

Why the 2-Year SAPHIRE Results Are So Good for Carotid Artery Stenting Enthusiasts

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The SAPHIRE study was the first completed randomized trial to compare protected carotid stenting to carotid endarterectomy. The patient population included those at potentially increased surgical risk because, at the time of the trial's design, clinical equipoise did not exist for the randomization of low-surgical-risk patients to an interventional treatment.

The primary end point events (stroke, death, and myocardial infarction) were similar in patients randomized to stenting and endarterectomy, 19.6% versus 26.4% at 2 years. Thus, the primary aim of the SAPHIRE trial was achieved; the outcome of stenting was not inferior to endarterectomy. In fact, superiority in the primary composite end point was almost achieved, with a p value of .11. Numerically, stenting resulted in equivalent or lower complication rates for all event types (death, stroke, or myocardial infarction) and patient subsets (symptomatic or asymptomatic). Stroke alone occurred with similar frequency in the stent and endarterectomy groups; 6.4% and 6.8%, respectively, at 2 years. Interestingly, target lesion revascularization was performed in a greater number of endarterectomy patients than stent patients, 6.1% versus 1.4% at 2 years ($p = .03$). Bleeding complications were comparable in the two groups and cranial nerve palsies, repeat revascularization and duration of hospitalizations were greater in the carotid endarterectomy group.

Concerns have been raised regarding the generalizability of the SAPHIRE results to the population of patients undergoing carotid endarterectomy in the United States. But a large study of over 100,000 Medicare patients undergoing carotid endarterectomy by Wennberg found that overall perioperative mortality rate at hospitals that had participated in the NASCET and ACAS trials was 1.4%, similar to that observed in SAPHIRE.¹ Since the mortality rate in NASCET was 0.6% and 0.1% in ACAS, the authors concluded that the trials were not representative of the patients being routinely treated with carotid endarterectomy. In a recent review of Medicare patients in Ohio undergoing carotid endarterectomy, 1 in 6 were over 80 years of age and would have been excluded from both NASCET and ACAS.² In the Cleveland Clinic prospective surgical registry of over 3,000 carotid endarterectomy patients, the high-risk group had a perioperative death, stroke, and myocardial infarction rate of 7.4% versus 2.9% for the low-risk group.³ The cranial nerve palsy rate in the present trial was lower than in NASCET (5.3% vs 7.6%) even though many of these patients had previous carotid endarterectomies, radical neck surgery, or radiation therapy.⁴ This supports the technical excellence of the surgeons in this study. In sum, these data suggest that the SAPHIRE results in the endarterectomy group are, in fact, similar to those observed in clinical practice as well as in the larger carotid endarterectomy study data sets.

One should also be careful to evaluate the definition of the primary end point when contrasting the outcome of two studies. The SAPHIRE primary end point was much broader than that of previous carotid surgery trials: in the peri-procedural period myocardial infarction was included. Further, in the post-30-day period all cause mortality was included. The ACAS primary end point was death or stroke to 30 days and ipsilateral stroke to 5 years.⁵ The NASCET primary end point was fatal or non-fatal ipsilateral stroke.⁴ The inclusion of myocardial infarction increased the rate of the primary end point, but the investigators included it because patients with atherosclerotic vascular disease are at substantial risk of myocardial infarction with either intervention or surgery, and either a Q wave or non-Q wave infarction, in the postoperative period carries a substantial risk of future morbidity and mortality.⁶⁻¹⁰ A perioperative non-Q wave infarction confer a sixfold increase in mortality and a 27-fold increase in myocardial infarction in the subsequent 6 months.⁹

In conclusion, the SAPHIRE study demonstrated non-inferiority of stenting compared to endarterectomy in patients at higher than normal risk for open surgery. These findings persist to the 2-year follow-up time point and confirm the durability of the initial results. Patients who have medical or anatomic factors that place them in a higher risk subgroup should be offered stenting as a viable alternative to carotid endarterectomy.

References

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