Efficacy of Carotid Endarterectomy Translates to Being Efficacious With Appropriate Surgical Skill

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SURGICAL INITIATIVE and hematological and pharmaceutical research have achieved substantial measures of success in the prevention and treatment of ischemic stroke. The key to this progress has been the conduct of large randomized trials. For none of the strategies shown to have efficacy (benefit) has the dialogue stopped with the publication of the primary results. The results may be presented in such a way as to appear beneficial, but closer scrutiny must examine the efficaciousness or practicality of transferring the results to clinical practice. Questions may also arise about the clinical significance of a statistically significant result.

Efficacy of a treatment can be assured for some patients and may exist for others, but the information remains buried within large generically defined populations. In addition, claims of efficacy have been confused by speculative assumptions made as a prelude to analyses. For example, in the CAPRIE (clopidogrel vs aspirin in patients at risk of ischemic events) trial, the analyses assumed all ischemic events to be of equal importance independent of the mode of clinical presentation. Thus all ischemic or fatal outcomes in the 3 arterial territories (peripheral, coronary, cerebral) were aggregated and overall benefit, albeit modest, was claimed for clopidogrel bisulfate over aspirin. Closer scrutiny failed to be convincing as to the significant benefit in stroke prevention for patients presenting with stroke. Many stroke neurologists are unhappy with the assumptions and want to see a repeat trial specifically testing the 2 drugs confined to patients presenting with cerebral ischemic event(s) before administering the new agent at 80 times the cost.

Efficacy may be absent from a large series in which lumping together produces a broad case-mix. It may be misleading to suggest blanket negativity when there are wide variations in the cause of stroke in populations being evaluated. Specific causal subgroups may be hidden as may patients within different time frames of symptom onset, thereby overlooking their unique benefit. Notable examples here include the thrombolytic trials. Benefit was not found in the European trials that used a 6-hour time-frame; the National Institute of Neurological Disorders and Stroke trial used 3 hours as the cutoff and found benefit. The International Stroke Trial, a huge trial, allowed entry of ischemic stroke of any cause. No benefit of anticoagulant therapy emerged. The trial did not specifically exclude patients with nonvalvular atrial fibrillation. Fortunately, proof of benefit and superiority of anticoagulants over aspirin was achieved in trials confined to this cardiac disorder.

In the surgical field, the report on the absence of efficacy for extracranial/intracranial bypass in stroke prevention may have overlooked a small number of patients with ongoing hemodynamic compromise threatening new events. Combing through the By-pass Study database would not provide the answer to this enigma. A high-risk subgroup in whom the circulatory compromise can be shown with positron emission tomographic scan are currently being randomized to seek evidence of benefit.

Because carotid endarterectomy (CE) for symptomatic patients and asymptomatic subjects has been subjected to trials in sufficient numbers, many answers are available about efficacy or its lack. The neurologist who would recommend and the surgeon who would perform CE must recognize that the mere existence of symptoms within the territory of a stenosed artery or the presence of an asymptomatic lesion only represents the first level of information required to decide on treatment for any individual patient.

The protocol of the North American Symptomatic Carotid Endarterectomy Trial (NASCET) was designed to accumulate sufficient data to answer a number of predetermined secondary questions. By virtue of these secondary analyses we can state that the factors associated with patients facing the highest risk of future stroke are severe (>70%) stenosis, male gender, absence of visible collaterals, hemispheric and nonretinal events, absence of intracranial stenosis, and age older than 75. Because none of these subgroups had increased perioperative complication rates, the differential between medical and surgical therapy was widest and strongly favors them as the ideal candidates for carotid endarterectomy. Conversely, lesser medical risk and lesser benefit can be predicted with lesser degrees of stenosis (50%-69%), and with this lesser degree of stenosis, female gender, retinal symptoms only, good collaterals, and presentation with lacunar symptoms are among the characteristics that militate against benefit and are against a sweeping declaration of efficaciousness of CE for them.
In generalizing NASCET results, one must not lose sight of the fact that patients with heart lesions likely to lead to thrombo-embolism, with impending organ failure, with recent evidence of myocardial infarction or congestive heart failure, with nonarteriosclerotic carotid lesions, or in whom symptoms stopped more than 6 months ago were not studied. Most patients in these categories should be told that they are not likely to benefit from the procedure, their operative risk is high, and subsequent strokes may be from other than a large-artery cause, not one preventable by CE.

