CEA Events Halved in Symptomatic Patients

BY KERRI WACHTER

FROM THE VASCULAR ANNUAL MEETING

BOSTON – Perioperative stroke and death rates associated with carotid endarterectomy have improved for symptomatic patients over the last 20 years, based on a comparison of newly released data.

"The periprocedural stroke and death rate has not changed dramatically in asymptomatic patients, whereas it has almost halved in patients with symptomatic disease," Dr. Brajesh K. Lal observed at the meeting.

Dr. Lal and his coinvestigators compared periprocedural stroke and death rates associated with carotid endarterectomy (CEA) in CREST (Carotid Endarterectomy vs. Stenting Trial), NASCET I and II (North American Symptomatic Carotid Endarterectomy Trials I and II), and ACAS (Asymptomatic Carotid Atherosclerosis Study).

The perioperative stroke plus death rate for symptomatic patients who underwent CEA was 5.8%, 6.7%, and 3.2% in the NASCET I and II (N. Engl. J. Med. 1991;325:445-53; 1998; 339:1415-25) and CREST (N. Engl. J. Med. 2010;363:11-23) trials, respectively. "Operative stroke and death in symptomatic patients [in the CREST trial] were lower than in NASCET and could be related to increased intraoperative shunting, patch angioplasty, antilipid therapy, or antihypertensive therapy," said Dr. Lal of the division of vascular surgery at the University of Maryland in Baltimore.

Although antiplatelet therapy following CEA was used at similar rates in all of the trials, postprocedure antilipid therapy was used much more frequently in the CREST trial: 76% for both symptomatic and asymptomatic patients in CREST, compared with 14% in NASCET I and 40% in NASCET II. Likewise, postprocedure antihypertensive therapy was used more frequently in CREST than in NASCET I and II: 80%, 54%, and 68%, respectively.

For asymptomatic patients, the perioperative stroke plus death rate was 2.3% and 1.4% in ACAS (JAMA 1995;273:1421-8) and CREST, respectively. However, the ACAS rate included a 1.2% angiography complications rate, Dr. Lal noted. If angiographic complications are excluded from the ACAS results, the perioperative stroke plus death rate for asymptomatic patients was comparable for ACAS and CREST (1.5% for ACAS vs. 1.4% for CREST).

The researchers also compared inclusion criteria, enrollment details, criteria used to credential surgeons, criteria used to define perioperative stroke, surgical technique, and perioperative medical therapy.

Inclusion Criteria

NASCET I was open to patients older than 80 years, and ACAS was open to patients aged 40-79 years. NASCET II and CREST were open to patients of all ages.

VITALS

Major Finding: Carotid endarterectomy, perioperative stroke, and death rates for symptomatic patients have declined over the last 2 decades.

Data Source: NASCET I and II, ACAS, and CREST trials.

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NASCET I included symptomatic patients with 70%-99% stenosis; NASCET II was open to symptomatic patients with 50%-69% stenosis. ACAS was open to asymptomatic patients with 60% or greater stenosis. CREST was open to asymptomatic patients with 60% or greater stenosis and symptomatic patients with 50% or greater stenosis.

In patients in both NASCETs and roughly half of the patients in ACAS, the percentage of stenosis was determined by means of preoperative angiograms. In CREST, the percentage of stenosis was determined by ultrasound, CT angiography, MR angiography, and angiogram. There were only slight differences among the trials in terms of the definition of symptomatic status.

Enrollment

Both NASCETs as well as ACAS started enrolling patients in 1987 and stopped enrolling patients in the 1990s, whereas CREST enrolled patients during 2000-2008. Both NASCET I and ACAS were conducted in a smaller number of centers (50 and 39, respectively). NASCET II and CREST were conducted in more than 100 centers each (106 and 117, respectively). There were more patients randomized to CEA in the CREST trial (1,240) than in the other three trials (328 for NASCET I, 430 for NASCET II, and 825 for ACAS).

In terms of baseline characteristics, patients in the trials did not differ by age, sex distribution, or race. The rates of smoking, cardiovascular disease, and preprocedure antiplatelet therapy also did not differ among the trials. However, CREST enrolled more patients with hypertension, diabetes, and dyslipidemia. Also, shunting and patch angioplasty were used more frequently in CREST.

