Letters to the Editor 595

Regarding “Carotid endarterectomy in SAPPHIRE–eligible high-risk patients: Implications for selecting patients for carotid angioplasty and stenting”

A recent article by Mozes and associates (J Vasc Surg 2004; 39:958-965) seeks to compare 2 groups of patients who underwent carotid endarterectomy at a single institution over a 5-year period. These 2 groups were defined as high risk and low risk, ostensibly on the basis of the eligibility criteria of the high-risk SAPPHIRE randomized trial of stenting versus endarterectomy. The reference that the authors quote, however, is not from the SAPPHIRE trial. Rather, the high-risk criteria were extracted from an article by Jordan and colleagues.

That aside, the authors aptly concluded that endarterectomy can be performed in high-risk patients with acceptable risks of stroke and death. The question of whether carotid stenting should be considered in such high-risk patients, however, cannot be resolved by a comparison of outcome in high- and low-risk patients. Rather, this question is best answered through a randomized comparison of stenting and endarterectomy, either in lower-risk patients (eg, the CREST trial) or higher-risk patients (eg, SAPPHIRE).

The authors reasoned that similar results with endarterectomy in high-risk versus lower-risk patients raise questions about the appropriateness of stenting as an alternative to endarterectomy. But the authors’ own data document a mortality rate of 0.6% in high-risk patients versus 0.0% in low-risk patients (P = .11, calculated with the χ² test and from their data). When the high-risk subgroups were compared with lower-risk subgroups, the stroke rate was 1.9% versus 1.1% (P = .45), the frequency of perioperative myocardial infarction was 3.1% versus 0.9% (P = .05), and the rate of the composite stroke and death myocardial infarction was 9.3% versus 1.6% (P = .000001). For each end point, the point estimates were higher in the high-risk patients. While some end points did not achieve statistical superiority, the failure to detect statistical superiority does not exclude an end point with conviction. Said another way, the P value of .11 suggests that we are only “69% certain that the mortality rate was greater in the high-risk patients. Although the SAPPHIRE data have not yet appeared in the literature, the data presented to the Food and Drug Administration panel this April suggested that the results of stenting were equivalent or superior to endarterectomy. The demonstration of non-inferiority of stenting is all that will be required for patients to preferentially choose a procedure that avoids a neck incision.

Vascular surgeons appear best-equipped to care for patients with carotid disease: they understand the anatomy, the indications for intervention, and the necessity for long-term follow-up. We can choose to become proficient at carotid stenting and be able to offer it as one potential treatment option. Alternatively, we can discount this new modality, but we will risk relinquishing the responsibility for carotid diagnosis and treatment to other specialty groups who may be unaccustomed to caring for patients with cerebrovascular disease.

Kenneth Onriel, MD
The Cleveland Clinic Foundation
Cleveland, Ohio

References


REFERENCES


doi:10.1016/j.jvs.2004.05.030

Reply

I appreciate the opportunity to respond to Dr Ouriel’s reflections regarding our article documenting the carotid endarterectomy experience from the Division of Vascular Surgery, Mayo Clinic, Rochester, Minn. The purpose of this study was to examine the implications of high-risk criteria (as defined by the Food and Drug Administration–approved, industry-sponsored SAPPHERE study) on outcomes following carotid endarterectomy (CEA). It is our perception that these criteria are overly inclusive, that they envelope a group of patients on whom we frequently operate, and that the endarterectomy results from SAPPHERE are inferior to those achieved in our own practice (and likely in many other centers of excellence). In our retrospective study in 776 consecutive patients, we found no difference in the individual end points of death, stroke, or myocardial infarction (MI) when comparing high- and low-risk groups. The combined end point of death, stroke, and MI did reach significance (P < .05) when comparing high- and low-risk symptomatic patients, but not asymptomatic patients. In addition, we identified only 4 factors predictive of perioperative stroke: cervical radiation therapy, class III/IV angina, age <60 years and, to a lesser degree, symptomatic presentation. The high-risk patients in our series were, in fact, comparable to those in SAPPHERE, as defined in Tables I–III. Although these tables faithfully reproduce the SAPPHERE criteria, they are incorrectly referenced within the text; we appreciate Dr Ouriel’s bringing this typographic error to our attention.

Dr Ouriel correctly points out that statistical analyses are sometimes flawed or misinterpreted; to quote Mark Twain, “There are lies, damn lies, and statistics.” Nevertheless, our practices, especially as they relate to cerebrovascular disease—and particularly in asymptomatic patients, where margins of efficacy are thin—are typically guided by evidenced-based medicine and determined by rigid analysis of peer-reviewed data, not by trends, perceptions, or industry hype. These methods of exacting analysis have been applied to the SAPPHERE data set (which has not yet been published or subject to peer review), demonstrating equivalency of carotid angioplasty/stenting (CAS) to endarterectomy in high-risk patients; these data will hopefully be used to achieve Food and Drug Administration approval. As such, we stand by our conclusions, as stated in the article, which are based on currently accepted statistical analysis. In addition, while the composite end point of stroke, death, and MI in our study was statistically different in symptomatic patients, this difference was largely driven by the occurrence of non-Q MI, much like SAPPHERE. While “myocardial enzyme leak” is clearly not a positive outcome, its significance remains uncertain. Depending on the sensitivity of the biomarker used, nearly 40% of patients having percutaneous coronary intervention suffer this complication, and although these patients are at increased risk of subsequent cardiac death, a cause-and-effect relationship remains to be determined. Biomarker release following coronary angioplasty, carotid endarterectomy, or CAS may simply identify a group of patients already at risk for future coronary events.1,2

With respect to Dr Ouriel’s final point, we could not be in better agreement—vascular surgeons represent the group of physicians best able to manage patients with carotid artery disease. I have personally been involved with carotid angiography and intervention for nearly a decade, and remain active in clinical trials of CAS. I have trained many of my vascular surgical colleagues and have encouraged them to become proficient in these techniques so that we, as a specialty, can remain at the forefront. It is imperative that we take a leading role in carotid intervention, lest we become a historical footnote.3 Perhaps, however, we see our respective roles differently; I believe that it is my obligation to counsel patients as to the risks, benefits, and long-term outcomes of all available therapies (medical, interventional, and surgical) that relate to their particular disease, and to make a recommendation to that specific individual on the basis of the available peer-reviewed literature and the results of procedures performed within my own institution.4 I will have neglected my duty by simply performing the procedure “that the patient wants”—the one that “avoids a neck incision” or is currently in vogue. While CAS may ultimately become first-line therapy, carotid endarterectomy remains the treatment of choice for the vast majority of patients with high-grade carotid artery stenosis in our practice; further prospective, randomized studies will hopefully further define the role of CAS in both high-risk and low-risk patients.

Timothy M. Sullivan, MD
Mayo Clinic
Rochester, Minn

REFERENCES


doi:10.1016/j.jvs.2004.06.016