Neither referring physicians nor patients can take it for granted that the results published from the randomized trials are an accurate reflection of the scenario awaiting them in their local hospitals. The skill of the individual surgeon who will perform the procedure must be known. In a well-designed and clearly documented study in this issue of the ARCHIVES, Feasby and colleagues\(^6\) draw attention to convincing evidence of the unacceptably high rate of perioperative stroke and death when the procedure is performed by surgeons whose annual experience in the performance of CE is low. Where the hospital case volume is low (<150) and the single surgeon's annual performance of CE is less than 15 patients, a 13.6% stroke and death rate emphatically indicates that these patients would have survived stroke free more often had they received only medical treatment. We do not know what percentage of the 14 268 patients reported by Feasby et al had no symptoms or how many had only moderate disease. Reference to Figure 1 demonstrates that when the symptoms are related to moderate stenosis and when the complications of CE are at this unacceptably high level "CE is harmful out to 3 years postprocedure."

Asymptomatic carotid stenosis is accompanied by a low risk of stroke. The annual risk for patients in the 2 largest trials of asymptomatic subjects was 2.4% for stroke and 2.3% for stroke and death in the Asymptomatic Carotid Atherosclerosis Study\(^8\) (ACAS) and Veterans Administration trial\(^9\), respectively. Excluding angiography, the phenomenally low complication rate in the 826 subjects randomized to endarterectomy in the ACAS trial was 1.5%. The perioperative stroke and death risk in the 1214 subjects who underwent to CE with asymptomatic disease in the Aspirin and Carotid Endarterectomy (ACE) trial was 4.4% and was not better (4.1%) when analyzed only for 320 the subjects operated on by ACAS surgeons also working within the ACE trial.\(^10\) When the surgical complication rate in the ACE trial and the medical rate of events in the ACAS are subjected to analysis, the asymptomatic patients in the ACE trial had more strokes than the comparable medically treated subjects. The estimated allowable surgical risk of stroke and death to achieve benefit in asymptomatic subjects is 3%.

The Feasby et al report is of the Canadian-wide experience. In a study of equally compelling importance, Kresowik et al\(^11\) verified complication rates occurring in a total of 10 561 CEs performed in 10 states in the United States during 1995 and 1996. The study distinguished between symptomatic and asymptomatic individuals and had data for the 30-day post-CE period. For the 7604 subjects who underwent CE without any symptoms or with only nonspecific, nonhemispheric events, the rate of stroke and death was 5.3%. Fewer strokes would have occurred if medical care alone had been given. The authors acknowledge that the complication rate may have been underestimated. Figures from administrative databases are totally dependent on the accuracy of the discharge diagnosis. In most instances this is decided by the operating surgeon or more probably by surgical residents. As a rule their training has not involved the acquisition of refined skill in neurological examination. One report has drawn attention to a 3-fold increase in post-CE stroke occurrence when stroke neurologists rather than surgeons are responsible for determining the incidence of unfavorable outcomes.\(^12\) It is a reasonable speculation to suggest that minor postoperative strokes can commonly be overlooked or forgotten.

The accumulation of evidence-based data including the information in this issue of the ARCHIVES demands that more attention be paid to each individual patient and to the proven skill of every surgeon who will perform a procedure that carries a minimum of a 2% risk of disabling stroke or death. If the best possible results are to be based on what we know of the efficacy and efficaciousness of CE, the following are strongly recommended:

1. Hospitals and surgeons with low volumes of patients requiring CE should advise potential candidates for CE that they must go to high-volume hospitals with surgeons of known skill.
2. Surgical audits should be conducted annually by nonsurgical members of each institutional staff and the results made public.
3. Physicians sophisticated in the examination of the nervous system should be involved in decision making about the appropriateness of CE in each patient and be responsible for signing off on the diagnosis and complication sheets on the discharge summary.
4. Administrative databases for CE should be expanded to include the important prognostic variables now known to influence risk. As bare minimums, this will include the presence or absence of symptoms and the degree of stenosis.

To some readers, these recommendations may sound like constraints on professional freedom. The delicate function of the brain at risk annually in scores of thousands of patients and the posttrial record of CE results that are less than perfect require that nothing short of these recommendations should be tolerated.

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