

The emerging role of carotid artery stenting in the management of high-risk patients with carotid artery disease



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'Carotid artery disease represents a significant health risk with stroke being a leading cause of disability and mortality'

Stroke is a major cause of morbidity and mortality in the USA where approximately 500,000 new cases occur annually [1]. Approximately 150,000 of these occur as a result of extracranial atherosclerotic carotid arterial disease. Risk factors for the development of carotid artery stenosis include tobacco use, hypertension, dyslipidemia and diabetes mellitus [2].

The risk of morbidity and mortality from carotid stenosis depends largely upon the degree of stenosis and the presence or absence of symptoms. Asymptomatic patients with hemodynamically significant carotid stenosis have an annual stroke event rate of 2 to 5%. The annual stroke event rate for symptomatic carotid stenosis is approximately 4 to 13% [2]. Baseline stenosis severity, rate of progression, plaque composition and ulceration all increase the risk of events. Several studies have demonstrated the superiority of carotid endarterectomy (CEA) over medical management in patients with severe carotid arterial disease – either asymptomatic or symptomatic.

CEA is the traditional method of treating carotid artery stenosis and is the gold standard for revascularization of extracranial carotid artery disease. The first carotid repair for symptomatic carotid disease was performed in 1951. Since then, several studies have investigated the safety and efficacy of CEA. Trials such as the North American Symptomatic Carotid Endarterectomy Trial (NASCET), European Carotid Surgery Trial (ECST) and the Asymptomatic Carotid Atherosclerosis Study (ACAS) have demonstrated the safety and efficacy of CEA in the treatment of severe carotid artery stenosis with or without symptoms.

The NASCET studied 326 patients with symptomatic stenosis of 70% or more and found that these patients had a significant benefit after undergoing CEA that persists for at least 5 years. Patients treated medically had a 2-year event rate of approximately 26% whereas those

who underwent CEA had a 2-year event rate of 9% [3]. Similarly, the ECST studied 778 symptomatic patients with severe carotid artery stenosis and demonstrated that CEA can substantially reduce the risk of ipsilateral ischemic strokes at 3 years, 6.0% for CEA versus 11.0% for medical therapy [4].

The ACAS evaluated 1659 patients with asymptomatic but hemodynamically significant carotid artery stenosis. The study found that CEA is beneficial in patients with hemodynamically significant yet asymptomatic carotid artery stenosis. In patients with greater than or equivalent to 60% carotid artery stenosis, those treated with CEA had a 5-year event rate of 5.1%, while those treated medically had an event rate of 11% [5].

The major limitations of surgical trials for the treatment of carotid artery stenosis are the strict inclusion and exclusion criteria which resulted in a relatively low-risk patient population being studied. High-risk patients including those with occlusion of the contralateral carotid artery, recurrent restenosis following CEA, prior neck irradiation, coronary artery disease requiring revascularization, congestive heart failure, chronic obstructive pulmonary disease, and chronic renal insufficiency were not included in the trials studying the efficacy and safety of CEA. Historical as well as emerging data from carotid stent trials suggest that these patients have a significantly higher risk when treated either medically or surgically. The Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) trial suggests that high-risk patients have a 15.4% 30-day risk of myocardial infarction (MI), stroke or death following CEA [6].

Carotid artery stenting (CAS) has become an alternative approach to treating patients with severe carotid artery stenosis. This approach is attractive in patients with comorbid conditions that increase the surgical risk. Furthermore, this procedure may be better suited for patients with high-risk anatomic considerations such as prior neck irradiation, high carotid bifurcations, a tracheostomy or restenosis following CEA. Two recently published trials suggest the efficacy and safety of CAS.

The ACCULINK for Revascularization of Carotids in High Risk Patients (ARCHEr) trials were designed as noninferiority trials comparing CAS with historical control of CEA in high-risk patients. The findings of this trial confirmed the prespecified noninferiority end points. Major or fatal strokes occurred at rates similar to the major CEA trials. The 30-day composite end points (stroke, death or MI) were 7.6, 8.6 and 8.3% for ARCHEr 1, 2 and 3, respectively. The 1-year event rate (30-day composite end point and day 31 to 1 year ipsilateral stroke) was 8.3% for ARCHEr 1 and 10.2% for ARCHEr 2 [7]. The weighted historical control for the ARCHEr 1 and 2 trials was 14.5%. The SAPPHERE trial was a randomized trial with intention to treat analysis comparing CEA and CAS in high-risk patients. There was a significant reduction in the primary end point in the stent arm compared with the CEA arm – 12.2 versus 20.1%, respectively [8].

Atherosclerotic lesions are composed of calcium, lipid, fibrin and platelets with a high propensity for distal embolization during percutaneous interventions. Because of this, many companies have developed embolic protection devices (EPDs) [9]. There are three principle types of EPDs:

- Filters
- Distal balloon occlusion
- Proximal balloon occlusion with flow reversal

The first group act as filters – the lesion is initially crossed unprotected and then the filter is deployed distal to the lesion in the internal carotid artery (ICA). Following angioplasty and stenting, the filter is removed. The AngioGuard™ (Cordis Corp.) filter, the AccuNet™ (Guidant Corp.) filter, the FilterWire EX™ (Boston Scientific) embolic protection device, and the MedNova NeuroShield™ (Mednova

Inc.) are all examples of filter EPDs. Distal balloon occlusions occlude flow distally in the ICA during the procedure. Upon completion of the intervention, the column of blood with any potential embolic debris is removed with an aspiration catheter. The PercuSurge® device (Medtronic), which is approved for aortocoronary saphenous vein graft interventions, is an example of the distal balloon occlusion device [9]. The third group of EPDs – proximal balloon occlusion – function with a balloon at the end of a sheath and in the external carotid artery, which allows flow reversal during the intervention. The Parodi Anti-Emboli System (PAES) is an example of this group. Each group of embolic protection devices has its own advantages and shortcomings [9].

Carotid artery disease represents a significant health risk with stroke being a leading cause of disability and mortality. Treatment of carotid artery stenosis has traditionally involved surgical excision of the plaque – CEA. However, there are significant complications with this procedure, especially in high-risk patients who were generally excluded from large trials comparing CEA with medical therapy. CAS is an emerging modality which has been demonstrated to be noninferior to CEA and in some studies, superior in the reduction of periprocedural complications. This technology remains in its infancy and lacks the long-term outcome data which is available for patients who have undergone CEA. With the recent US Food and Drug Administration approval of the Guidant CAS platform, patients who have either high-risk comorbidities or anatomic features now have the option of a new treatment modality – CAS. There are also trials underway evaluating the efficacy of carotid artery stenting in lower risk patient populations such as the Carotid Revascularization Endarterectomy versus Stent Trial (CREST).

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