

In Women, Limit Use of Carotid Endarterectomy

BY HEIDI SPLETE
Senior Writer

The perioperative risks of carotid endarterectomy outweigh the benefits in symptomatic women with less than 70% stenosis, especially those with few other risk factors, Sonia Alamowich, M.D., reported.

For women with lesser stenosis, medical management is both safer and more effective than surgery, according to Dr. Alamowich of Tenon Hospital in Paris, and her colleagues.

They performed subset analysis on pooled data from two trials of endarterectomy. The North American Symptomatic Carotid Endarterectomy Trial (NASCET) involved 873 women and 2,012 men with internal carotid artery stenosis and a history of recent transient ischemic attack or nondisabling ischemic stroke, randomized to best medical treatment alone or in combination with carotid endarterectomy. The Aspirin and Carotid Endarterectomy (ACE) trial was designed to study the best dose of aspirin to reduce the risk of stroke and death in 2,804 women and men scheduled for endarterectomy.

The 30-day risk of death after endarterectomy was higher in women than men (2.3% vs. 0.8%). Women's higher mortality was due largely to fatal stroke, based on a subgroup analysis of 1,415 patients in the surgery arm of NASCET and 1,148 symptomatic patients from ACE (Stroke 2005;36:27-31).

With stenosis of at least 70%, the absolute stroke risk reduction 5 years after endarterectomy was 15.1% for women and 17.3% for men. When carotid stenosis fell within the

50% to 69% range, endarterectomy reduced women's absolute stroke risk by only 3% versus 10% for men. Endarterectomy bestowed no significant benefit on either women or men with carotid stenosis under 50%.

When managed medically, men and women with at least 70% stenosis of the carotid had a similar 5-year absolute relative risk of ipsilateral ischemic stroke (28.9% vs. 29.8%). With stenosis from 50% to 69%, medically managed women had a lower risk of stroke, compared with men (16.1% vs. 25.3%).

Women scoring 0-3 on the stroke prognosis instrument measuring risk factors had no likelihood of stroke, and those scoring 2-5 had 6.3% risk of stroke. The stroke risk in men in the same two score categories were 18.5% and 19.2%, respectively. Thus, men with moderate stenosis benefit from surgery, regardless of their risk score.

Only 29% of the women with 50%-69% stenosis fell in that group with the highest risk score of 8-15. Carotid endarterectomy reduced their absolute relative risk of stroke by 8.9%; surgery provided little or no benefit to women with low risk scores and only moderate stenosis.

Certain stroke risk factors were significantly more common among women: obesity, smoking, hypertension, and hyperlipidemia. Other risk factors were significantly more likely among men: prior stroke and/or myocardial infarction, intermittent leg pain, irregular or ulcerated internal carotid artery plaques, occluded contralateral internal carotid arteries, and brain infarct on imaging.

Review of 28 Studies Links Hormone Therapy to Higher Stroke Risk

BY HEIDI SPLETE
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Hormone therapy is associated with a significantly increased risk of stroke, based on studies involving nearly 40,000 patients.

A review of 28 studies ranging in size from 59 to 16,608 adults and with follow up times of 0.7-6.8 years showed a significant association between hormone therapy use and an increased risk of total stroke, with an odds ratio of 1.29. The review supports previous studies that showed an association between increased risk of stroke and hormone therapy, reported Philip Bath, M.D., and Laura Gray of the University of Nottingham (England) [BMJ [Epub ahead of print], January 2005. Article DOI number: 10.1136/bmj.38331.655347.8F. Available from: www.bmj.com).

Twelve studies included women taking estrogen only; 16 included women taking estrogen plus progesterone. The average ages ranged from 55 to 71 years, and three studies of estrogen combined with progesterone included men. All but five studies were placebo-controlled, and 11 small trials recorded no stroke events.

Overall, 2% of patients randomized to no hormone therapy suffered strokes, but the risk of stroke among women randomized to hormone therapy increased 29%, primarily because of the increase in ischemic stroke. In

addition, severity of stroke increased with hormone therapy use; the chance of a poor functional outcome, defined as either death or disability and dependency, was 56% higher among women randomized to hormone therapy.

In particular, hormone therapy use was associated with a significant increase in the risk of ischemic stroke in 16 studies (OR 1.29). Hormone therapy use also was significantly associated with an increased risk of nonfatal stroke in 21 studies (OR 1.23), and with an increased risk of stroke leading to death or dependency in 14 studies (OR 1.56).

Hormone therapy was not significantly associated with hemorrhagic stroke or transient ischemic attacks in 17 studies and 22 studies, respectively. However, none of the studies showed any association between hormone therapy and a reduction of stroke risk, despite data from previous observational studies suggesting a protective effect of hormone therapy against cerebrovascular events.

