic arch. Arch angiography is then performed. If the decision is made to attempt an intervention, systemic anticoagulation must be initiated. Anticoagulation is achieved routinely using intravenous heparin and activated clotting times are monitored to ensure efficacy. The goal activated clotting time is between 250 and 350 s. Therapeutic anticoagulation is important prior to initiating the intervention to reduce the likelihood of thrombosis or emboli.

The increased stroke rate seen in patients older than 70 years is likely due, in part, to an increased amount of atherosclerosis in the aortic arches of the elderly [14,15]. Furthermore, as demonstrated by Lam *et al.*, challenging aortic arch morphology, which is more commonly seen in older patients, can impact the embolic risk by increasing the technical difficulty associated with selecting the target carotid artery and advancing the long vascular sheath [14].

Once arch angiograms have been obtained, the target CCA and ipsilateral external carotid artery must be selected. This selective cannulation, especially when the great vessel origins are stenosed, has the potential to generate debris [14]. With an adequate length of wire in the ipsilateral external carotid artery, a long, 90–100-cm, vascular sheath is advanced into the ipsilateral CCA. At this stage, a 0.014-inch wire is advanced across the target stenosis. It is important to stress that all of the aforementioned steps are performed without an embolic protection device. Once across the target lesion, an embolic protection filter is positioned distal to the target lesion. The filter should be placed in a straight portion of the ICA and should be sized to the appropriate lumen diameter to optimize embolic protection. Traversing the carotid plaque during these last two steps, especially when treating high-grade stenosis, friable lesions and symptomatic patients, can generate emboli.

Once the embolic protection device is in place, distal embolization beyond the filter is dramatically reduced [19]. This safeguard allows further manipulation of the carotid bifurcation and treatment of the intended stenosis. After the administration of glycopyrrolate, the intervention is initiated. This antimuscarinic agent is used owing to the improved hemodynamic stability observed with its use [20]. Postdilatation hypotension can negatively impact outcomes.

Ackerstaff *et al.* demonstrated significant reductions in middle cerebral artery blood flow by transcranial Doppler in patients with postdilatation asystole and hypotension [21].

Routinely, the area of stenosis is gently predilated with a low-profile angioplasty balloon. This step facilitates the smooth delivery of the chosen stent. A carotid-specific stent is then advanced and deployed based on the selection process described in this review. Stents are cautiously postdilated after stent deployment as this step can generate significant debris. Using transcranial Doppler, Ackerstaff *et al.* demonstrated that embolic showers generated after postdilatation were significantly associated with neurologic adverse events [21]. Therefore, a residual waste is usually acceptable as the source of embolization has been covered and additional dilatation can generate emboli. The type of stent used can impact distal embolization and neurologic sequelae at this stage of the procedure and during the postoperative period. Exceptions to the authors' stent selection algorithm are made when CAS is carried out as part of a clinical trial.

The embolic protection device is then removed. Care should be taken when retrieving the filter. Overzealous collapse of the filter may extrude captured debris causing a stroke. The long vascular sheath is also watchfully extracted from the ipsilateral CCA. This step should be performed over a wire before completely removing the sheath from the patient.

Identifying high-risk patients, limiting unnecessary maneuvers, modifying techniques and selecting appropriate devices to compensate for challenging anatomy and plaque morphology will likely reduce the cerebrovascular sequelae of CAS and optimize results. Careful attention to detail at each stage of a CAS procedure is crucial to achieving this goal and to improving procedural outcomes to a level comparable with endarterectomy.

Advances in CAS technologies, including the use of alternative embolic protection systems, may reduce the incidence of periprocedural stroke further. In particular, flow reversal embolic protection appears to be very promising with perioperative stroke and death rates of 2.9%, which is comparable with CEA [22]. However, these results need to be scrutinized further by conducting randomized trials comparing CAS with flow reversal embolic protection to CEA.

Basics of stent types & design

Carotid artery stents come in various configurations and are made of several materials. Generally,

these stents are self-expanding bare-metal stents. The two common metals used to construct these stents are nickel–titanium alloy (Nitinol) and cobalt–chromium alloy. Nitinol, at present, is more commonly used in the construction of carotid stents (TABLE 1). Carotid stents are further categorized as ‘open cell’ or ‘closed cell’ based on the free-cell area between the stent lattices [23]. These stents have important mechanical and structural differences that are unique [24–26]. Each stent has a set of properties that make their utilization advantageous in distinct scenarios. Thoughtful device selection based on preprocedural symptomatic status, specific stent characteristics, anatomic challenges and plaque morphology is crucial to optimizing the results of CAS.

■ Characteristics of open- & closed-cell stents

The concept of open- and closed-cell stents and selecting the best stent in a given situation is multifaceted. Classifying a stent as either open cell or closed cell is based on the free-cell area of a given stent. The free-cell area is a measure of the amount of space between stent lattices (TABLE 1) [24].

