Carotid Artery Stenting
Applications and Technical Considerations

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Abstract

Purpose of The Review
To examine current understanding of diverse etiologies of extracranial carotid disease, including clinical and imaging manifestations as well as treatment approaches.

Recent Findings
Increasing availability of advanced cerebrovascular imaging modalities continues to elucidate atherosclerotic and nonatherosclerotic carotid steno-occlusive disease as a common culprit of cerebral ischemia. Individualized treatment strategies targeting each etiologic subset would optimize preventive measures and minimize recurrence of cerebral ischemia.

Summary
Ischemic stroke is a prominent cause of mortality and long-term disability worldwide. The magnified effect of carotid disease warrants constant and close inspection.
Stroke is the second leading cause of mortality in developed countries and the foremost culprit of long-term disability. Ischemic events account for more than 85% of all strokes and are commonly caused by carotid artery disease. Steno-occlusive disease of the cervical carotid is often caused by atherosclerotic disease, but it may also be secondary to nonatherosclerotic conditions including carotid webs (CaW) and dissections. It is important to recognize the entity of cervical carotid artery pseudo-occlusion, a flow-related phenomenon where blood/contrast stagnation occurs at the cervical level in the setting of intracranial internal carotid artery (ICA) occlusion. This may occur either acutely due to embolic or in situ thrombotic events or chronically due to moyamoya syndrome or intracranial atherosclerotic disease.

Atherosclerosis constitutes a frequent cause of steno-occlusive disease, typically affecting the carotid bifurcation. Luminal narrowing and ulceration is the consequence of atheromatous plaque progression, which could yield to cerebral ischemic events due to artery-to-artery embolization after in situ thrombosis or hemodynamic compromise. As the population ages, it is likely that the impact of carotid artery disease will grow as up to 7.5% and 5% of elderly (80 years) men and women, respectively, have asymptomatic carotid stenosis ≥50%. Despite the evolution of medical management, substantial morbidity and mortality are associated with the presence of carotid atherosclerotic disease. This can be found incidentally or can be diagnosed after an ischemic event, which may need to be urgently or emergently treated, or may be approached with revascularization for secondary prevention according to the clinical presentation.

Without revascularization, the ischemic stroke rate among asymptomatic carotid patients has been reported as 19%–33%, depending on the degree of stenosis, within 18 months of medical management. Among the nonatherosclerotic conditions, dissections account for a sizable amount of ischemic strokes in the young due to the development of thromboembolism or hemodynamic insufficiency. CaW, an intimal form of fibromuscular dysplasia, has emerged as a relevant thromboembolic source of recurrent ischemic stroke in the young.

Stenting of Atherosclerotic Disease

Carotid artery stenting (CAS) was initially developed as an alternate treatment option for carotid occlusive disease in high surgical risk patients. Retrospective, prospective, and controlled data have compared this minimally invasive procedure to carotid endarterectomy (CEA). Accrued evidence indicates that both procedures share similar safety and efficacy, and thus appropriate patient selection is the most critical factor for optimal outcomes. Major randomized trials addressing carotid artery revascularization are nearly 3 decades old; studies factoring in more intensive current medical management are needed.

Patient Selection/Risk Assessment

Numerous anatomic and structural elements should be considered when deciding the modality of choice for carotid revascularization. Classically, high surgical risk patients who have one or more of the following should be preferentially considered for CAS:4-9

- High carotid bifurcation: risks of cranial nerve injury are increased with surgical exploration in lesions located above the second vertebral level
- Contralateral vocal cord paralysis, as significant airway compromise could result from bilateral laryngeal nerve palsy
- Lesions located below the level of the clavicle
- Previous ipsilateral CEA
- Greater than 50% contralateral carotid artery stenosis
- Prior coronary artery bypass graft surgery
- Prior tracheostomy, radical neck surgery, or radiation
- Heart failure New York Heart Association Class III or IV
- Chronic obstructive pulmonary disease

Conversely, CAS revascularization may be unfavorable in the following situations:10,11

