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ICSS: Continued Higher Event Rates With Stenting vs Surgery for Symptomatic Carotid Stenosis

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February 25, 2010 — Interim safety results at 120 days in the International Carotid Stenting Study (ICSS) appear to favor carotid endarterectomy over carotid stenting for patients with symptomatic carotid stenosis.

The results show higher rates of stroke, death, or periprocedural myocardial infarction (MI) in patients treated with stenting vs endarterectomy. The primary outcome of the study is the 3-year rate of fatal or disabling stroke in any territory, and results are expected in 2012.

"I think the conclusions from our trial are very much that, overall, surgery is a better option, but there may be some patients in whom it's reasonable to do stenting, perhaps the younger patients or those at high risk of surgery," principal investigator Martin M. Brown, MD, from University College London, Institute of Neurology, in the United Kingdom, told Medscape Neurology.

The 120-day results of the ICSS and those of the ICSS magnetic resonance imaging (MRI) substudy were published online February 26 in Lancet and Lancet Neurology, respectively.

Results of the long-awaited Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST), comparing carotid stenting with endarterectomy in patients with both symptomatic and asymptomatic carotid stenosis eligible for either procedure, will be presented tomorrow here at the International Stroke Conference in San Antonio, Texas.

The results are expected to give as clear a picture as possible comparing the 2 modalities while at the same time addressing issues regarding operator experience and use of distal protection devices that have been raised with other comparative trials.

Trials Find Surgery Superior

The ICSS brings to 3 the number of large randomized trials that have reported results evaluating the use of carotid stenting as an alternative to endarterectomy to treat symptomatic carotid artery stenosis. In the first, called the Stent-Supported Percutaneous Angioplasty of the Carotid Artery vs Endarterectomy (SPACE) trial, carotid stenting failed to meet criteria for noninferiority vs endarterectomy and in fact showed slightly higher rates of ipsilateral ischemic stroke and death at 30 days (SPACE Collaborative Group. Lancet. 2006;368:1239-1247).

Results of the Endarterectomy vs Angioplasty in Patients With Symptomatic Severe Carotid Stenosis (EVA-3S) were published within 2 weeks of the SPACE trial and again failed to show noninferiority with carotid stenting vs endarterectomy. Stroke and death rates were again lower with surgery (Mas JL, et al. N Engl J Med. 2006;355:1660-1671).

Longer-term follow-up of both of these trials, however, presented in 2008 at the European Stroke Conference, showed that rates of ipsilateral stroke were low and similar between carotid stenting and endarterectomy groups at 2 and 4 years of follow-up.

ICSS is a multicenter, international randomized controlled trial comparing carotid artery stenting with carotid endarterectomy in patients with recently symptomatic carotid stenosis. The trial enrolled 1713 patients, with 855 randomized to stenting and 858 randomized to surgery.

An earlier version of these safety data from the ICSS was presented at the European Stroke Conference in Stockholm, Sweden, in May 2009. The results, presented by Professor Brown and reported by Medscape Neurology at that time, showed that carotid stenting was associated with twice as many strokes as with carotid endarterectomy in both intention-to-treat and per-protocol analyses.

The difference was driven largely by nondisabling strokes and was balanced by a much higher frequency of cranial nerve palsy with endarterectomy.

Still, the researchers concluded at the time that carotid endarterectomy should be the treatment of choice for suitable patients with recently symptomatic carotid artery stenosis. These more complete results with slightly higher patient numbers do not appear to change that conclusion.

Stroke, death, or procedural MI at 120 days was higher in the stenting group than among those who underwent endarterectomy, as was the incidence of stroke, death, and periprocedural MI, any stroke, and all-cause death.