Closed-cell stents have a smaller free-cell area between the stent lattices. As a consequence, closed-cell stents are more rigid, and therefore, less conformable in tortuous vessels. These characteristics can make advancing a closed-cell stent more challenging in serpentine vessels. Excessive device manipulation should be avoided when possible, and therefore, closed-cell stents should be avoided in these situations. Furthermore, an inflexible stent placed in a compliant, but coiled vessel may create kinks due to forced straightening of a curved structure. The theoretical advantage of a closed-cell stent is in its ability to better scaffold labile carotid plaques that are at an increased risk of generating particulate debris. These high-risk plaques are more commonly seen in symptomatic individuals [27,28]. This enhanced scaffolding effect may decrease distal embolization [24]. An added benefit, observed by Gurbel *et al.* in a porcine model, is that closed-cell stents may result in less platelet aggregation [29]. This observation is theorized to result from less intimal prolapse and a smoother stent–arterial wall interface seen with closed-cell stents.

Alternatively, the larger free-cell area between the stent struts in an open-cell stent creates a more malleable structure. Therefore, open-cell stents readily navigate through tortuous vessels allowing smooth device delivery in unfavorable anatomy. By reducing the manipulation

necessary to traverse a target lesion with a stent, embolic potential may be reduced. In addition, the flexible nature of open-cell stents helps avoid arterial kinking due to unnecessary vessel straightening. Arterial kinking may increase the risk of cerebrovascular insufficiency and sustained hypertension [30]. However, due to the increased area between the stent lattices, these stents do not exclude the plaque as well as their tightly woven counterparts.

It is important to realize that the free-cell area of a given stent, whether open cell or closed cell, is variable. This changeability is dependent on several factors. For example, when implanted, the stent’s free-cell area of a constrained stent will differ from when it is freely expanded [31]. Stent oversizing will result in a reduced free-cell area when constrained within an arterial lumen. Similarly, due to the natural taper that occurs from the CCA to the ICA, free-cell area will vary along the length of the stent. Distally, these stents will have less space between the stent inter-cises. This has resulted in the production and availability of tapered stents to accommodate the caliber difference between the CCA and ICA.

Auricchio *et al.* demonstrated, in a carotid model, that after stenting, free-cell area variability is most pronounced with open-cell stents [31]. This inconsistency is most prominent at the carotid bifurcation due to observed caliber changes and the presence of diverging vessels. Muller-Hulsbeck *et al.* also created a model to assess the impact of various forces on carotid stents [25]. In their *in vitro* model, carotid stents were subjected to 20 and 30° of bend, and 10 and 15° of twist. These investigators demonstrated that closed-cell stents generate a higher force when contorted. Therefore, deploying these tighter and more rigid structures in unfavorable vessels will result in a counter effect. Simply, if the forces generated by

Table 1. Various carotid stents, stent materials and associated free-cell areas.

Carotid stent	Metal	Free-cell area (mm ²)
Closed cell		
Wallstent®	Cobalt–chromium	1.1
Xact®	Nitinol	2.7
NexStent®	Nitinol	4.7
Open cell		
Precise®	Nitinol	5.9
Protégé®	Nitinol	10.7
Acculink®	Nitinol	11.5
<i>Data taken from [23].</i>		

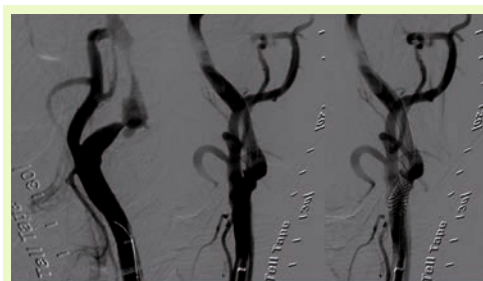


Figure 1. 74-year-old man with symptomatic carotid disease with high-risk plaque characteristics stented using a closed-cell stent.

the stent exceed that of the recipient artery, the treated vessel will inherently accommodate the unyielding structure. As described above, the extreme manifestation of this effect is arterial kinking due to the straightening of a previously meandering vessel. An ideal stent will conform to a winding vessel without generating excess force. Importantly, this model also established that free-cell area will vary along the proximal, middle and distal portions of the stent. This unevenness appeared most pronounced in open-cell stent configurations corroborating the study performed by Auricchio *et al* [25,31]. Furthermore, this study verified that open-cell stents allow penetration of larger particles. The

fact that open-cell stents permit infiltration of larger embolic material was further illustrated in the authors' own analysis of debris captured by embolic protection devices following CAS [32]. In the authors' study, filter analysis identified significantly larger caliber particles in recipients of open-cell stents.