- Type II or III aortic arch
- Greater than 50% stenosis of the arch artery origin
- Long segment stenosis (≥12.85 mm)
- Severe ipsilateral intracranial stenosis
- Common or ICA tortuosity >30°
- Concentric plaque calcifications

Carotid Revascularization Endarterectomy vs Stenting Trial (CREST) data have demonstrated that, contrary to the previous assumptions, CAS is safer in younger individuals. This is mainly related to increased stroke risks with aging, likely secondary to age-related effect on the arch and craniocervical angioarchitecture. Age was observed to be a primary end point effect modifier in the CREST trial. The efficacy of CAS and CEA was found to be comparable at age 70 years for the composite endpoint of stroke/myocardial infarction/death.12 This is in line with data from different randomized trials as well as prospective and retrospective registries that indicated...
higher risk of 30-day stroke and death in ≥80-year-old patients undergoing CAS.\textsuperscript{12–19} Other features that may be unfavorable for an endovascular approach are the presence of pedunculated thrombus or nonconcentric but thick calcifications. Long and contiguous lesions may favor endarterectomy whereas short and contiguous lesions can be safely treated with stenting.\textsuperscript{11} Underlying lesion ulcers has not been clearly established as a specific risk factor for modality of revascularization.\textsuperscript{11} Initiating dual antiplatelet therapy prior to carotid revascularization is critical and has been demonstrated to markedly decline in recurrent ischemic events without significant increase in bleeding complications.\textsuperscript{20}

**Procedural Safety**

There are 2 types of embolic protection devices (EPDs): filters and flow reversal devices. Filters are more frequently used and aim to maintain antegrade carotid flow while capturing dislodged debris during angioplasty and stent placement (Figure 1). Significant reduction in overall stroke and death rates has been demonstrated in those patients in whom EPD was used.\textsuperscript{21} Proximal protection methods are designed to arrest or reverse proximal ICA flow while performing carotid revascularization. This is usually performed by temporarily inflating balloons in the external carotid artery and common carotid artery (CCA). Following stent deployment, the proximal ICA is suctioned to remove debris prior to deflating the balloon. These devices are typically navigated into the common carotid artery via a transfemoral artery sheath. A more recent novel approach of flow reversal is the transcarotid artery revascularization (TCAR) approach. This is performed by gaining direct proximal CCA vascular access through surgical vessel exposure, as well as femoral venous access, and CCA clamping. While angioplasty and stenting are performed, passive reversal of blood flow from the carotid artery into the femoral vein aids in preventing cerebral embolization. Early data indicate that patients undergoing TCAR may have similar outcomes with lower risks of cranial nerve injury compared to those undergoing CEA.\textsuperscript{22}

**Carotid Stent Technology**

Self-expandable open- and closed-cell stent designs are the 2 main types of carotid stent. Closed-cell stents have been associated with lower chances of plaque protrusion through stent cells due to the aligned annular rings and tighter free space, which could lead to a lower periprocedural thromboembolic risk. Conversely, open-cell stents have improved flexibility and conformability in curves and tortuous vessels. Despite theoretical advantages of each design, most registries have demonstrated no significant clinical advantages of one type over the other. Periprocedural cerebrovascular risks were grossly comparable with both open and closed stent according to a review of multiple retrospective studies.\textsuperscript{22} The use of drug-eluting stents or drug-coated balloons is generally reserved for those with recurrent in-stent stenosis due to intimal hyperplasia. Novel micromesh/ultra-closed-cell stent technology with very small aperture areas has been designed to minimize the chances of plaque prolapse through stent cells.\textsuperscript{23} In the CREST trial, 40% of the periprocedural strokes occurred after the first day of treatment, suggesting that plaque prolapse is a potential culprit.\textsuperscript{24} Plaque prolapse has been linked to open-cell stent use, new lesions on MRI, and perioperative strokes.\textsuperscript{25}