Table. ICSS: 120-Day Interim Safety Results

Endpoint	Stenting Group, No. (%)	Carotid Endarterectomy Group, No. (%)	Hazard Ratio (95% CI)	P Value
Disabling stroke or death	34 (4.0)	27 (3.2)	1.28 (0.77 – 2.11)	0.34
Stroke, death, or procedural MI	72 (8.5)	44 (5.2)	1.69 (1.16 – 2.45)	0.006
Any stroke	65 (7.7)	35 (4.1)	1.92 (1.27 – 2.89)	0.002
All-cause death	19 (2.3)	7 (0.8)	2.76 (1.16 – 6.56)	0.017

CI = confidence interval; ICSS = International Carotid Stenting Study; MI = myocardial infarction

Three procedural MIs, all of which were fatal, occurred in the stenting group vs 4, all nonfatal, in the surgery group.

Cranial nerve palsy was seen in 1 stenting patient but in 45 of the endarterectomy patients. Hematomas of any severity were also less frequent with stenting with 31 vs 50 events with surgery (P = .0197).

Although they conclude that endarterectomy should be the treatment of choice, Professor Brown and colleagues acknowledge that some patients will still prefer stenting. "Most patients had no complications from either procedure," they write. "Thus, some patients might still opt for stenting after being presented with the available evidence, especially if they have a strong preference for avoiding surgery."

ICSS-MRI Study

In a separate paper published simultaneously in Lancet Neurology, the ICSS investigators with lead author Leo H. Bonati, MD, from University Hospital Basel, Switzerland, report results of an MRI substudy in 7 ICSS centers, scanning patients before, 1 to 3 days after, and then again 27 to 33 days after their assigned intervention.

A total of 231 patients were scanned, 124 from the stenting group and 107 from the surgery group. The primary outcome was the presence of at least 1 new ischemic brain lesion on diffusion-weighted imaging (DWI) on the posttreatment scan.

They report that 62 stenting patients (50%) had at least 1 new lesion on DWI performed a median of 1 day after treatment compared with 18 endarterectomy patients (17%) (odds ratio, 5.21; 95% confidence interval [CI], 2.78 – 9.79; P < .0001).

When they compared this outcome in centers that did and did not use distal protection devices, the odds ratio for a new lesion on DWI was 12.20 (95% CI, 4.53 – 32.84) in centers using cerebral protection devices as a policy but only 2.70 (95% CI, 1.16 – 6.24) in centers where stenting was unprotected.

"One of the reasons we wanted to get the MRI study out at the same time is it really demonstrates how you get a lot of silent damage to the brain after stenting that doesn't occur after endarterectomy," Professor Brown noted. "I find that rather worrying as a neurologist," he added.

He also finds their results with regard to protection devices consistent with both their MRI findings and findings from other studies. One of the ICSS centers has done cognitive testing to gauge any subtle deficits associated with these lesions, he noted, and the results are now being analyzed.

"I think there will be a lot more interesting analysis coming out of the trial, and we're hoping to combine all our data together with the CREST results in due course so we can look at risk factors," Professor Brown said.

"Clear Advantage" for Endarterectomy

In a Reflection and Reaction article accompanying the publication of the ICSS-MRI substudy in Lancet Neurology, Klaus Gröschel, from the Department of Neurology at Georg-August-Universität Göttingen, Germany, points out that results of the MRI substudy suggest that "the widespread use of carotid stenting, especially its routine use as first-choice treatment for symptomatic carotid stenosis, does not seem to be justified for the time being.

"However," he adds, "it is not only about whether stenting or endarterectomy will win the race, presently with a clear advantage for endarterectomy, but more about individual patient selection. Stenting and endarterectomy could both have their place as different treatment options for carotid stenosis and should preferably complement each other, with advantages of either technique in certain patient subgroups, which need to be further identified."

The association seen between the filter-based neuroprotection and new DWI lesions is "striking" though, Dr. Gröschel notes, "because they do not seem to accomplish the job they were invented to do."

At present, he concludes, these devices should be done on an individual basis "according to, for example, a potentially difficult endovascular access to reach the stenosis or lesion characteristics."

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