Free-cell area will vary along the length of a stent, and therefore, will offer different degrees of scaffolding along its course. Normally, extracranial carotid disease is localized to the carotid bifurcation and extends into the ostium of the ICA. An ideal stent must scaffold this area to prevent distal embolization. A small free-cell area is less important proximal and distal to this high-risk zone. These observations are being utilized to optimize the design of newer generation carotid stents. For example, the Cristallo Ideale (Medtronic, MN, USA) stent implements a hybrid design [31]. The midportion of this stent has a closed-cell configuration, while the proximal and distal ends are open cell. The theoretical benefit of such a design is an optimal balance of conformability and scaffolding.

■ Stent selection

Selecting the ideal stent for specific carotid anatomy and plaque morphology becomes applicable once the long vascular sheath is in

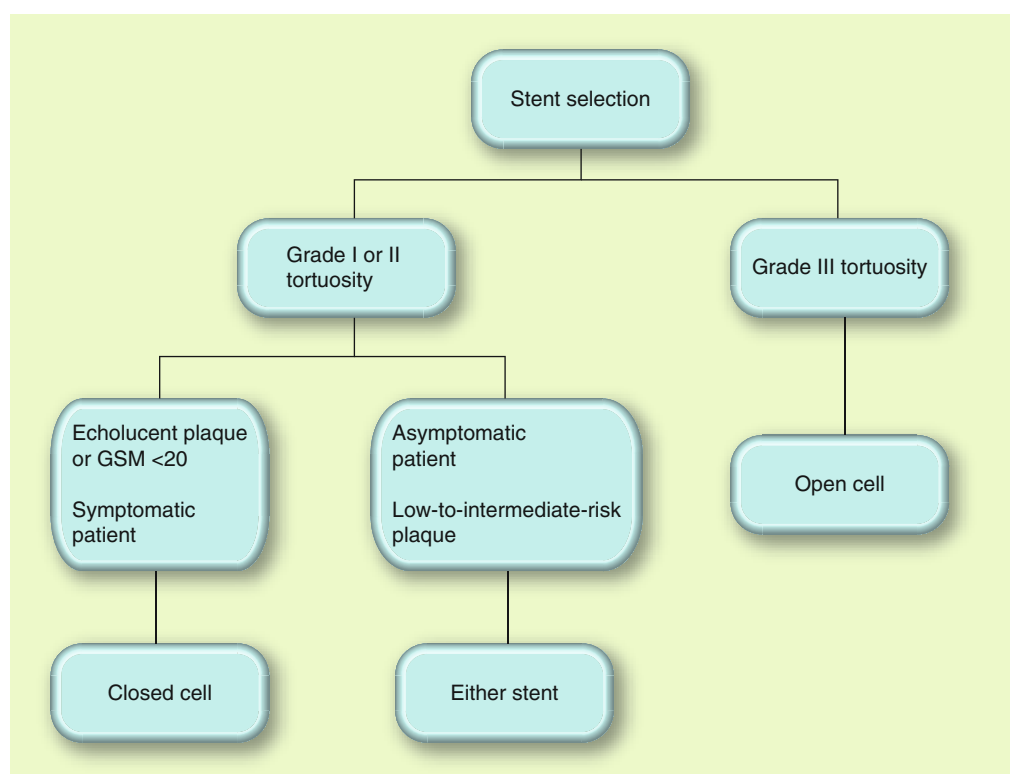


Figure 2. Algorithm for carotid stent selection.

GSM: Gray scale median.

position within the CCA, the target lesion has been crossed and an embolic protection filter is positioned. At this stage, selecting the best stent possible can impact procedural outcomes [23,33]. When choosing a stent, the embolic potential of the plaque and carotid tortuosity should be considered (FIGURES 1 & 2).

Preprocedural assessment of the target carotid stenosis or an individual's presentation can identify friable plaques. These high-risk lesions will benefit most from the increased scaffolding seen with closed-cell stents. In particular, duplex ultrasound is the most helpful tool used to categorize these plaques. Lesions that appear more echolucent are more prone to distal embolization and stroke (FIGURE 3) [27,28]. Furthermore, calculating the gray scale median (GSM) can be a useful adjunct (FIGURE 4) [34]. GSM uses plaque imaging and an assessment of the number of white and black pixels within a plaque. More black pixels results in a lower GSM score and represents a more echolucent plaque. Malik *et al.* demonstrated a propensity to generate more embolic debris and particulates of larger calibers in patients undergoing CAS with a calculated GSM <20 [34]. Symptomatic patients often demonstrate high-risk plaque morphology [27,28].

The degree of carotid tortuosity can be determined by assessing intraprocedural angiograms [15]. Alternatively, these measurements can be determined using preoperative computed tomographic angiography or magnetic resonance angiography by constructing 3D images and analyzing angles along the centerline. Using either technique, the amount of tortuosity can be calculated and categorized (TABLE 2) [15]. In patients with grade I (<30°) or grade II (30–60°) ICA tortuosity, both open- and closed-cell stents are conformable enough to allow safe positioning. In this scenario, the plaque morphology should influence the stent utilized. However, in patients with very serpentine carotid arteries (grade III, >60°), open-cell stents are ideal due to their malleable properties.

