Editorial

Carotid artery stenosis

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Qureshi and colleagues report the results of a prospective longitudinal pilot registry to test the short-term (30-day) and intermediate-term (1-year) safety and efficacy of a novel coiled sheet stent used for extracranial carotid artery (CA) angioplasty and stent placement. The major advantage of this new stent, compared with current stent designs, apparently lies in its improved flexibility and maneuverability. Treatment was attempted in 45 patients who had high-grade internal CA stenosis (> 70% according to North American Symptomatic Carotid Endarterectomy Trial [NASCET] criteria) with or without symptoms; the patient cohort had multiple medical comorbidities that are usually associated with CA stenosis. The primary outcome was a technically successful stent placement that produced less than 30% stenosis on angiograms with no incidence of mortality or ipsilateral stroke within 30 days. Most patients (35 of 45) were observed for 1 year for ipsilateral stroke and recurrent stenosis (> 70%) by using Doppler ultrasonography.

Effective delivery of the stent was achieved in 44 of 45 patients. It is not clear why the one patient in whom the authors were unable to pass a guidewire for stent delivery was not included as an example of primary outcome treatment failure in the intent-to-treat analysis. Inclusion of this patient would change the primary outcome measure from 93 to 91%. Among the 44 patients who underwent stent placement, within 30 days there were two ipsilateral strokes (4.5%), two transient ischemic attacks (4.5%), and two deaths (4.5%), one of which occurred in a patient who suffered a stroke. These stroke rates are comparable to those previously reported by Roubin, et al., in a prospective longitudinal registry of CA angioplasty and stent placement, in which the 30-day stroke and death rate was 7.4%. The rates are also comparable to those of a larger retrospective analysis, in which the 30-day stroke and death rate was reported to be 3.1%. In the current study, although primary outcome was restricted to ipsilateral stroke, an additional vertebrobasilar stroke occurred within 30 days. Thus, the total 30-day incidence of cerebral ischemia in patients who received the stent was 11.3% (strokes 6.8%, transient ischemic attacks 4.5%). Distal protection devices were not used in the current study. Presumably, their use would lower the incidence of cerebral ischemia, although direct proof of this is lacking.

The natural history of symptomatic CA stenosis treated medically or by carotid endarterectomy (CEA) is well known. A recent metaanalysis covering more than 6000 patients in the three endarterectomy trials for symptomatic stenosis has yielded data on the natural history and risk factors that were derived from more than 25,000 patient-years of follow up. Although many patients in the current study would not have been candidates for endarterectomy trials (36% of the patients had undergone endarterectomy previously), the risk profile for medical comorbidities in this cohort was not otherwise significantly higher. It should be noted that several exclusions for stent placement in this study (calcification, ulceration, aortic or peripheral vascular disease, contra-indication for antiplatelet agents) would not be contraindications to CEA. Differences in medical and wound complications have been proposed as favorable features of CA angioplasty and stent placement when compared with CEA. In the current study, however, medical events were relatively common, including hypotension (23%), bradycardia (13.6%), need for transfusion (4.5%), and significant hematoma (4.5%). Although the periprocedural stroke rate observed in this study is roughly comparable to that observed in the surgical arm of several prospective, randomized trials for CEA in patients with symptoms (NASCET; European Carotid Surgery Trial [ECST]; and Veterans Affairs Trial), such a comparison is potentially misleading. Differences in study design, patient characteristics, selection of patients for inclusion, and cohort size preclude any meaningful comparison of studies. Clearly, prospective randomized trials in which CA angioplasty and stent placement is compared with CEA are necessary to resolve the issue. The Carotid Revascularization Endarterectomy versus Stent Trial (CREST) is in progress, but results may not be known for several years. The results of a recent randomized prospective trial in which a comparison was made between CA angioplasty and stent placement performed using a distal protection device and CEA in high-risk patients has been reported in abstract form (P Fayad for the SAPHIRE Investigators: Stenting and angioplasty with protection in patients at high risk for endarterectomy: the SAPHIRE Study. American Academy of Neurology 55th Annual Meeting, Honolulu, Hawaii, March 29–April 5, 2003 [unpublished data]). Among 309 patients, a significant advantage for CA angioplasty and stent placement over CEA was found in the composite primary end point...
(30-day rate of stroke, death, or myocardial infarction; 5.8 compared with 12.6%, respectively; \( p = 0.04 \)). The rate of stroke and death (4.4 compared with 7.5%, respectively) was not significantly different between groups; much of the observed difference was related to the rate of myocardial infarction (2.6 compared with 7.3%, respectively), which included non-Q-wave infarctions.

