ALTHOUGH ASYMPTOMATIC CAROTID BRUITS are an established risk factor for ischemic stroke, the management of asymptomatic patients with carotid bruits and carotid stenosis remains controversial. Carotid endarterectomy is performed in increasing numbers of patients although its efficacy has not been demonstrated convincingly for either asymptomatic or symptomatic disease. Since a requirement of any treatment is that benefits should outweigh risks, unless a subgroup with spontaneous stroke risk of at least 5% can be identified.

The reported outcome of asymptomatic patients with neck bruits varies widely but the best perspective is obtained from community studies in patients with transient ischemic attacks (TIAs), figures which may not apply to asymptomatic patients. Both the Extracranial Arterial Occlusion Joint Study and the Mayo Clinic reported a two-thirds reduction in stroke rates following uncomplicated carotid endarterectomy. The reduced long-term risk is offset by the more immediate complications of surgery. For carotid endarterectomy, surgeons with a high level of expertise achieve peri-operative stroke and death rates less than 5% (table I), whereas operative stroke and death occur with about equal frequency. Angiographic complications should also be considered, but are omitted from further discussion because recent technological refinements have reduced permanent neurological sequelae to well below 1%. The data are the basis for evaluating the merits of carotid endarterectomy in patients with asymptomatic carotid stenosis.

Selection of Endpoints

If stroke risk alone is considered, the net stroke reduction at three years in the surgical group is 42%, and the ‘break-even point’ is 13 months (fig. 1). The ‘break-even point’ is the moment when the number of strokes in each group is equal. A randomized surgical trial would require 1214 patients in each group to achieve a statistically significant result (table 2, trial 1).

If both stroke and death risks are considered (fig. 2), the net (stroke and/or death) risk reduction at three
years becomes only 6%, the break-even point is 28 months and the required sample size for an endarterectomy trial 3582 in each group (table 2, trial 1). Even if 7000 patients could be recruited, such results would not be clinically important.

The inclusion of mortality in this calculation is debatable as some patients might gamble on their survival to avoid long-term disability from stroke. In an endarterectomy trial fulfilling ethical requirements, deaths must be counted because peri-operative death is a significant hazard. In practice, patients should choose between conservative and surgical treatment on the basis of their personal attitudes toward surgery, stroke and death.

### Spontaneous Stroke and Death Risk

Knowledge of the natural history of asymptomatic carotid disease is incomplete. The Evans County1 and Framingham studies have determined the overall stroke rate but the relationship between stroke and underlying carotid disease is uncertain. Substantial variation in reported outcome suggests that subgroups do exist within the ACB population. For example,

![Figure 1. Endarterectomy results, assuming stroke is the sole endpoint, spontaneous stroke rate = 2% rate annum, stroke risk reduction after surgery = 1/3, and peri-operative stroke rate = 1.5%. Net stroke risk reduction at 3 years = 42%, and intersection of the curves occurs at 13 months.](http://stroke.ahajournals.org/)

Cooperman et al17 and Thompson et al9 reported higher spontaneous stroke rates of 3% and 4.3% per annum (respectively), probably because a greater proportion of surgical referrals have carotid stenosis.

Carotid endarterectomy is more acceptable if the spontaneous stroke rate is at least 5% per annum (table 2, trial 2). If the combined risks of stroke and death are considered, the net risk reduction at three years is 26% and the break-even point is 10 months (fig. 3). This effect could produce a dramatic decline in the overall incidence of stroke in the community. A multi-centre randomized trial would require a more feasible total study population of 1206 patients (table 2, trial 2).

Of 500 patients followed for up to 30 months in the Toronto Asymptomatic Cervical Bruit Study, neurological ischemic events have occurred in 28. Twenty-two of 25 patients with carotid events had ipsilateral carotid stenosis. The event rate in patients with internal carotid artery (ICA) stenosis greater than 75% was 15% per annum, compared with 3% per annum in patients with ICA stenosis less than 75% and 2% in patients without carotid stenosis (fig. 4).

Patients with progressing lesions had a higher incidence than non-progressors. However, 26 of the 28 patients presented with TIA's and only three of these suffered a stroke. Only two patients presented with stroke without prior
TIAs. The risk of cerebral ischemic events was related to the presence, severity and progression of carotid stenosis, but the incidence of stroke, especially unheralded stroke, in our 'high-risk' patients was well below 5% per annum. Cerebral ischemic events were also more frequent in patients with heart disease, males and patients over 65 years. Multivariate analysis demonstrated that the initial severity of carotid stenosis and the presence of heart disease were the best predictors of cerebral ischemic events.

Risk Reduction after Carotid Surgery
A two-thirds reduction in stroke rate may be unduly optimistic and the long-term therapeutic effect of endarterectomy in asymptomatic patients may be less than for symptomatic patients. The overall stroke rate is less and therefore, stroke syndromes less likely to be prevented by endarterectomy, such as cerebral hemorrhage, lacunar infarction and middle cerebral artery thrombosis may assume a greater proportion. Assuming a high-risk subgroup exists, if the stroke risk reduction from carotid endarterectomy is only one-third (table 1, trial 3), the net surgical stroke and/or death risk reduction is only 7%, and again of doubtful clinical importance.

Risks of Carotid Surgery
Although the reported peri-operative complication rates in major referral centres are less than 5%,8-13 city-wide audits in Springfield, Illinois18 and Cincinnati, Ohio19 have shown alarmingly high stroke and/or death rates, 21.1% and 11.4% respectively (table 1). The complication rate of 16.7% in 24 patients withdrawn from the Toronto Asymptomatic Carotid Bruit Study following endarterectomy was also significantly higher.20

A peri-operative stroke and/or death rate around 15% places the surgical group at a clear disadvantage (table 2, trial 4 and figure 3), while a lesser rate of 10% confers no advantage to either group. Although rates between 5% and 10% result in a small benefit to the surgical group, the large sample required to achieve statistical significance would preclude a randomized trial.

Conclusion
The efficacy of carotid endarterectomy is extremely responsive to the choice of endpoint and variations in the spontaneous stroke rate, the risk reduction from surgery and the peri-operative complication rate. The role of carotid endarterectomy in asymptomatic patients has not yet been clearly defined. A randomized trial should be deferred until a subgroup is identified with at least a 5% per annum stroke risk. Only those who are at high risk for stroke should be considered for surgical treatment.
surgical units with a documented peri-operative complication rate of less than 5% should participate.

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