In addition to choosing the appropriate stent configuration, it is important to choose the correct diameter and length of the device. The stent should be of an adequate caliber to appose the vessel wall. Therefore, carotid stents are usually oversized. To achieve a better size match given the incongruent CCA and ICA diameters, a tapered stent configuration is preferred. The use of a radiopaque ruler can help determine the best length. The extent of the stent should be long enough to cover the target stenosis without excess intrusion into the relatively normal proximal and distal vessel. If

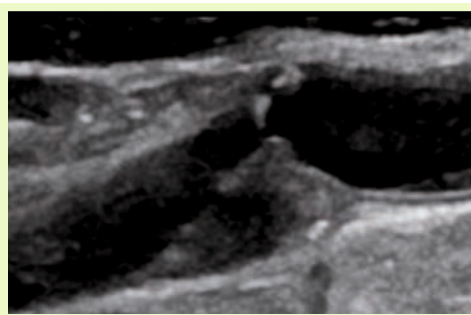


Figure 3. Echolucent carotid plaques are a high risk for embolization.

possible, landing the stent in a straight arterial segment will achieve the best result.

■ Impact of stent design on outcomes

To date, large prospective, randomized control studies have not been performed comparing stent configurations. Therefore, definitive data are lacking. Several retrospective studies of varying size and one randomized control trial with insufficient power have been executed. Despite the theoretical advantage of plaque stabilization when closed-cell stents are used, comparisons of outcomes have produced varying results. Closed-cell stents have not uniformly resulted in decreased periprocedural neurological events when compared with open-cell stents. These results may be confounded by selection bias as operators may inherently use specific stents in vulnerable situations. Furthermore, a disparity exists when evaluating the impact of stent design on outcomes in symptomatic and asymptomatic treatment groups. A clear and consistent improvement in outcomes due to stent configuration has not been demonstrated. These observations are due to the multiple confounding factors that

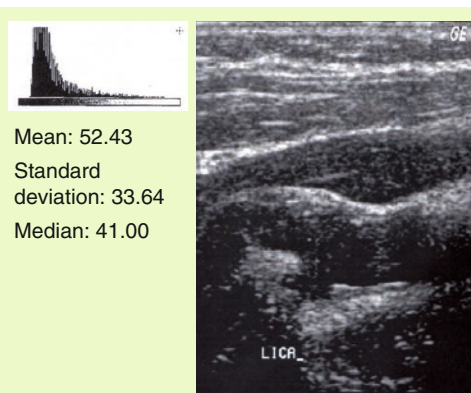


Figure 4. Gray scale median <20 is correlated with more embolic particles and debris of larger caliber. The gray scale median of this plaque is 41.00; and therefore, this plaque is associated with less risk [31].

Table 2. Grading of carotid tortuosity.

Grade	Angle measured from centerline (°)
I	<30
II	30–60
III	>60

Data taken from [15].

influence the results of CAS. Furthermore, the process of stent selection encompasses complex decision-making that is difficult to capture without a well-structured and adequately powered randomized trial. Therefore, an agreement on an ideal stent design has not been reached.

Bosiers *et al.* and Hart *et al.* independently showed improved outcomes when using closed-cell stents [23,33]. Further analysis of their data, however, demonstrated that these benefits were not observed in asymptomatic patients. Bosiers *et al.* investigated the impact of carotid stent design in 3179 patients [23]. Their end points included 30-day and overall transient ischemic attack (TIA), stroke and death rates. Although the use of closed-cell stents resulted in a lower event rate at 30 days and overall in the entire study population, these benefits were mainly observed due to differences seen in the 1317 patients treated for symptomatic carotid disease. Similarly, the study by Hart *et al.* assessed the influence of stent type on 30-day TIA, stroke or death rates [33]. In their total cohort of 701 patients, stent design did not alter outcomes. However, in a subgroup analysis of symptomatic patients, open-cell stent use resulted in a higher likelihood of an adverse event (odds ratio: 4.1; 95% CI: 1.4–12; $p = 0.014$). Labile plaques are

more commonly seen in symptomatic patients [27,28]. Therefore, the benefits of scaffolding observed with closed-cell stents may account for the improved TIA, stroke and death rate seen exclusively in symptomatic patients treated with this configuration.

Conversely, in retrospective studies by Tadros *et al.*, Schillinger *et al.*, Jim *et al.* and Maleux *et al.* comparing stent designs in mixed populations of symptomatic and asymptomatic patients, no differences in outcomes were observed [32,35–37]. In the studies published by Schillinger *et al.* and Jim *et al.*, the results specifically for symptomatic patients were also similar between groups [35,36]. One underpowered randomized controlled trial also showed no measurable differences when comparing stent configurations in a diverse cohort of symptomatic and asymptomatic patients [38]. Furthermore, in a study comparing pre- and post-CAS diffusion-weighted MRI results, Blasel *et al.* found that stent type did not influence the number of new MRI lesions detected following CAS in 84 symptomatic patients [17].

