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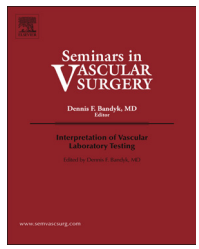

Will mesh-covered stents help reduce stroke associated with carotid stent angioplasty?

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ABSTRACT

Carotid stent angioplasty (CAS) has been shown to protect patient from future stroke long-term efficacy similar to carotid endarterectomy (CEA). The risk of minor stroke in the perioperative period is higher than with CEA and not related to cerebral protection during the CAS procedure since a significant portion of the neurologic events occur between 1 and 30 days following stent deployment. This observation suggests mechanisms integral to the stent itself may be pertinent such as plaque embolization thru the stent struts may occur. It appears that this embolic risk can be reduced by use of specific carotid stent designs that include a mesh covering to minimize the open struts areas and thus embolization through the carotid stent. Improvements in stent design that eliminate post-procedural debris embolization will expand the application of CAS for severe internal carotid artery atherosclerotic stenosis.

1. Introduction

After a decade and a half of clinical studies on carotid stenting, several factors have become clear. Both carotid artery stenting (CAS) and carotid endarterectomy (CEA) protect the patient from stroke over the long term [1,2]. However, in the perioperative period, the risk of stroke, especially minor stroke, is higher with stenting and often presents in a delayed fashion. That is, a significant portion of neurologic events occur between 1 and 30 days after stent placement, long after the cerebral protection device has been removed [3–5]. This appears to be a failure of the carotid stent itself. The morphology of the plaque changes after stent insertion and there is a risk of cerebral embolization through the struts of the stent. Mesh-covered carotid stents have been developed to address this issue [6–8].

2. Background

Treatment for internal artery carotid stenosis can effectively reduce the incidence of stroke, especially in correctly identified at-risk patient groups. Efficacy of CEA depends predominantly on a patent's symptoms, age, and sex. In its most effective setting, in symptomatic men, CEA has an absolute risk reduction for an ipsilateral event of 30.2% over 5 years [2,9]. CEA has remained the procedure of choice for the majority of patients for the last few decades. CAS is a more recently developed and less invasive therapy than CEA. However, there is a higher risk of stroke associated with CAS when compared with CEA, frequently relegating CAS to only patients too ill to undergo CEA or with contraindications to CEA [3,9–11]. Making CAS safer, especially with respect to minor strokes in the perioperative period, is required to make CAS a more broadly applicable therapy.

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Stroke rates between 30 days and up to several years are comparable between CEA and CAS. Procedurally CAS has a tangible benefit with an experienced operator and can avoid some of the potential complications of CEA, such as cranial nerve palsies and wound complications. It has been effectively shown in the Carotid Acculink/Accunet Post-Approval Trial to Uncover Unanticipated or Rare Events (CAPTURE) 2 trial that patient volume is inversely related to death and stroke events with CAS [12]. CAS also has a lower rate of myocardial infarction (MI) than CEA does, making CAS an option to consider in some patients [3,13–15]. Here we focus on a potential cause for concern related to current carotid stent design and the stroke risk posed by cerebral embolization through the stent. Could a mesh-covered carotid stent reduce this risk?

3. Trials that established current endarterectomy guidelines

To understand the current standard, one must look at CEA guidelines and how they were created. The risk reduction, and hence benefit, to intervention on carotid stenosis is different by sex, age, and percent stenosis, but most importantly by symptomatic status. Individuals with symptoms of carotid disease within the previous 6 months are defined as symptomatic patients. Patients with a more remote history of symptoms or none at all, are defined as asymptomatic [9,10,16]. A group of well-known trials established our current guidelines for intervention. The European Carotid Surgery Trial (ECST) enrolled more than 3,000 symptomatic patients and was published in 1998. They concluded that surgical intervention should be done in patients with carotid stenosis >80% for an absolute risk reduction of 11.6% of major disabling ischemic event over 3 years. There was some benefit with stenosis from 70% to 79%, but not enough to include this in their recommendations [17]. The North American Symptomatic Carotid Endarterectomy Trial (NASCET) enrolled more than 2,200 symptomatic patients and was also published in 1998. Their findings were similar to ESCT, but they recommended intervention for symptomatic patients with stenosis >70%. Patients with stenosis 50% to 69% saw a smaller benefit and those with <50% saw no benefit with surgical intervention [16]. The Asymptomatic Carotid Atherosclerosis Study (ACAS) enrolled more than 4,500 asymptomatic patients, comparing maximum medical management alone to medical management plus endarterectomy in patients with carotid stenosis. Patients with at least 60% stenosis had half the risk of stroke or death over a 5-year period when treated with carotid repair plus medical management as compared with patients managed nonoperatively [18]. These trials helped to create our current guidelines for intervention on carotid stenosis. It is imperative to note two significant things here. These trials are all nearly 20 years old and the trials that best established the use of endarterectomy were performed before the development of carotid stenting.

4. Results with carotid stenting

The most prominent contemporary carotid therapy trial is the Carotid Revascularization Endarterectomy Versus Stenting (CREST) trial. CREST was a randomized trial published in 2010 comparing CEA and CAS, composed of more than 2,000 patients in the United States and Canada. Symptomatic patients with stenosis ≥50% on ipsilateral angiography or ≥70% by duplex ultrasound were included. Asymptomatic patients were included if they had ≥60% stenosis by angiography or ≥70% by ultrasound. Among asymptomatic patients, there was no significant difference in risk for minor stroke, major stroke, or death with either CEA or CAS. There were more minor strokes after CAS than CEA (12 *v* 6 events). For symptomatic patients, however, there was an increased risk of minor stroke and death with CAS. Symptomatic patients had twice as many MIs with CEA versus CAS, however the difference was not statistically significant ($P = .083$). Restenosis rates did not differ by treatment arm or by symptom status. Additionally, CEA was associated with more cranial nerve palsies and wound complications, although the majority of nerve palsies resolved within 6 months [3,15,19].

The International Carotid Stenting Study (ICSS) evaluated stenting and endarterectomy for symptomatic carotid stenosis with a subset utilizing magnetic resonance imaging (MRI) analysis for 231 patients. An MRI was performed 1 to 7 days before treatment and again 1 to 3 days after treatment. Half of CAS patients had at least one new lesion post intervention compared with only 17% of CEA patients. In patients who had a symptomatic ischemic hemispheric stroke, the median lesion total volume was larger by diffusion-weighted imaging (DWI) at 9.4 mL compared with asymptomatic lesions at 0.12 mL, making symptomatic lesions 78 times larger than asymptomatic ones. In both symptomatic and asymptomatic groups, stented patients comprised a majority. Protection devices used in the stented group were not found to be effective [5].

The CAPTURE trial was a prospective study that evaluated high-risk surgical patients. Symptomatic patients with ≥50% stenosis and asymptomatic patients with stenosis ≥80% were enrolled. The primary endpoint was stroke, MI, or death

Table 1 – Timing of carotid artery stenting–related strokes or new diffusion-weighted imaging lesions in clinical trials.

Timing of stroke or development of a new MRI lesion after CAS	n
Crest [15]	
Day 0	29
Day 1 to 7	10
Day 8 to 30	9
Bosiers [4]	
Day 0	29
Day 1 to 30	61
ICSS-MRI lesions [5]	
Day 0	NA
Day 1	62
Day 2 to 30	28

Abbreviations: CAS, carotid artery stenting; ICSS, International Carotid Stenting Study; MRI, magnetic resonance imaging; NA, not applicable.