**Preoperative Management**

Similar to percutaneous coronary intervention, dual-antiplatelet therapy should be started preferably at least 48 hours prior to CAS.\textsuperscript{23} Generally, aspirin and clopidogrel are utilized. Those scheduled for CAS within 48 hours can receive aspirin 325–650 mg and clopidogrel 450–600 mg at least 4 hours before the CAS procedure. Following CAS, daily aspirin 81–325 mg and clopidogrel 75 mg should be maintained for at least 30 days, with a recommendation to continue aspirin indefinitely, per multispecialty consensus.\textsuperscript{26} Recent study suggested prolonged duration of dual antiplatelet therapy is associated with lower rates of post stenting ischemic events and higher rates of extracranial hemorrhages.\textsuperscript{26} In those who are intolerant or nonresponders to clopidogrel, ticagrelor (60–90 mg twice daily) or prasugrel (5–10 mg once daily) can be used. Comorbid renal disease as well as significant peripheral atherosclerotic vascular disease (which might limit vascular access) must be examined prior to CAS. The procedure is performed in the angiography suite most commonly under monitored anesthesia care. Continuous cardiac and blood pressure monitoring along with ample hydration and antihypertensives dosing modification are warranted prior to CAS to avoid persistent intra- and postprocedural hypotension. Systolic blood pressure (SBP) should be prudently monitored while performing revascularization to minimize risk of reperfusion or hyperperfusion syndrome and hemorrhagic transformation of ischemic infarct. Generally, stringent control of SBP lower than 140 mm Hg immediately after angioplasty or stent is pursued.

**Complications**

- Hemodynamic instability: the carotid bulb contains baroreceptors that modulate sympathetic and parasympathetic activity. Stretching/compressing these receptors with angioplasty and stent placement can inhibit sympathetic activity and increase vagal parasympathetic tone with consequent cardiovascular changes. Five to ten percent of patients can develop bradycardia and hypotension, but routine preprocedural measures with avoidance of beta-blockers close to intervention time and administering atropine with low heart rate baseline (less than 60 beats/minute) can minimize significant hemodynamic changes. Most of these changes are transitory and do not require prolonged postprocedural treatment but some patients may require short-term vasopressor therapy. We tend to favor the use of IV dopamine as it is a vasopressor with inotropic properties that increases cardiac output more than norepinephrine as well as improves renal and hepato-splanchnic blood flow.
- Iatrogenic vascular injuries: vasospasm is mostly benign, short-lived, and can be noticed in 10%–15% of cases. On the other hand, vascular dissections, thrombosis, or perforation
are more deleterious and can constitute a nidus for thrombosis; it is less common (<1%).

- External carotid artery stenosis: can potentially happen in the setting of straightening and dilation of the ICA with the stent deployment and is considered clinically insignificant.

- Device malfunctioning: rare, can occur in less than 1% and can be exemplified by stent migration, kinking, or fracture that can lead to vessel angulation and restenosis.27,28

- Stent restenosis or thrombosis: these can predispose to hypoperfusion or thromboembolism. Intimal hyperplasia is a healing sequela of vascular intervention post angioplasty and stenting. This usually affect the extracellular matrix and vascular smooth muscles leading to thickening of the intimal vessel wall layer. Excessive formation of intimal hyperplasia can constrain the luminal blood flow, leading to in-stent restenosis. Certain technical and demographic factors are tied to this, including higher stent length, stent diameter, multivessel intervention, residual underlying dissection as well as poor apposition to the vessel wall, older age, female sex, higher SBP and diastolic blood pressure, prior or active tobacco use, non-insulin-dependent diabetes, high serum cholesterol, and higher-grade contralateral carotid stenosis.29 A recent randomized study suggested promising results for cilostazol use in preventing in-stent carotid stenosis.30

- Cerebral hyperperfusion syndrome: like in CEA, patients with baseline and periprocedural impaired vasomotor reactivity in the setting of uncontrolled hypertension as well as occluded or severe contralateral carotid stenosis are exposed to higher risk of postprocedural intracerebral hemorrhage.31 Preprocedure studies to establish the presence of compromised cerebrovascular reserve may identify the patients at highest risk for cerebral hyperperfusion syndrome. Transcranial Doppler with monitoring of the pre- and postrevascularization mean flow middle cerebral artery velocities can be used to titrate the postoperative blood pressure levels.32

- Myocardial infarction: periprocedural incidence has been reported to be 1%–4%. Myocardial infarction defined as doubling of upper limits normal range of creatine kinase MB or troponin in addition to either chest pain or ECG evidence of ischemia.15 Hemodynamic instability after angioplasty/stenting may be the major trigger of cardiac ischemia.

