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Yadav JS, Wholey MH, Kuntz RE, et al: Protected carotid-artery stenting versus endarterectomy in high-risk patients. *N Engl J Med* 351:1493–1501, 2004.

Background. Carotid endarterectomy is more effective than medical management in the prevention of stroke in patients with severe symptomatic or asymptomatic atherosclerotic carotid-artery stenosis. Stenting with the use of an emboli-protection device is a less invasive revascularization strategy than endarterectomy in carotid-artery disease.

Methods. We conducted a randomized trial comparing carotid-artery stenting with the use of an emboli-protection device to endarterectomy in 334 patients with coexisting conditions that potentially increased the risk posed by endarterectomy and who had either a symptomatic carotid-artery stenosis of at least 50 percent of the luminal diameter or an asymptomatic stenosis of at least 80 percent. The primary end point of the study was the cumulative incidence of a major cardiovascular event at 1 year—a composite of death, stroke, or myocardial infarction within 30 days after the intervention or death or ipsilateral stroke between 31 days and 1 year. The study was designed to test the hypothesis that the less invasive strategy, stenting, was not inferior to endarterectomy.

Results. The primary end point occurred in 20 patients randomly assigned to undergo carotid-artery stenting with an emboli-protection device (cumulative incidence, 12.2 percent) and in 32 patients randomly assigned to undergo endarterectomy (cumulative incidence, 20.1 percent; absolute difference, -7.9 percentage points; 95 percent confidence interval, -16.4 to 0.7 percentage points; $P=0.004$ for noninferiority, and $P=0.053$ for superiority). At one year, carotid revascularization was repeated in fewer patients who had received stents than in those who had undergone endarterectomy (cumulative incidence, 0.6 percent vs. 4.3 percent; $P=0.04$).

Conclusions. Among patients with severe carotid-artery stenosis and coexisting conditions, carotid stenting with the use of an emboli-protection device is not inferior to carotid endarterectomy.

Comment

The prevention of stroke with carotid endarterectomy (CEA) compared with medical management in both symptomatic and asymptomatic patients with carotid artery (CA) stenosis has been well described in several large prospective clinical trials.^{4,6–8} The data from these clinical trials provide the standard by which to compare new interventions, including stent placement, for efficacy in stroke prevention and rate of complications. The article by Yadav and coworkers describes the first randomized clinical trial (Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy) in which CEA was compared with stent placement in patients with severe CA stenosis and coexisting conditions. Various coexisting conditions are included, such as significant heart disease, pulmonary disease, contralateral CA occlusion, contralateral laryngeal nerve palsy, previous radical neck surgery or radiation therapy, recurrent stenosis after CEA, or age older than 80 years. It is significant to note that these treatments have very different functions; endarterectomy works by the removal of a dynamic disease process in which plaque-related events lead to stroke caused by thrombosis and embolization, whereas stent procedures only provide luminal expansion and plaque compression.² Therefore, it is important to evaluate whether stent placement is as effective at stroke prevention and whether it has a comparable and acceptable rate of complications.

In the study by Yadav, et al., the authors used some of the typical primary end points for comparative CA stenosis studies, including stroke or death within the first 30 days or within 1 year after treatment. Also, in this study the authors used myocardial infarction occurring within 30 days after treatment, which was not included as a primary end point in the larger CEA clinical trials.^{1,3–5,7,8} The difference between the treatment groups occurred mainly because of the increased incidence of periprocedure myocardial infarcts in the CEA group. For example, using conventional end points (stroke or death at 30 days plus ipsilateral stroke or death from neurological causes within 31 days–1 year), nine patients (5.5%) who received stents and 13 (8.4%) who underwent CEA reached this end point ($p = 0.36$). The inclusion of myocardial infarction within 30 days of the procedure as an end point resulted in 20 (12.2%) patients who received stents and 32 (20.1%) who underwent CEA reaching the primary end point of the study ($p = 0.05$). Thus, a statistically significant difference was only attained with the addition of myocardial infarcts within 30 days of the procedure as an end point. Cambria² suggests that this end point was selected as a practical consideration because the study was not sufficiently powered to detect differences in stroke or death between the treatment groups. The overall incidence of stroke within 1 year posttreatment was 10 (6.2%) for the group with stents and 12 (7.9%) for the group receiving CEA ($p =$

0.6), and the incidence of ipsilateral stroke was seven (4.3%) and eight (5.3%), respectively (major stroke, $p = 0.09$; minor stroke, $p = 0.34$). Thus, there was no statistically significant difference in stroke prevention at 1 year posttreatment.

Secondary end points included the need for target vessel revascularization at 1 year and the incidence of cranial nerve palsy. Interestingly, cranial nerve injury is very specific to surgery, and in this study it occurred in 5% of surgical patients and in 0% of the patients who received stents. This finding is supported in other studies.³ Also, one (0.6%) of the patients treated with a stent and six (4.3%) of those who underwent CEA required a revascularization procedure within 1 year of treatment ($p = 0.04$). In another study in which stent placement was compared with CEA, 25 patients (14%) who received stents and seven (4%) who underwent CEA had ipsilateral severe stenosis (70–99%) at 1 year posttreatment ($p < 0.001$).³ One aspect that deserves close attention is the durability of treatment; it is unclear what the incidence of recurrence will be at follow-up durations longer than 1 year for the group that received stents.

Overall, Yadav, et al., concluded that among patients with severe stenosis and coexisting conditions, CA stent placement is not inferior to CEA. Compared with the larger trials evaluating CEA as opposed to medical therapy, this study had some limitations. First, it had a relatively small sample size (334 treated patients, 167 with stents and 167 with surgery). Other trials evaluating CEAs included more than 1600 to 3000 randomized patients.^{1,4,5,7} Second, the end point of the study was sooner than in previous trials. Ultimately, longer study periods will be needed to evaluate properly the relative efficacy for stroke prevention between these two interventions. Surgical studies have evaluated stroke prevention at 2 to 6 years after CEA.^{1,4,7,8}

This is an important study that helps further define the role of CA stent placement as a therapeutic option for atherosclerotic CA disease. There is a need for a larger-scale, multicenter trial with increased numbers of patients and longer follow-up duration to identify appropriate patients for either CEA or stent placement.

References

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