It is encouraging that the intermediate-term stroke rate (0%) and the recurrent stenosis rate (3%) were low in the current study, because these issues remain unresolved potential detriments to CA angioplasty and stent placement. The durability of CEA has been well defined; an analysis of 1728 surgically treated patients from the ECST (median follow-up period of 6 years) indicated that, based on a follow-up period of 10 years, the annual ipsilateral stroke rate was approximately 1% and half of the strokes were minor.\(^1\) Clearly, comparable data concerning long-term outcomes for stroke and recurrent stenosis for CA angioplasty and stent placement will be important.

I have some concerns about the suitability for publication of this article in the Journal of Neurosurgery. Although not stated, presumably the trial was funded by the manufacturer and the data may be part of an analysis conducted to obtain approval from the US Food and Drug Administration. Whether such data should be included in the scientific literature on a topic such as CA angioplasty and stent placement is debatable. In addition, two authors disclose financial support from the device manufacturer. Many institutional review boards preclude research in this setting, and many journals no longer accept manuscripts with a potential conflict of interest.

Extracranial and intracranial angioplasty and stent placement will clearly play an important role in the management of patients with cerebrovascular disease in the future. Although the stents currently in use can be placed in the extracranial CA of most patients, improved flexibility of stent devices will likely be an advance in this field, especially when dealing with intracranial vasculature. Technology in endovascular therapy is progressing much faster than clinical trials can be completed, and it may simply be impossible to evaluate these devices in the rigorous manner that was accomplished for CEA. Nevertheless, caution must be taken to avoid invalid comparisons with historical data and extrapolation of results to broader populations.

References

RESPONSE: We appreciate the valuable comments made by Dr. Mayberg in his authoritative editorial. As Dr. Mayberg appropriately pointed out, the efficacy of CEA for protection against stroke in patients with CA stenosis has been demonstrated in large, multicenter clinical trials such as the NASCET,\(^1\)\(^,\)\(^2\) Asymptomatic Carotid Atherosclerosis Study (ACAS),\(^3\) and ECST.\(^4\) Currently, CEA is one of the most common surgical procedures performed in the US. Nevertheless, it should be noted that markedly higher rates of procedure-related mortality and morbidity were reported for patients at community hospitals and for Medicare recipients than for patients enrolled in the NASCET and the ACAS.\(^5\)\(^,\)\(^6\)\(^,\)\(^7\)\(^,\)\(^8\)\(^,\)\(^9\)\(^,\)\(^10\)\(^,\)\(^11\)\(^,\)\(^12\)\(^,\)\(^13\) Carotid artery angioplasty with stent placement has emerged as a potential alternative to CEA for less invasive treatment of CA stenosis in patients deemed to be at high risk for surgery.\(^10\)\(^,\)\(^11\)\(^,\)\(^12\)\(^,\)\(^13\) Results such as those reported in the present study indicate that CA angioplasty and stent placement may be associated with a postprocedural stroke rate similar to that observed among low-risk patients undergoing CEA in several prospective studies.\(^1\)\(^,\)\(^3\)\(^,\)\(^4\)\(^,\)\(^12\)\(^,\)\(^14\)\(^,\)\(^15\) We agree with Dr. Mayberg that studies such as this one cannot be substituted for randomized controlled trials in which direct comparisons between CEA and CA angioplasty with stent placement are provided. Indeed, the present study highlights the need for randomized studies such as the CREST\(^8\) for low-risk patients. On the other hand, the SAPPHIRE trial (P Fayad for the SAPPHIRE Investigators: Stenting and angioplasty with protection in patients at high risk for endarterectomy: the SAPPHIRE Study. American Academy of Neurology 55th Annual Meeting, Honolulu, Hawaii, March 29–April 5, 2003) indicates that randomization of high-risk patients may result in an increased rate of cardiac morbidity, and that data from these patients are probably best studied in registries and compared with data from historical controls. The results provided by the present study may help spur the development of effective protocols to address the efficacy of CA angioplasty with stent placement for the patient population most likely to benefit from the procedure.

Dr. Mayberg has pointed out another important issue regarding commercial sponsorship of the study and a potential conflict of interest borne by the investigators. We completely agree that to help shape diagnostic and therapeutic decisions, current information must be provided in a manner free from commercial influence. This has become a challenge for every journal because relationships between authors and biomedical companies are growing. A healthy interaction between academia and industry may facilitate the dissemination of scientific knowledge and its application to patient care. Excessively stringent policies, however, may not be in the best interest of science, as stated in the *New England Journal of Medicine*:

Certainly, if we publish nothing on a given subject we run...