- Access site: more common complications are those related to transfemoral access injuries. Most issues relate to pain, and less commonly infections (<1%), pseudoaneurysm or arteriovenous fistulas (1%–2%), puncture-site hematoma (<5%), and retroperitoneal bleeding requiring blood transfusion (up to 2%–3%).33 The transradial artery approach for neuroendovascular procedures, including carotid stenting, has gained popularity and might be safer than the transfemoral access approach.34

**Stenting of Nonatherosclerotic Disease**

**Carotid Webs**

CaW is an intimal version of fibromuscular dysplasia. It is a radiologic diagnosis based on the observation of a shelf-like linear intraluminal protrusion at the posterior aspect of the

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**Figure 1** Dislodged Debris Captured by Emboli Protection Device Noted After Carotid Stenting

**Figure 2** Left Carotid Web in a 60-Year-Old Man Presenting With Middle Cerebral Artery Occlusion
Carotid bulb (Figure 2). It has been estimated to affect 8.9% of patients with TIA, 0.5% of all patients with ischemic stroke, and 9%–37% of young patients with cryptogenic stroke. It appears that these lesions lead to recurrent strokes in a substantial proportion of patients, with reported numbers indicating 83% of the patients with TIA had short-term (3 months) recurrent events, while in patients with stroke, the recurrent event rate ranged from 29% to 71%. The median time for recurrence varies from 9 to 12 months. CaWs appear to more commonly affect young Black female patients. These lesions are often missed or misdiagnosed. Among other entities, webs are commonly mistaken as dissections due to the appearance of a structure resembling a flap on axial images, or as atherosclerotic lesions that can present in the form of focal and endoluminal protruding lesions. Although the diagnosis can be made noninvasively, some modalities are limited for this condition. Ultrasonography has been shown to have lower sensitivity and specificity. Magnetic resonance angiography (MRA) can be helpful when performed with gadolinium, as the time-of-flight commonly leads to flow artifacts. CT angiography (CTA) has good special resolution and allows for multiplane reconstructions. It has been shown to have comparable performance to conventional angiography. Prominent flow stagnation has been demonstrated to occur within the web pocket, and this impairment of flow dynamics appears to predispose to local thrombosis. Superimposed thrombosis within the web has been reported in 12%–29% of patients with symptomatic CaW. The evidence related to treatment options is limited. Asymptomatic lesions have never been reported to lead to strokes, and therefore may not warrant specific treatment. Antiplatelet monotherapy can be used in symptomatic CaW, but recurrent events in patients following this strategy has been reported to occur in up to 30%. Anticoagulation or dual antiplatelets could be considered, despite the limited available data. The long-term preventative strategy needs to factor in that these patients are young and the lesion is static in nature. Revascularization with surgical resection or stenting is an option. A systematic review has indicated that surgery may be safe and effective in preventing recurrent strokes. Endovascular treatment with carotid stenting has more recently emerged as an alternative and appeared safe and effective in a recently published series. Multidisciplinary discussion and involvement of patients/family members in the treatment plan is encouraged.