In an effort to clarify the utility of closed-cell stents, data from four studies were pooled (FIGURE 5) [23,33]. Closed-cell stents are thought to reinforce labile plaques. These high-risk stenoses are more common in symptomatic patients [27,28]. Furthermore, the studies that demonstrated an advantage with closed-cell stents recognized these benefits strictly in symptomatic populations. Of the available retrospective studies, results specifically for symptomatic patients were reported by four investigators, Bosiers *et al.*, Hart *et al.*, Schillinger *et al.* and Jim *et al.* [23,33,35,36]. Moreover, these researchers uniformly detailed 30-day TIA, stroke and death rates as an end point in patients receiving either open- or closed-cell stents. Cumulatively, 4352 symptomatic patients were pooled, 1892 received a closed-cell stent and 2460 were stented with an open-cell device. Adverse events at 30-days were observed in 67 patients (3.5%) in the closed-cell group and in 116 individuals (4.7%) in the open-cell group. Overall, the combined odds ratio when comparing open-cell stents with closed-cell stents in symptomatic patients was 1.35 (95% CI: 0.99–1.83; $p = 0.057$) for the end point of 30-day TIA, stroke or death (FIGURE 5).

When considering periprocedural adverse neurologic events, it is important to recognize that the best results were achieved in the CREST trial, where operator experience was used as part of the study inclusion criteria [1]. The CREST trial, which demonstrated the lowest stroke rate of all of the CAS trials, utilized an open-cell

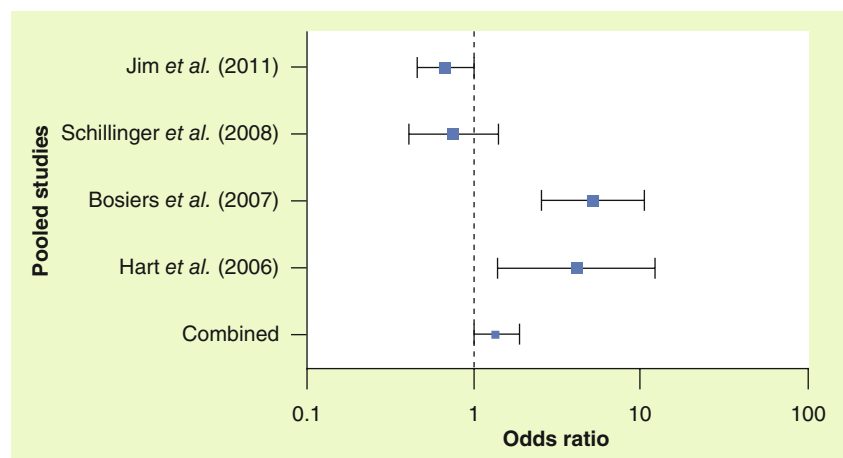


Figure 5. 30-day likelihood of transient ischemic attack, stroke or death in symptomatic patients receiving open- versus closed-cell stents.

Odds ratio: 1.35 (95% CI: 0.99–1.83; $p = 0.057$).

Data taken from [23,33,35,36].

stent. Therefore, stent design and selection is one modifiable variable that may impact upon procedural outcomes. However, more than any other variable, operator experience has the most impact on improving outcomes. This observation is further exemplified by the authors' own low adverse event rate [32,35–37].

Postprocedural surveillance

An important consideration, specifically during postprocedural observation, is that stent design will impact the results of surveillance duplex ultrasound. Pierce *et al.* demonstrated that the peak systolic velocities, peak diastolic velocities and ICA/CCA ratios were significantly higher

Executive summary

Background

- Adopting strategies aimed at minimizing the embolic risk during carotid artery stenting through appropriate patient selection, embolic protection and device selection will likely reduce cerebrovascular complications.

Procedural steps & the potential for embolization

- Imprudent wire and catheter advancement, and challenging aortic arch morphology can impact the embolic risk.
- With a wire in the ipsilateral external carotid artery, a long vascular sheath is advanced into the ipsilateral common carotid artery.
- A 0.014-inch wire is advanced across the target stenosis.
- Once across the target lesion, an embolic protection filter is positioned.
- Using glycopyrrolate before dilating will improve hemodynamic stability.
- Gently predilate the area of stenosis with a low-profile angioplasty balloon.
- Advance and deploy a carotid-specific stent.
- Cautiously postdilate the stent; a residual waste is usually acceptable.
- The embolic protection device is then removed.

Basics of stent types & design

- Carotid stents are self-expanding bare-metal stents that are categorized as 'open cell' or 'closed cell' based on the free-cell area between the stent lattices.
- These stents have important mechanical and structural differences that are unique.

