Patient Age Affects Carotid Treatment Results

BY MITCHEL ZOLER

SAN ANTONIO — The largest-ever, head-to-head comparison of stenting versus surgery for treating severe carotid artery stenosis showed a marked effect of age, with patients older than 70 having fewer adverse outcomes after carotid endarterectomy and patients younger than 70 having fewer complications following carotid angioplasty and stenting.

Although the highly anticipated results from the decade-long Carotid Revascularization Endarterectomy vs. Surgery Trial (CREST) seemed, in simplest terms, to show a dead heat between carotid stenting and surgery, the results reported at the International Stroke Conference actually revealed statistically significant and clinically important differences between the two treatments. (See box.)

The statistically significant interaction between patient age and outcome will likely play a major role when physicians and patients now decide which intervention to favor for a specific patient.

The CREST results also showed another significant difference between carotid surgery and stenting: Surgery led to a 1.2% increased absolute rate in the incidence of periprocedural myocardial infarctions, while stenting produced a 1.8% increase absolute rate of periprocedural strokes. This finding will force patients and their physicians to consider which complication they would rather risk.

The patients in CREST answered that question, at least in part, via another outcome measure. Assessment of patient physical and mental quality of life with the 36-item Short Form (SF-36) Health Survey a year after treatment showed that patients who developed new strokes, even "minor" strokes, had significant reductions from baseline in both their mental and physical well-being, while patients who developed new myocardial infarctions had, on average, no significant changes in their SF-36 mental and physical scores, Dr. Wayne M. Clark reported while presenting the CREST results.

"This study, at the bottom line, was an endorsement for surgery," commented Dr. James C. Grotta, chairman of neurology at the University of Texas in Houston.

The CREST findings also renewed concerns about the appropriateness of any invasive intervention, be it stenting or surgery, for asymptomatic carotid stenosis. The findings raised questions about how CREST differed from another large comparison of stenting and surgery, the International Carotid Stenting Study (ICSS), the results of which also appeared online, coincidentally, on the same day as the CREST report (Lancet 2010 Feb. 26 [doi:10.1016/S0140-6736(10)60239-5]).

Some experts noted that the CREST stenting results came from selected, experienced operators and that it would be a leap to expect comparable results from less-experienced physicians.

CREST randomized 2,502 patients with either symptomatic carotid stenosis or asymptomatic, severe carotid stenosis (at least 60% blockage) at 108 sites in the United States and 9 in Canada. The patients' average age was 69 years, a third were women, and 47% were asymptomatic. The analysis showed no significant effect from gender or symptom status on outcomes.

Impact of Age

The age effect produced the sharpest distinction between stenting and surgery, and confirmed evidence that began emerging a few years ago that carotid stenting poses a special problem for elderly patients. "As we went into this [trial], most of us thought that the less invasive procedure would be best suited for the older patients," said Dr. Thomas G. Brott, professor and director of neurology at the Mayo Clinic in Jacksonville, Fla., and co–principal investigator for CREST.

The problem has been attributed to the increased difficulty and danger of placing stents and embolic protection devices through elderly patients' tortuous and atherosclerotic arteries.

"It's likely that putting in the embolic protection device sets off strokes. Until we have more data to show whether or not the age effect is real, I will take it into account in my patients," commented Dr. J. Donald Easton, a neurologist at the University of California, San Francisco.

"I'm tending to look at the age cut-point very carefully," said Dr. Philip B. Gorelick, professor of neurology and rehabilitation and director of stroke research at the University of Illinois in Chicago.

Dr. Clark reported the age effect as a continuous variable, without specifying any point estimates. But based on the line graph he showed, patients who underwent stenting at age 65 had a roughly 20% reduced risk for an adverse perioperative or long-term outcome compared with those who underwent surgery. At age 60 the relative benefit from stenting was about 35%. At age 50, the rate of adverse outcomes after stenting was less than half the rate after endarterectomy.