Carotid Dissection
Among young and middle-aged individuals, spontaneous carotid dissections account for a significant proportion of ischemic strokes. The prevalence of carotid dissections is 2.6 (95% confidence interval, 1.9–3.3) per 100,000 inhabitants per year. The mean age at diagnosis in North American and European published data is 45.8 years with 13%–16% harboring multiple cervical carotid and vertebral dissections. It is rare for dissections to involve patients older than 65 years. Carotid dissections are more prevalent in men and patients are, on average, 5 years older at time of presentation. The pathophysiology of carotid dissections is poorly understood. They often occur spontaneously in healthy individuals without significant vascular risk factors. Traumatic dissections usually result from ICA trauma. The classic theory is that an intimal tear may yield to blood seepage into the false lumen between the vessel wall layers, forming dissecting intramural hematoma that creates a false lumen. Alternatively, underlying arteriopathy could be the culprit in cases of multiple and recurrent dissections, although it may also explain dissections related to trauma. Arteriopathy with microhemorrhages could lead to intramural hemorrhages that would tear into the lumen. Luminal stenosis or occlusion (due either to hematoma compressing the intima or the exposure of subendothelial collagen leading to thrombosis) are more commonly associated with subintimal dissections. Conversely, subadventitial dissections may result in outward expansion leading to an aneurysmatic (imprecisely called “pseudoaneurysm”) formation.

Noninvasive imaging including CTA or MRA is used in most centers to diagnose cervical carotid dissections. Generally, conventional angiography is used infrequently to supplement noninvasive imaging findings. Dissections are demonstrated as long tapered lesions with subsequent luminal stenosis or occlusion. Dissecting aneurysms or an intimal flap with a double lumen can be observed. Acutely, the surface is commonly irregular due to contrast filling defects related to in situ thrombosis. Stenotic carotid artery disease appears to be the most common presentation (48%), followed by occlusive and aneurysmal morphology in 35% and 17%, respectively.

A third of patients with carotid dissection may have only local signs and symptoms without cerebral or retinal ischemia, which could in part be related to the underestimation of this disease given lack of central ischemic symptoms. Retrospective data indicate that the risk of ischemic stroke can vary from the first few hours to a couple of weeks after the diagnosis of cervical dissection. Different mechanisms may contribute to the risk of stroke, including thromboembolism, hypoperfusion, or a combination of both. In addition, local mass effect of the aneurysmatic dilation may cause compression of adjacent nerves, their feeding vessels, leading to Horner syndrome, lower cranial neuropathies, and cervical nerve root involvement. Extracranial internal carotid dissection usually occurs 2 cm distal to the carotid bifurcation, near or adjacent to the skull base. S-shaped cervical ICA curves without superimposed atherosclerotic disease have been suggested as independently associated with a higher risk for carotid dissections. Arterial fenestrations and cerebral aneurysms have been associated with extracranial cervical dissections as well.

Although rare, when dissection extends into the intradural portion of the vessel, it could result in subarachnoid hemorrhage as intracranial arteries are more prone to rupture due to thinner media/adventitia and lack of external elastic lamina. The first intracranial carotid segment (petrous segment) is protected in the petrous bone, making it less common for rupture.
Antithrombotic therapy with anticoagulation or antiplatelet drugs has been used as the mainstay treatment for symptomatic cervical carotid dissection post ischemic stroke or TIA. Single or dual antiplatelet treatment were compared with anticoagulation for cervical artery dissection in the Cervical Artery Dissection in Stroke Study (CADISS), which found no significant difference between the 2 treatment groups. A total of 46% of the antiplatelets group received dual antiplatelet coverage.48 The duration of treatment may vary as the average time for endothelialization is much shorter than the time for spontaneous arterial remodeling, making it reasonable to maintain dual antiplatelets from a few weeks up to a few months.

Endovascular reconstruction with stent placement is generally reserved for those who failed medical management and encountered recurrent ischemic insults despite antithrombetics, have symptoms of cranial nerve compression, or have rapid aneurysm growth. Despite potential benefit of vessel reconstruction, stenting is considered a Class IIb, Level of Evidence C treatment.49 Low procedural risks and safe outcome were reported with endovascular stenting of carotid dissections involving the CCA or ICA. If dissections are proximal and in a relatively straight segment, carotid stents can be used. Intracranial self-expandable stents can be used in more distal occlusions.50 When significant tortuosity is present, flow-diverting stents can be used for vessel remodeling. The use of proximal or distal protection devices should be encouraged, especially in presence of in situ thrombosis.

