Sept. 26, 2005 — The American Academy of Neurology (AAN) has updated its guidelines on carotid endarterectomy (CE). The revised recommendations and underlying evidence are reported in the Sept. 27 issue of *Neurology*.

"The evidence of this guideline points out an effective method of stroke prevention in certain people," guideline author Seemant Chaturvedi, MD, from Wayne State University in Detroit, Michigan, says in a news release. "CE is beneficial for those with severe to moderate narrowing in their carotid artery."

The objective of the AAN Therapeutics and Technology Assessment Subcommittee was to evaluate the efficacy of CE for stroke prevention in asymptomatic and symptomatic patients with internal carotid artery (ICA) stenosis. Additional considerations were the use of endarterectomy in different clinical settings, such as combined with cardiac surgery.

Depending on the population studied, extracranial ICA stenosis accounts for 15% to 20% of ischemic strokes. Although CE is the most frequently performed surgery to prevent stroke, the last AAN statement regarding CE was published in 1990. This revision was prompted by several multicenter trials and other major developments since 1990.

To address nine important clinical questions, the authors performed a systematic search for articles from 1990 through 2001, as well as additional articles from 2002 through 2004 that met prespecified criteria. Case reports, review articles, technical studies, and single-surgeon case series were excluded.

The nine clinical questions identified by the panel, and key studies addressing each, were as follows:

1. *Does CE benefit symptomatic patients?*

The North American Symptomatic Carotid Endarterectomy Trial (NASCET) and the European Carotid Surgery Trial (ECST) are two completed class I studies. The Veterans Affairs Cooperative Studies Program 309 Trial was stopped prematurely after announcement of the initial NASCET results, which showed a significant benefit of CE in patients with 70% to 99% symptomatic stenosis. Two-year ipsilateral stroke risk was 26% in the medically treated patients and 9% in the CE group (P <.001; absolute risk reduction [ARR], 17.0%; number needed to treat [NNT] = six at two years.

A combined analysis of trials of symptomatic patients, which included 6,092 patients with 35,000 patient-years of follow-up, showed a benefit for CE for 50% to 69% stenosis (ARR, 4.6% over five years; NNT = 22), more than 70% stenosis (not near occlusion; ARR, 16% over five years; NNT = 6.3). For near occlusion, ARR was 5.6% over two years (P < .19) but only –1.7% (P < 0.9) over five years. The overall rate of perioperative stroke or death for all surgical patients within 30 days of trial surgery was 7.1%, yielding a number needed to harm (NNH) of 14.

2. *Does CE benefit asymptomatic patients?*

Three class I studies are the Asymptomatic Carotid Atherosclerosis Study (ACAS), the Veterans Affairs Study, and the Asymptomatic Carotid Surgery Trial (ACST). The Veterans Affairs study

showed a nonsignificant trend favoring CE for prevention of ipsilateral stroke (9.4% vs 4.7% at four years). In ACAS, the five-year projected rate of ipsilateral stroke was 11.0% for medical treatment patients and 5.1% for CE (53% relative risk reduction; *P* = .004).

3. *Is emergent CE beneficial in patients with progressing stroke of less than 24 hours?*

Four class IV studies were identified, but they were fairly small, lacked objective evaluation of the reported neurologic outcomes, and analysis of one study was hindered by coexisting treatments.

4. *What are the most important clinical variables that impact the risk/benefit ratio?*

Sex and presenting symptoms may be most relevant. In both the NASCET 50% to 69% group and in ACAS, womenderived no benefit from CE. NASCET also showed that patients presenting with retinal ischemia have a lower subsequent stroke risk than do patients with hemispheric events.

5. *What are the most important radiologic factors that impact the risk/benefit ratio?*

The NASCET and ACAS studies suggest that for symptomatic patients with a contralateral occlusion, the surgical complication rate is higher than if the contralateral ICA is patent, but there is still a better outcome than with medical management for patients with 70% to 99% stenosis. However, for patients with asymptomatic stenosis and a contralateral occlusion, the only randomized evidence suggests that patients do slightly better with medical management (2.0% absolute increase in risk with CE at five years). For symptomatic patients with angiographic near-occlusion, CE is associated with a trend toward benefit at two years but no clear benefit at five years.

6. *What is the ideal dose of aspirin preoperatively in patients undergoing CE?*

The ACE trial, a class I study, showed a lower combined rate of stroke, myocardial infarction, and death in the low-dose groups (81 mg and 325 mg) than in the high-dose groups (650 mg and 1,300 mg) at 30 days (5.4% vs 7.0%; *P* = .07) and at three months (6.2% vs 8.4%; *P* = .03).

7. *What is the evidence/practice gap?*

The panel noted that CE results achieved in the clinical trials may not be reproducible in routine clinical practice.

8. *What are the data regarding CE concurrent with or prior to coronary artery bypass graft (CABG)?*

There were no randomized clinical trials addressing this question. Retrospective reports suggest similar perioperative complication rates in CE before or simultaneous with CABG data, although the death rates with combined CE-CABG are higher than with CE alone.

9. *How long should one wait after a stroke to perform CE?*

None of six retrospective cohort studies comparing the timing of CE in patients after a stroke found any differences in operative morbidity and longer-term outcomes, but there were significant limitations in study designs.

Compared with medical therapy alone, CE reduces the stroke risk for patients with 70% to 99% symptomatic stenosis (16% absolute risk reduction at five years). For patients with 50% to 69% symptomatic stenosis, absolute risk reduction is 4.6% at five years. Provided there is a low perioperative complication rate, there is a small benefit for asymptomatic patients with 60% to 99% stenosis. The guidelines recommend that patients undergoing endarterectomy take aspirin at a dose of 81 to 325 mg per day rather than at higher doses of 650 to 1,300 mg per day.

The evidence supports CE for severe (70% to 99%), recently symptomatic (within the previous six months) stenosis (level A evidence). CE is moderately useful for symptomatic patients with 50% to 69% stenosis (level B), but it is not indicated for symptomatic patients with less than 50% stenosis (level A).

Asymptomatic patients with 60% to 99% stenosis have a smaller benefit/risk ratio than do symptomatic patients, mandating individual decision-making on a case-by-case basis, according to the guidelines. It is reasonable to consider CE for patients between the ages of 40 and 75 years and with asymptomatic stenosis of 60% to 99% if the patient has an expected life span of five years, and if rates of surgical stroke or death frequency can be reliably documented to be less than 3% (level A).

If the perioperative stroke/death rate is lower than 3%, CE can reduce the future stroke rate (level A). To reduce the rate of stroke, myocardial infarction, and death, low-dose aspirin (81-325 mg) is preferred for patients before and after carotid endarterectomy (level A).

The panel made no recommendations regarding the value of emergent CE in patientswith a progressing neurologic deficit (level U).

Patients with severe stenosis and a recent transient ischemic attack or nondisabling stroke should undergo CE without delay, preferably within two weeks of the most recent symptoms (level C). Evidence is insufficient to support or refute the performance of CE within four to six weeks of a recent moderate to severe stroke (level U).

"We recommend further high-quality studies to evaluate the evidence/practice gap in the future," Dr. Chaturvedi says.

Recommendations for topics for future research include the setting of urgent CE in patients with progressing stroke, the appropriateness of CE in community settings, the management of coexisting carotid and coronary artery disease, the timing of CE in patients with recent stroke, the role of newer antiplatelet agents in the perioperative setting, and comparison of CE with stenting in patients with symptomatic and asymptomatic carotid stenosis.

The authors report no conflicts of interest.

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Reviewed by Gary D. Vogin, MD