Credentialing

"The credentialing criteria for surgeons were fairly consistent across all of the trials," said Dr. Lal. Both CREST and ACAS required surgeons to perform at least 12 CEAs each year. However, there were no established surgeon volume requirements in the two NASCETs. All four trials included surgical management committees, site evaluations, and reviews of indications, hospital courses, and outcomes in the 50 most recent CEAs.

The minimum stroke plus death rate was no more than 3% for asymptomatic patients and no more than 5% for symptomatic patients in both CREST and ACAS; both NASCETs had a minimum rate of less than 6% in symptomatic patients.

End Points

The primary end point for both NASCETs as well as ACAS was the number of strokes plus deaths. For CREST, however, the primary end point was the number of strokes, MIs, and deaths. Importantly, the definition of stroke (an acute neurologic ischemic event of at least 24 hours' duration with focal signs and symptoms) was consistent across the trials. In all cases, strokes were adjudicated by neurologists, who were blinded to the treatment. ■

Vitamin B Failed to Reduce Poststroke Vascular Events

BY SHARON WORCESTER

FROM THE LANCET NEUROLOGY

Daily B vitamin supplementation is no more effective than is placebo for reducing the incidence of major vascular events in patients who have had a recent stroke or transient ischemic attack, according to findings from the Vitamins to Prevent Stroke (VITATOPS) trial.

Among 8,164 patients enrolled in the multicenter, parallel, double-blind trial, major vascular events (nonfatal stroke, nonfatal myocardial infarction, or death from any vascular cause) occurred in 15% of patients randomized to B vitamin supplementation and in 17% randomized to placebo after a median follow-up period of 3.4 years. This translated into a nonsignificant relative risk of 0.91, Dr. Graeme J. Hankey of Royal Perth (Australia) Hospital and his colleagues from the VITATOPS Trial Study Group reported.

When each type of vascular event was analyzed separately, B vitamin supplementation was not associated with a significant reduction in the relative risk for nonfatal or fatal stroke, nonfatal or fatal MI, or death from any cause. However, there was a slight, but statistically significant, reduction in the risk of death from vascular causes (relative risk, 0.86).

Dr. Hankey and his associates wrote that the findings suggest that B vitamins, while safe in poststroke and post-TIA patients, should not be recommended to prevent recurrent stroke (Lancet Neurology 2010 Aug. 4 [doi:10.1016/S1474-4422(10)70187-3]).

Study participants were enrolled between November 1998 and December 2008, within 7 months of experiencing stroke or TIA and were randomized to receive placebo or 2 mg of folic acid, 25 mg of vitamin B_6, and 0.5 mg of vitamin B_{12} daily in addition to usual medical care.

No unexpected adverse events occurred during follow-up, and no significant differences were seen between the treatment and placebo groups in regard to common adverse events, the investigators noted.

Although prior cross-sectional and observational epidemiological studies have suggested that raised plasma concentrations of total homocysteine are associated with increased risk for major vascular events, and that B vitamin supplementation can lower total homocysteine – as it did in the current study – this did not translate to a reduced incidence of subsequent vascular events in the study, they said.

Fasting blood tests performed at the end of follow-up in 1,164 patients showed that the B vitamin group had 3.8 micromol/L lower homocysteine than the placebo group (10.5 vs. 14.3 micromol/L). An analysis of a subset of 925 patients with fasting blood levels of homocysteine available from baseline and follow-up indicated that each 1.0-micromol/L decrease in total homocysteine was associated with only a nonstatistically significant 2% reduction in risk of the primary outcome.

The study is limited by incomplete adherence to trial drugs and by incomplete follow-up, as well as by a relatively short duration of follow-up, which "might not have been long enough to adequately identify or exclude any long-term effects of B vitamins," the investigators noted.

To control for random error, the researchers added their data to those from other randomized controlled trials of homocysteine-lowering therapy in patients with or without preexisting cardiovascular disease. This "updated meta-analysis" also showed that B vitamins are not significantly more effective than placebo for reducing the risk of the composite outcome of stroke, myocardial infarction, or vascular death (RR, 0.99). ■

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