**Stenting in Acute Tandem Occlusions**

Concomitant tandem steno-occlusive disease of the extracranial carotid and intracranial large vessels is associated with lower revascularization rates after IV thrombolysis and with poorer clinical outcomes.51 Underlying proximal occlusion can be attributed to various pathologies including dissections, atherosclerotic occlusions, embolic events, or re-occlusions of previously revascularized carotid arteries with CEA or CAS. The decision to address both lesions makes an emergent endovascular intervention for acute ischemic stroke considerably more challenging as compared to isolated intracranial occlusion cases. In most patients, intracranial reperfusion is the main goal when dealing with acute tandem occlusions (TOs). However, some patients may not have adequate compensation (e.g., via circle of Willis, leptomeningeal, or external to internal carotid collateralization) and may need to have their cervical carotids secured patent. Therefore, there is lack of consensus as to the best way to approach the extracranial lesion.

The peri- and postprocedural need for IV antithrombotic agents (e.g., glycoprotein IIb/IIIa inhibitors) and oral antithrombetics (e.g., aspirin, clopidogrel, ticagrelor) has raised safety concerns as some series revealed high rates of intracerebral hemorrhage, ranging from 18% to 43%. On the other hand, stent thrombosis can be encountered in up to 17% despite optimal periprocedural antithrombotic use.52 Most published data reported low rate of hemorrhagic transformation with acute stenting but there is no established consistency of choice and dosing of antithrombotic, especially in those who received IV alteplase.52,53
Some of the stroke thrombectomy randomized trials excluded patients with TO, while others included them, with a variable rate of TO inclusion ranging between 17% and 32%.54 Several series, meta-analyses, and reviews have been published demonstrating the potentially safe, yet technically complex, endovascular treatment of TO.52,54-57

Various strategies of endovascular treatment have been suggested, including performing both intracranial and extracranial revascularization (with angioplasty or stenting) or utilizing a more minimalistic approach, only approaching the intracranial occlusion without addressing the cervical carotid.59 There are benefits and disadvantages to each method and controlled data are lacking. Data from the Systematic Evaluation of Patients Treated With Neurothrombectomy Devices for Acute Ischemic Stroke (STRATIS) registry demonstrated feasible, safe, and better clinical outcome with acute stenting of extracranial carotid stenosis during neurothrombectomy. A great subset of the published literature involves an anterograde approach that addresses the proximal carotid occlusion (with angioplasty or stent placement) first followed by reperfusion of the intracranial lesion. This could facilitate flow-related recanalization of the intracranial occlusion while securing antegrade flow and optimizing collaterals, as well as stabilizing the internal carotid artery stenosis and easing passage of the base catheter to approach the intracranial lesion. Antegrade revascularization, however, may delay intracranial reperfusion. Prior studies suggested an average delay in intracranial reperfusion of 20 minutes with anterograde approach.53 On the other hand, performing upfront intracranial thrombectomy may allow faster restoration of intracranial blood flow58 (Figure 3). Well-known differences in clinical outcomes between the antegrade and retrograde approaches are lacking.54 In cases of atherosclerotic occlusions, there are generally well-developed collaterals and targeting intracranial reperfusion alone may suffice (leaving the carotid occluded or narrowed); this approach would minimize the effect of cerebral recanalization with abrupt increase in perfusion pressure in the setting of an acute ischemic stroke (especially if thrombolysis has been used) and make the use of dual antiplatelet therapy relatively safer. Revascularization can then be considered within the first 2 weeks based on the final infarct volume, stroke topography, the presence of hemorrhagic changes, and the clinical examination.

CAS can be performed safely in acute and elective settings following stroke. Nonatherosclerotic extracranial carotid disease such as CaW or dissection might benefit from CAS in carefully selected patients. Future studies addressing the optimal techniques and technologies are warranted.

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