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EDITORIAL COMMENT

New Insights Into Improving Acute and Long-Term Outcomes of Carotid Stenting*

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Carotid stenting is now a Food and Drug Administration-approved procedure for high surgical risk patients and has Centers for Medicare and Medicaid Services reimbursement for symptomatic patients who are at high surgical risk. The Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) randomized trial demonstrated the superiority of carotid stenting with emboli protection to endarterectomy in high surgical risk patients, and there are currently three approved carotid stents and emboli prevention devices in the U.S. (1). The interventional community can take some satisfaction in the maturation and mainstreaming of carotid stenting; however, much work remains to be done, and the two studies published in this issue of the *Journal* (2,3) contribute to the advancement of carotid stenting.

See pages 2384 and 2390

There have been a limited number of prospective multicenter carotid stenting studies published, and therefore the Carotid Revascularization with EV3 Arterial Technology Evolution (CREATE) trial by Safian et al. (2) is an important addition to the carotid literature. The CREATE trial was a non-randomized study of carotid stenting with a unique over-the-wire emboli protection filter. Only 30-day data is reported, and the technical success rate was good at 97.4%. The overall 30-day complication rate of 6.2% for death, stroke, and myocardial infarction (MI) was in the general range for high surgical risk carotid patients. However, the results have to be interpreted with caution due to the end point definitions; the standard all stroke 30-day end point was not used. Instead, only ipsilateral strokes and procedure-related contralateral strokes were considered, which would lead to some periprocedural contralateral strokes not being counted. Furthermore, a more liberal definition of MI, creatine kinase of three times normal, was utilized, potentially excluding some MIs that were included in other carotid stenting studies. The inclusion criteria were the generally accepted high surgical risk criteria and were similar to the SAPPHIRE trial with the exception of the age definition, which was age ≥75 years instead of the age ≥80 years used in the SAPPHIRE trial. Further limitations of the study are the lack of an independent data center or an angiographic core lab to verify the degree of stenosis.

This study does, however, provide several insights that have not been previously reported. A carefully conducted multivariate analysis indicates that the presence of symptoms, baseline renal insufficiency, and duration of filter deployment are predictors of stroke. While the mean duration of filter deployment was approximately 18 min, patients with major strokes had a mean filter deployment time of almost 26 min. Furthermore, in patients with filter durations of >20 min there was almost double the risk of death and stroke compared with patients with filter deployment times of <20 min. This provides the first systematic evidence that filter deployment times, and by inference overall procedure times, are important predictors of acute outcomes in carotid stenting. Because the most difficult part of carotid stenting is typically the guide catheter placement and filter placement, it is surprising that it still took an average of 18 min to complete the procedure after the filter was deployed. This finding would suggest inexperienced operators or a lack of appreciation of the need for speed after the filter is deployed. This study drives home the point that all materials such as the stent and post-dilatation balloons should be prepared before filter deployment, and the procedure should be finished with all due speed once the filter is deployed. Typically, it should take no more than 5 to 10 min once the filter is deployed to complete stent deployment, post-dilatation, and capture and removal of the filter.

Another procedural insight from this study was regarding the occurrence of hemorrhagic stroke. The major stroke rate of 3.5% and the intracranial hemorrhage rate of 1.3% were higher in this study than in other studies in high-risk patients. This is particularly surprising because patients with strokes within 30 days were excluded from this study, which was not the case in other high surgical risk studies. The authors note that these strokes were not associated with excessive procedural anticoagulation, but specific data are not provided. Two of the patients were on concomitant warfarin therapy, and one had poorly controlled hypertension. One patient potentially had hyperfusion syndrome.

The high incidence of intracranial hemorrhage in this study highlights the importance of periprocedural patient management. As we become better at reducing the risk of ischemic stroke, the relative importance of intracranial hemorrhage will increase. Hyperperfusion syndrome is an important predictor of this catastrophic event after endarterectomy as well as carotid stenting (4). Hypertension, severe stenosis, and severe contralateral disease have been shown in a multivariate analysis to be predictors of hyperperfusion and intracranial hemorrhage (4). The periprocedural identification of patients at risk for hyperfusion and

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June 20, 2006:2397–8

careful post-procedure management reduced the risk of hyperfusion and intracranial hemorrhage in a prospective study (5). Reversal of heparin with protamine at the end of the procedure and careful management of blood pressure for the first week are important steps that can be taken in patients at increased risk of hyperperfusion to reduce the risk of hemorrhage.

Clark et al. (3) conducted the first systematic intravascular ultrasound (IVUS) study of carotid artery stenting and provided us with some important mechanistic insights into the short- and medium-term behavior of carotid stents. This study suffers from having been in the mid-to-late 1990s and utilizing primarily the Wallstent (Boston Scientific, Natick, Massachusetts). All of the currently approved carotid stents are made from nitinol and have quite different behavioral characteristics than the elgiloy-based Wallstent. The authors demonstrated great courage in conducting this study before emboli protection was widely available and report no complications with the performance of IVUS both during the index procedure as well as at follow-up. Although the post-procedural stent expansion was poor, being only 70% by IVUS, there was considerable stent enlargement (49%) at six months. However, new intimal hyperplasia increased proportionately being 37% at six months. As in the coronaries, there was a relationship between the minimum luminal diameter (MLD) at the end of the procedure to restenosis. In fact, MLD was the only predictor of stenosis, with no correlation found for other variables including, surprisingly, gender, previous endarterectomy, diabetes, or calcification.

There has been a tendency in current carotid stenting practice to leave the stent underdilated in order to reduce embolization. This study suggests that there may be a price to pay in terms of restenosis if an adequate MLD is not obtained; unfortunately, it does not tell us what MLD is associated with an acceptable risk of restenosis. It is possible that the behavior of nitinol stents may be different in this regard, but the relationship between MLD and restenosis should apply to nitinol stents also.

These studies give us several insights into improving the performance of carotid stenting. Foremost, short procedure time and particularly filter deployment times are essential to minimizing complications. The best way to insure short procedure times is with adequate operator training and careful patient selection. Although avoiding procedural embolization is of paramount importance, it is essential to obtain a reasonable angiographic result and MLD in order to avoid restenosis. Periprocedural management requires greater attention if we are to continue to reduce the complications of carotid stenting.

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