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Carotid Stenting or Carotid Surgery in Average Surgical-Risk Patients: Interpreting the Conflicting Clinical Trial Data

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Abstract There are generic as well as carotid-specific trial design considerations that have the potential to materially affect the outcomes and interpretation of comparative studies between carotid artery stenting and carotid endarterectomy. Recently, a series of trials in patients who are at average risk for carotid surgery have been reported. The European trials have all suffered from allowing an imbalance in operator experience between stenting and surgery and have consistently allowed stenting procedures without embolic protection. The combination of inexperienced operators and lack of embolic protection may be responsible for their negative stenting results. The Carotid Revascularization with Endarterectomy vs. Stenting Trial avoided both of these problems, having a threshold of experience for operators as well as mandating embolic protection be used. The Carotid Revascularization with Endarterectomy vs. Stenting Trial demonstrated noninferiority for stenting compared with surgery in average-risk symptomatic and asymptomatic patients, leading to Food and Drug Administration approval of a stent and protection for this indication. This has been recently followed by guidelines supporting the role of stenting compared with surgery from a broad range of professional societies. (Prog Cardiovasc Dis 2011;54:14-21)

Although the concept of a percutaneous approach to obstructive carotid atherosclerotic disease using balloon angioplasty was first introduced in the early 1980s and followed by the advent of stent use in the 1990s, the ensuing 30 years have not brought clarity as to the role that carotid artery stenting (CAS) plays in the management of patients with carotid bifurcation disease (Fig 1). This is in spite of the fact that there have been thousands of patients treated in multicenter controlled trials, both randomized and single-armed. This article will discuss the remaining controversy in the use of CAS and attempt to clarify its role based on the currently available data. There is no question regarding the equal effectiveness of longer term stroke prevention in all the CAS vs carotid endarterectomy (CEA) trials to be discussed (and this is not in question); most of the following discussion will focus on the comparative short-term safety of CAS vs CEA (30-day outcomes) and attempt to explain the differences among the trials in this regard.

Carotid angioplasty

Although never compared directly to CAS in any randomized fashion, carotid angioplasty (CA) without stenting is felt to be inferior to CAS because it likely results in a more incomplete initial result, possibly less acute plaque stabilization, and less robust long-term patency. So, outcomes from the Carotid Angioplasty: The Endovascular versus Surgical Treatment in Patients with Carotid Stenosis in the Carotid and Vertebral Artery Transluminal Angioplasty Study trial (CAVATAS)[1] for which the endovascular arm received CA alone in 74% of cases must be taken as less than definitive and more as legacy results, a sort of pre-CAS exploratory.

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Abbreviations and Acronyms

CA = carotid angioplasty

CAS = carotid artery stenting

CEA = carotid endarterectomy

CREST = Carotid Revascularization with Endarterectomy vs. Stenting Trial

ECG = electrocardiogram

EPD = emboli protection device

EU = European Union

EVA-3S = Endarterectomy vs. Stenting in Patients with Symptomatic Severe Carotid Stenosis

FDA = Food and Drug Administration

ICSS = International Carotid Stenting Study

MI = myocardial infarction

SPACE = Stent-supported Angioplasty vs. Carotid Endarterectomy in Symptomatic Patients

Initiated in 1992, very early in the technique development for CA, and completing enrollment in 1997, this study randomized patients with symptomatic carotid disease (defined here and in upcoming trial discussions as nondisabling stroke, hemispheric transient ischemic attack, or amaurosis fugax within the past 6 months). Five hundred four patients were randomized to either CEA or CA. There were no prespecified end points because the investigators positioned the trial as an exploratory one meant to inform future endovascular treatment, but the primary outcome variable was disabling stroke or death. No embolic protection device (EPD) was available for use in this trial. At 30 days, there was no difference between the 2 therapies either for disabling stroke or death (6.4% vs 5.9%, P=NS) or for any stroke lasting more than 7 days and death (10.0% vs 9.9%, P=NS). In a survival analysis, after 3 years, there was no difference in ipsilateral stroke between the 2 therapies, the first indication that an endovascular approach to carotid bifurcation disease would be effective in longer term stroke prevention. There was more restenosis in the CAS group at 1 year (14% vs 4%, $P < .001$) and more cranial nerve injury in the CEA group (8.7% vs 0%, $P < .0001$).

CAVATAS investigators concluded that although the data had wide confidence intervals and that the 2 therapies had similar major risks and effectiveness in preventing strokes to 3 years, endovascular therapy offered fewer minor complications. Most observers felt that the rates of 30-day complication in both arms were excessive and not representative of current experience. This trial, albeit with the stated limitations in technique, represents a legacy data set of limited import but was the first demonstration that an endovascular carotid treatment could have comparable safety and undoubtedly helped shape future trial design consideration.

Carotid artery stent trials: descriptors

Before considering the available data comparing CAS with CEA, several important features must be defined. First, only the trials performed in an era with EPD will be considered in this review. Second, all the trials to be presented were performed in patients at standard or usual risk for CEA. The only available randomized data in high–surgical-risk patients in the era of EPD, the Stenting and angioplasty with protection in patients at high risk for endarterectomy (SAPPHIRE) trial,[2] resulted in a finding of equivalence between the 2 therapies. And last, only multicenter efforts are to be considered. Table 1 is a compilation of the studies and their periprocedural outcomes to be presented for analysis.

Carotid artery stent trials: design considerations

There are generic as well as carotid-specific trial design considerations that have the potential to materially affect

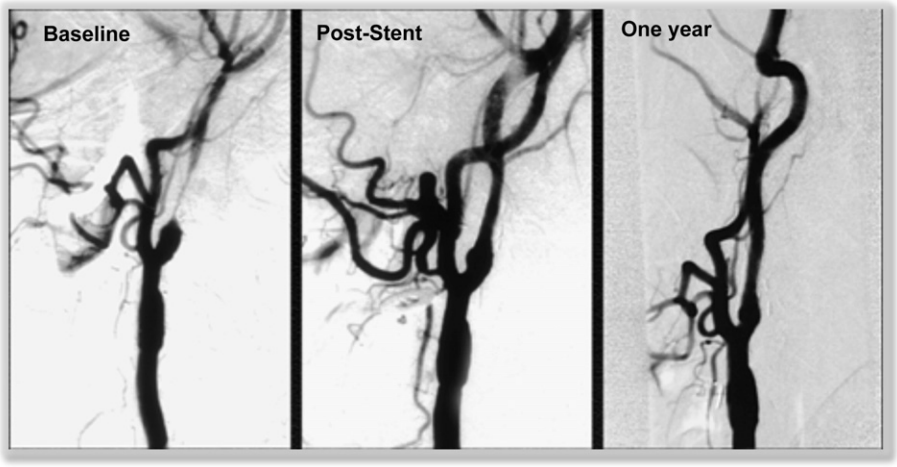

Fig 1. Image of a baseline internal carotid stenosis (left). An angiogram of a poststent image (center). A 1-year follow-up angiogram (right).