Characteristics of open- & closed-cell stents

- Closed-cell stents have a smaller free-cell area between the stent lattices.
- Closed-cell stents are more rigid and less conformable, and therefore, advancing a closed-cell stent is more challenging in serpentine vessels.
- Rigid stents placed in a coiled vessel may create kinks.
- Closed-cell stents scaffold labile carotid plaques better; this enhanced scaffolding effect may decrease distal embolization.
- The larger free-cell area in an open-cell stent creates a more malleable structure, and therefore, open-cell stents readily navigate tortuous vessels.

Stent selection

- When choosing a stent, the embolic potential of the plaque and carotid tortuosity should be considered.
- Lesions that appear more echolucent are more prone to distal embolization and strokes.
- Symptomatic patients often demonstrate high-risk plaque morphology.
- In patients with grade I (<30°) or grade II (30–60°) internal carotid artery tortuosity, both open-cell and closed-cell stents are conformable enough to allow safe positioning, and therefore, the plaque morphology should influence the stent utilized.
- In patients with grade III tortuosity (>60°), open-cell stents are ideal.

Impact of stent design on outcomes

- Closed-cell stents have not uniformly resulted in decreased periprocedural neurological events when compared to open-cell stents.
- The studies that demonstrated an advantage with closed-cell stents recognized these benefits strictly in symptomatic populations.
- To clarify the utility of closed-cell stents, 4352 symptomatic patients were pooled: 1892 patients received a closed-cell stent and 2460 patients were stented with an open-cell device.
- The combined odds ratio when comparing open-cell stents with closed-cell stents in symptomatic patients was 1.35 (95% CI: 0.99–1.83; $p = 0.057$) for the end point of a 30-day transient ischemic attack, stroke or death.

Postprocedural surveillance

- Knowing the stent type used during carotid artery stenting when surveying patients is necessary to accurately gauge the possibility of recurrent or residual stenoses.

Conclusion

- Patients categorized as having symptomatic extracranial carotid disease are most susceptible to distal embolization during surgical or endovascular revascularizations.
- The increased scaffolding effect seen with closed-cell stents appears to be most beneficial in this population with symptomatic disease.
- When the level of tortuosity permits, utilizing a stent with a smaller free cell is ideal.
- The stent type used in asymptomatic individuals with low-risk plaque characteristics does not appear to influence periprocedural adverse event rates.

in recipients of closed-cell stents compared with open-cell stents 5 days after CAS [39]. Their duplex measurements would have resulted in the diagnosis of a >50% stenosis in 45% of patients receiving closed-cell stents had the criteria to assess nonstented carotid arteries been used. These results were further corroborated by Hussain *et al.* in a similar study [40]. In this second study, the authors demonstrated higher peak systolic velocities and ICA/CCA ratios in the closed-cell stent population. Their findings were observed immediately after CAS and maintained at 20-month follow-up. Therefore, knowledge of the stent type used during CAS when surveying patients is necessary to accurately gauge the possibility of recurrent or residual stenoses. Moreover, parameters other than velocity measurements and ICA/CCA ratios should be utilized for a more reliable determination of procedural success. In the authors' vascular laboratory, a combination of B-mode ultrasound and color Doppler are used to better assess patency following stenting.

Conclusion

Carotid stenting has advanced significantly and is a viable alternative to endarterectomy in select patients. Patients categorized as having symptomatic extracranial carotid disease clearly have the highest future stroke risk if treated with medical therapy alone. This same cohort of individuals, due to the presence of labile carotid plaques, are

most susceptible to distal embolization during surgical or endovascular revascularizations. The increased scaffolding effect seen with closed-cell stents appears to be most beneficial in this population with symptomatic disease. Therefore, when the level of vascular tortuosity permits, utilizing a stent with a smaller free-cell area to treat this subgroup is ideal. Based on the available data, the stent type used in asymptomatic individuals with low-risk plaque characteristics does not appear to influence periprocedural adverse event rates.

Future perspective

Many advances have already been made in the area of CAS. Improvements in this technology, device design and embolic protection will ultimately result in improved stroke and death rates. These advances may reduce the complications associated with CAS. Ultimately, CAS may supersede CEA as the treatment of choice in patients with extracranial carotid disease.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

References

Papers of special note have been highlighted as:

