Hotline Editorial

Carotid endarterectomy in patients with recently symptomatic moderate (30–69%) carotid stenosis: no overall benefit

Atherothrombotic stenosis at or around the carotid bifurcation is associated with an increased risk of ipsilateral ischaemic stroke. This risk increases with the severity of stenosis, and is further increased, at least for a few years, after the occurrence of transient ischaemic attacks or minor ischaemic strokes in the distribution of the diseased artery. The risk of stroke is reduced by treatment with aspirin, and in certain patients, by carotid endarterectomy[1,2]. Whether or not the operation is beneficial is determined by the balance between the risk of stroke and death due to the operation itself and the risk of ipsilateral ischaemic stroke without surgery. Patients at greatest risk of stroke on medical treatment are likely to have the most to gain from surgery. For this reason the analyses of the recent randomized controlled trials of endarterectomy were stratified by the degree of stenosis of the symptomatic carotid artery; a powerful predictor of stroke risk.

In 1991, the European Carotid Surgery Trial (ECST) and the North American Symptomatic Carotid Endarterectomy Trial (NASCET) both reported that endarterectomy reduced the overall risk of stroke in patients with recently symptomatic severe (70–99%) carotid stenosis[1,2]. The ECST also demonstrated that surgery was harmful in patients with mild stenosis (0–29%), in whom the risk of stroke on medical treatment was too low to offset the operative risks. Both trials continued to randomize patients with moderate (30–69%) stenosis. However, comparison of the trial results was complicated by the fact that they had measured the degree of stenosis differently on the pre-randomization angiogram. The NASCET method of measurement underestimated the degree of stenosis compared to the ECST method. Stenoses reported to be 70–99% by the NASCET trialists were equivalent to 82–99% by the ECST method, and stenoses reported to be 70–99% by the ECST trialists were 50–99% by the NASCET method[3]. Nevertheless, both trials were in agreement about the benefit of endarterectomy in patients with 'severe' stenosis: a reduction in risk of stroke at 3 years of about 50% in relative terms and between 10% and 20% in absolute terms.

In June 1996, the ECST collaborators reported the result for patients with moderate i.e. 30–69% stenosis[4]. 1599 patients were randomized to surgery (60%) or to avoid surgery (40%) and were followed-up for a mean of over 4 years. The primary outcome measures were survival and survival free of stroke (in fact, strokes lasting longer than 7 days), and the results were reported separately for patients with stenosis of 30–49% and 50–69% by the ECST method of measurement. The operative risks of stroke and death were 8.0% and 7.9%, respectively; consistent with previous series in which outcome was assessed by neurologists[4]. Log rank tests for all-cause mortality in both groups showed a non-significant trend against endarterectomy: 1.29 (95% CI 0.88–1.90) in the 30–49% group and 1.18 (0.88–1.58) in the 50–69% group. For survival free of major stroke, surgery was significantly harmful during the early years of follow-up (P<0.05 for 0–3.4 years in the 30–49% group and 0–2.3 years in the 50–69% group). This reflects the fact that most of the hazard in the surgery patients occurs within the first few days after the operation, whereas the hazard in the medical group accrues gradually over years of follow-up. However, despite nearly 10 000 patient-years of follow-up in the moderate stenosis patients, there was no evidence of any benefit from endarterectomy up to 8 years after operation in either the 30–49% or the 50–69% stenosis groups. More information will be available in about 2 years when the NASCET trialists complete follow-up of their 'moderate' stenosis patients: approximately 50–82% stenosis by the ECST method of measurement[3].

Currently, endarterectomy is only indicated in patients with 70–99% recently symptomatic stenosis by the ECST method. The vast majority of the benefit in this group occurs in patients with 80–99% stenosis (ECST unpublished data). However, even in these patients, it is still necessary to perform about seven operations to prevent one patient having a stroke over the next 3 years. The cost-effectiveness of the
operation could be improved considerably if it was possible to identify those patients at highest risk of stroke without surgery, and operate on them, and avoid surgery in those patients, who, despite having a severe carotid stenosis, have a low risk of stroke on medical treatment. The degree of the stenosis is only one of several independent clinical and angiographic characteristics which predict the risk of stroke on medical treatment. For example, the risk of stroke is higher distal to an irregular plaque than smooth plaque\(^6\), and lower following amaurosis fugax than a cerebral ischaemic event\(^7\).

Stratification of the ECST results by predicted risk of stroke on medical treatment, using an independently derived prognostic model, has demonstrated that endarterectomy is ineffective in a significant proportion of ‘low risk’ patients with 70–99% stenosis\(^8\). Similar results have been shown for coronary bypass grafting in low risk patients\(^9\). More powerful prognostic models have been derived using the ECST data, but these await validation when NASCET is complete. However, it is likely that we will be able to identify patients with severe stenosis who do not benefit from endarterectomy and patients with moderate stenosis, and a high risk of stroke on medical treatment, who do benefit. In the meantime, since stratification of the results of the ECST and NASCET trials according to the degree of stenosis of the symptomatic carotid artery was the only prespecified subgroup analysis, this must remain the major determinant of likely benefit from carotid endarterectomy.

Finally, with a total of 3026 patients randomized, and nearly 20 000 patient years of follow-up (complete in 99·5% of patients), the ECST has shown that large randomized controlled trials of surgical procedures are possible, and that they can change clinical practice, as indeed they have done in coronary artery surgery. Further trials are evaluating the role of endarterectomy in patients with asymptomatic carotid stenosis, and the efficacy of angioplasty compared with endarterectomy in patients with symptomatic carotid stenosis. The effectiveness of prophylactic carotid endarterectomy for asymptomatic stenosis in patients undergoing cardiac or coronary artery surgery remains to be determined.

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**References**