The investigators suggested that phytoestrogens, which were not included in these studies, may have yielded different results. They also noted that the estrogen dose in several trials was higher than the standard starting doses of conjugated equine estrogen and estradiol in Great Britain, 0.625 mg and 1 mg, respectively, and studies of lower doses may yield different results.

CLINICAL CAPSULES

Drainage, Chemo for Malignant Effusions

Neoplastic pericardial effusions should be treated aggressively with intracavitary infusions of thiotepa, a low-cost, low-risk procedure that extends life expectancy and improves quality of life, according to Alessandro Martinoni, M.D., and associates at the University of Milan's European Institute of Oncology.

Malignant pericardial effusions are common in cancer patients, and until now the resulting pericardial tamponade has been the immediate cause of death in 85% of affected patients. But developing the condition should no longer "be considered as a terminal event, but [rather] as a treatable condition requiring true therapeutic intervention instead of a mere palliative approach," the investigators noted (Chest 2004;126:1412-6).

They performed percutaneous pericardiocentesis in 33 patients with metastatic breast, lung, skin, or endometrial cancers. All had pericardial effusions causing severe dyspnea, weakness, chest pain, and tachycardia, and 24 had cardiac tamponade. The malignant effusions were drained and thiotepa was administered in stages over a 5-day period. "All patients showed rapid and almost complete improvement of symptoms," without any adverse effects, pain, or myelosuppression.

Pericardial effusions recurred in only three patients (9%) over several months of

follow-up, and resolved with a repeat pericardiocentesis and thiotepa infusion. The treatment thus not only eliminated existing neoplastic effusion but also inhibited further effusion from developing. Median patient survival was 115 days (range 22-1,108 days), an "unexpected" result considering their extremely poor prognoses.

New Marker for HF Mortality in Elderly

The serum level of cystatin-C appears to be a stronger predictor of mortality in elderly people with heart failure than serum creatinine, reported Michael G. Shlipak, M.D., of San Francisco Veterans Affairs Medical Center, and his associates.

Cystatin-C, a serine protease inhibitor released by all functioning cells, can be used as a serum measure of renal function. Unlike creatinine, cystatin-C does not appear to be influenced by patient age, gender, or body mass, and so should be a particularly useful marker in elderly heart failure (HF) patients, the investigators said (J. Am. Coll. Cardiol. 2005;45:268-71).

They conducted a pilot study comparing cystatin-C with creatinine as a predictor of mortality, using data from a community-based longitudinal study of nearly 6,000 elderly subjects. During a median follow-up of 6.5 years, cystatin-C level was a better predictor of mortality in those who had HF. If larger studies confirm this finding, this new marker of re-

nal function could replace traditional markers in risk assessment for HF patients, they said.

Injected Anti-VEGF for Macular Disease

Intravitreal injections of pegaptanib, an agent that blocks the activity of vascular endothelial growth factor, arrests the loss of visual acuity in patients with age-related macular degeneration due to choroidal neovascularization, according to Evangelos S. Gragoudas, M.D., of the Massachusetts Eye and Ear Infirmary, Boston, and associates.

They conducted two concurrent randomized trials involving 1,186 patients aged 50 years and older treated at 117 medical centers worldwide. The subjects, who had a broad spectrum of lesion sizes, angiographic types of lesions, and baseline levels of visual loss, were randomly assigned to receive either pegaptanib or sham eye injections every 6 weeks for 48 weeks.

Reductions in both moderate and severe losses of visual acuity were noted as early as at the time of the second injection, and benefit increased over time. The treatment also reduced the chance that patients would progress to legal blindness, and it actually improved vision in 33% of patients, the investigators said (N. Engl. J. Med. 2004;351:2805-16).

Racial Disparity Persists in ICD Use

The racial disparity in the use of im-

plantable cardioverter defibrillators improved throughout the 1990s but still remained "substantial" by the year 2000, reported Peter W. Groeneveld of Veterans Affairs Medical Center, Philadelphia, and his associates.

The researchers analyzed Medicare data on more than 570,000 elderly patients hospitalized with ventricular arrhythmias during 1990-2000. At the beginning of that period, subjects of any race living in geographic areas where at least 10% of the population was African American had a 19%-23% lower chance of receiving an implantable cardioverter defibrillator (ICD) than did those living in areas with smaller black populations. But by 2000, ICD implantation rates had essentially equalized among geographic groups. For the study, geographic areas were defined using zip codes, and demographic data were obtained from the 1990 and 2000 U.S. Census.

It appears that early in the decade, ICD use "may have insufficiently 'penetrated' the health care systems where black patients were more likely to receive care." Although this geographic situation has largely been ameliorated, a racial disparity still persists. "Even as late as 1999-2000, elderly black patients with ventricular arrhythmias continued to have approximately two-thirds the likelihood of receiving an ICD" as whites, the investigators said (J. Am. Coll. Cardiol. 2005;45:72-8).

—Mary Ann Moon