The primary adverse-event measure in CREST was the composite rate of any stroke, myocardial infarction, or death during the 30 days following treatment plus the rate of any ipsilateral stroke during long-term follow-up of up to 4 years. This rate was 7.2% for stenting and 6.8% for endarterectomy, with similar rates of ipsilateral strokes occurring from 31 days to 4 years (2.0% vs. 2.4%).

In contrast to younger patients, at age 75, the rate of adverse outcomes after stenting rose by about 35% compared with surgery; at age 80, the adverse outcome rate was more than 50% higher with stenting than with surgery; and at age 85, the adverse event rate was roughly doubled by stenting. In patients who were 70 years old, the adverse event rates were essentially identical regardless of which procedure was used.

No Data on Asymptomatic Patients

The CREST results reported so far gave no details on how endarterectomy and stenting fared in asymptomatic patients, compared with patients who already had symptoms of carotid disease. In the absence of these data, several experts cautioned that the findings should not be taken as an endorsement of aggressive carotid interventions for asymptomatic patients, especially now that medical therapy has become so effective.

"It's worth revisiting the role of interventions in asymptomatic patients. Even low [adverse event] rates do not mean that everyone with an asymptomatic lesion needs to have endarterectomy or a stent," Dr. Grotta said.

"We need to look carefully at the asymptomatic data. Asymptomatic patients walk a fine line. There is not much room for any additional morbidity and mortality," Dr. Gorelick said.

"We think that a reasonable question to ask today, after a couple of decades of advancement in medical therapy, is whether in asymptomatic patients best medical therapy is the equal of carotid revascularization. That's something to investigate," Dr. Brott said.

In contrast to CREST, the results from ICSS showed a clear benefit from endarterectomy over stenting. Experts offered several possible explanations for this difference.

Dr. Ralph L. Sacco, professor and chairman of neurology at the University of Miami, cited differences between the two studies: CREST enrolled both asymptomatic and symptomatic patients, while ICSS involved only symptomatic patients; CREST used a single stent and embolic protection device, while ICSS allowed participating physicians to use whichever device they wanted; and CREST had results during follow-up of as long as 4 years, while the ICSS report focused on outcomes within the first 120 days of treatment.

But perhaps the most important difference was that CREST included a lead-in phase for participating operators to hone their stenting skills, something that ICSS lacked.

"We had in CREST a very detailed credentialing process, including about 1,600 lead-in cases that were not included in the randomized trial," noted Dr. Clark, a CREST participant and professor of medicine and director of the Oregon Stroke Center at the Oregon Health and Science University in Portland.

But the careful training phase of stent operators in CREST raised issues on the generalizability of the results.

"The results of this trial are not generalizable to the medical community as a whole," said Dr. Mary E. Jensen, a professor of radiology at the University of Virginia in Charlottesville. "They should not be interpreted to mean that carotid stenting is ready to be rapidly adopted as a standard practice at every hospital. Other studies have shown that carotid stenting can be more dangerous than carotid endarterectomy if the operators lack the technical expertise and experience required to maintain a low complication rate. I hope that if the Centers for Medicare and Medicaid Services uses the CREST data to expand coverage [of carotid stenting], it will include a credentialing/training/competency requirement that matches CREST in addition to insisting that all patients are seen before and after by neurologists so that independent observation of complications occurs."

"This is another reason we need comprehensive stroke centers," Dr. Grotta said. "Part of the licensing of stroke centers is having acceptable complication rates for carotid surgery and stenting."■

VITALS

Major Finding: The composite adverse event rate during up to 4 years of follow-up was 7.2% for stenting and 6.8% for endarterectomy, with the adverse event rate after stenting rising significantly higher than after surgery among patients older than 70 years.

Data Source: The Carotid Revascularization Endarterectomy vs. Stenting Trial (CREST), which randomized 2,502 patients with either symptomatic or asymptomatic carotid stenosis to treatment by endarterectomy or carotid stenting with embolic protection at 117 U.S. and Canadian sites.

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