■ of interest

■ of considerable interest

- 1 Brott TG, Hobson RW 2nd, Howard G *et al.* Stenting versus endarterectomy for treatment of carotid-artery stenosis. *N. Engl. J. Med.* 363(1), 11–23 (2010).
- 2 Yadav JS, Wholey MH, Kuntz RE *et al.* Protected carotid-artery stenting versus endarterectomy in high-risk patients. *N. Engl. J. Med.* 351(15), 1493–1501 (2004).
- 3 Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. *N. Engl. J. Med.* 325(7), 445–453 (1991).
- Landmark study comparing endarterectomy with the best medical therapy in a patient with symptomatic cerebrovascular disease.
- 4 Endarterectomy for asymptomatic carotid artery stenosis. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. *JAMA* 273(18), 1421–1428 (1995).
- Landmark study comparing endarterectomy with best medical therapy in patient with asymptomatic cerebrovascular disease.
- 5 Randomised trial of endarterectomy for recently symptomatic carotid stenosis: final results of the MRC European Carotid Surgery Trial (ECST). *Lancet* 351(9113), 1379–1387 (1998).
- 6 Halliday A, Mansfield A, Marro J *et al.* Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomised controlled trial. *Lancet* 363(9420), 1491–1502 (2004).
- 7 Silver FL, Mackey A, Clark WM *et al.* Safety of stenting and endarterectomy by symptomatic status in the Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST). *Stroke* 42(3), 675–680 (2011).
- 8 Kinlay S. Fire in the hole: carotid stenting versus endarterectomy. *Circulation* 123(22), 2522–2525 (2011).
- 9 International Carotid Stenting Study investigators, Ederle J, Dobson J *et al.* Carotid artery stenting compared with endarterectomy in patients with symptomatic carotid stenosis (International Carotid Stenting Study): an interim analysis of a randomised controlled trial. *Lancet* 375(9719), 985–997 (2010).
- 10 Amarenco P, Labreuche J, Mazighi M. Lessons from carotid endarterectomy and stenting trials. *Lancet* 376(9746), 1028–1031 (2010).
- 11 Bangalore S, Kumar S, Wetterslev J *et al.* Carotid artery stenting vs carotid endarterectomy: meta-analysis and diversity-adjusted trial sequential analysis of randomized trials. *Arch. Neurol.* 68(2), 172–184 (2011).
- Excellent review and meta-analysis of the carotid artery stenting (CAS) trials demonstrating a higher stroke and death rate with carotid artery stenting compared with endarterectomy.
- 12 Eckstein HH, Ringleb P, Allenberg JR *et al.* Results of the Stent-Protected Angioplasty versus Carotid Endarterectomy (SPACE) study to treat symptomatic stenoses at 2 years: a multinational, prospective,

- randomised trial. *Lancet Neurol.* 7(10), 893–902 (2008).
- 13 Bonati LH, Jongen LM, Haller S *et al.* New ischaemic brain lesions on MRI after stenting or endarterectomy for symptomatic carotid stenosis: a substudy of the International Carotid Stenting Study (ICSS). *Lancet Neurol.* 9(4), 353–362 (2010).
 - 14 Lam RC, Lin SC, DeRubertis B, Hyncek R, Kent KC, Faries PL. The impact of increasing age on anatomic factors affecting carotid angioplasty and stenting. *J. Vasc. Surg.* 45(5), 875–880 (2007).
 - **Reviews the anatomic challenges associated with CAS.**
 - 15 Lin SC, Trocciola SM, Rhee J *et al.* Analysis of anatomic factors and age in patients undergoing carotid angioplasty and stenting. *Ann. Vasc. Surg.* 19(6), 798–804 (2005).
 - 16 Gurm HS, Yadav JS, Fayad P *et al.* Long-term results of carotid stenting versus endarterectomy in high-risk patients. *N. Engl. J. Med.* 358(15), 1572–1579 (2008).
 - 17 Blasel S, Hattingen E, Berkefeld J *et al.* Evaluation of angiographic and technical aspects of carotid stenting with diffusion-weighted magnetic resonance imaging. *Cardiovasc. Intervent. Radiol.* 32(4), 666–671 (2009).
 - 18 Malik RK, Vouyouka A, Salloum A, Marin ML, Faries PL. Tips and techniques in carotid artery stenting. *J. Vasc. Surg.* 50(1), 216–220 (2009).
 - **Reviews CAS technique and provides helpful tips to facilitate procedural success.**
 - 19 Bosiers M, Peeters P, Verbist J *et al.* Belgian experience with FilterWire EX in the prevention of embolic events during carotid stenting. *J. Endovasc. Ther.* 10(4), 695–701 (2003).
 - 20 Chung C, Cayne NS, Adelman MA *et al.* Improved hemodynamic outcomes with glycopyrrolate over atropine in carotid angioplasty and stenting. *Perspect. Vasc. Surg. Endovasc. Ther.* 22(3), 164–170 (2010).
 - 21 Ackerstaff RG, Suttorp MJ, van den Berg JC *et al.* Prediction of early cerebral outcome by transcranial Doppler monitoring in carotid bifurcation angioplasty and stenting. *J. Vasc. Surg.* 41(4), 618–624 (2005).
 - **Highlights the impact of various CAS maneuvers on cerebral embolization as measured by transcranial Doppler.**
 - 22 Clair DG, Hopkins LN, Mehta M *et al.* Neuroprotection during carotid artery stenting using the GORE flow reversal system: 30-day outcomes in the EMPiRE Clinical Study. *Catheter Cardiovasc. Interv.* 77(3), 420–429 (2011).
 - 23 Bosiers M, de Donato G, Deloose K *et al.* Does free cell area influence the outcome in carotid artery stenting? *Eur. J. Vasc. Endovasc. Surg.* 33(2), 135–141; discussion 142–143 (2007).
 - **Excellent paper reviewing the impact of carotid stent free-cell area on procedural outcomes.**
 - 24 Bosiers M, Deloose K, Verbist J, Peeters P. Carotid artery stenting: which stent for which lesion? *Vascular* 13(4), 205–210 (2005).
 - 25 Muller-Hulsbeck S, Schafer PJ, Charalambous N, Schaffner SR, Heller M, Jahnke T. Comparison of carotid stents: an *in vitro* experiment focusing on stent design. *J. Endovasc. Ther.* 16(2), 168–177 (2009).
 - 26 Schillinger M, Minar E. Matching carotid anatomy with carotid stents. *J. Cardiovasc. Surg. (Torino)* 49(6), 723–727 (2008).
 - 27 Mathiesen EB, Bona KH, Joakimsen O. Echolucent plaques are associated with high risk of ischemic cerebrovascular events in carotid stenosis: the tromsø study. *Circulation* 103(17), 2171–2175 (2001).
 - 28 Aldemir E, Apaydin M, Varer M, Uluc E. Echolucency of carotid plaques and cerebrovascular events. *J. Clin. Ultrasound* 40(7), 399–404 (2012).
 - 29 Gurbel PA, Callahan KP, Malinin AI, Serebruany VL, Gillis J. Could stent design affect platelet activation? Results of the Platelet Activation in STenting (PAST) Study. *J. Invasive Cardiol.* 14(10), 584–589 (2002).
 - 30 Pokrovskii AV, Beloiartsev DF, Timina IE, Adyrkhaev ZA. Clinical manifestations and diagnosis of pathological deformity of the internal carotid artery. *Angiol. Sosud. Khir.* 17(3), 7–18 (2011).
 - 31 Auricchio F, Conti M, Ferraro M, Reali A. Evaluation of carotid stent scaffolding through patient-specific finite element analysis. *Int. J. Numer. Method. Biomed. Eng.* 28(10), 1043–1055 (2012).
 - 32 Tadros RO, Spyris CT, Vouyouka AG *et al.* Comparing the embolic potential of open and closed cell stents during carotid angioplasty and stenting. *J. Vasc. Surg.* 56(1), 89–95 (2012).
 - 33 Hart JP, Peeters P, Verbist J, Deloose K, Bosiers M. Do device characteristics impact outcome in carotid artery stenting? *J. Vasc. Surg.* 44(4), 725–730; discussion 730–731 (2006).
 - 34 Malik RK, Landis GS, Sundick S, Cayne N, Marin ML, Faries PL. Predicting embolic potential during carotid angioplasty and stenting: analysis of captured particulate debris, ultrasound characteristics, and prior carotid endarterectomy. *J. Vasc. Surg.* 51(2), 317–322 (2010).
 - 35 Schillinger M, Gschwendtner M, Reimers B *et al.* Does carotid stent cell design matter? *Stroke* 39(3), 905–909 (2008).
 - 36 Jim J, Rubin BG, Landis GS *et al.* Society for Vascular Surgery Vascular Registry evaluation of stent cell design on carotid artery stenting outcomes. *J. Vasc. Surg.* 54(1), 71–79 (2011).
 - 37 Maleux G, Marrannes J, Heye S, Daenens K, Verhamme P, Thijs V. Outcome of carotid artery stenting at 2 years follow-up: comparison of nitinol open cell versus stainless steel closed cell stent design. *J. Cardiovasc. Surg. (Torino)* 50(5), 669–675 (2009).
 - 38 Timaran CH, Rosero EB, Higuera A, Ilarraza A, Modrall JG, Clagett GP. Randomized clinical trial of open-cell vs closed-cell stents for carotid stenting and effects of stent design on cerebral embolization. *J. Vasc. Surg.* 54(5), 1310–1316.e1 (2011).
 - 39 Pierce DS, Rosero EB, Modrall JG *et al.* Open-cell versus closed-cell stent design differences in blood flow velocities after carotid stenting. *J. Vasc. Surg.* 49(3), 602–606 (2009).
 - 40 Hussain HG, Aparajita R, Khan SZ, Rezayat C, McKinsey JF, Dayal R. Closed-cell stents present with higher velocities on duplex ultrasound compared with open-cell stents after carotid intervention: short- and mid-term results. *Ann. Vasc. Surg.* 25(1), 55–63 (2011).