The role for carotid endarterectomy (CEA) in reducing the subsequent stroke risk following an ipsilateral transient ischaemic attack (TIA) or non-disabling ischaemic stroke in patients with a significant internal carotid artery (ICA) stenosis is well established. A lesser benefit occurs after surgery for asymptomatic carotid stenoses. Nevertheless CEA is associated with a 30-day stroke risk of 5–7% and strategies that reduce this risk would be important.

The GALA (general versus local anaesthesia) Trial was conceived following publication of data from non-randomised studies suggesting that local or regional anaesthesia (LA) was associated with a 50% reduction in stroke and death rates for CEA compared to general anaesthesia (GA). A subsequent Cochrane Review of both non-randomised and randomised studies reached similar conclusions. The potential advantages of LA CEA include accurate assessment of neurological function (awake testing) following carotid clamping and clear identification of patients with cerebral hypoperfusion requiring a carotid shunt and preservation of cerebral autoregulation. Thus fewer shunts are used under LA, reducing the risk of air or particulate embolism to the brain and of arterial injury that might promote post-operative carotid thrombosis. Further, GA could result in more cardiorespiratory risks in elderly patients. Although both anaesthetic techniques have been used with varying enthusiasm since the 1950s there has been no consensus as to which is safer. Thus, the GALA Trial was designed to determine whether the type of anaesthesia influenced peri-operative morbidity and mortality (particularly from stroke), quality of life in the short term, and stroke and myocardial infarction-free survival to one year.

GALA is the largest randomised surgical/anaesthetic trial ever performed and included 3526 patients recruited by 95 centres in 24 countries. Although power calculations suggested that up to 5000 patients might be required to confirm a one third reduction in the primary outcome events of stroke (including retinal infarction), myocardial infarction and death (from 7.5% to 5%) within 30 days of surgery this was a more conservative effect than that suggested by the previous meta-analysis and recruitment was terminated after a one-year extension to the proposed recruitment period. Primary outcome data is available for 99.9% of patients.

Analysis of the results has shown that primary outcome events were observed (randomisation — 30 days post-surgery) in 84/1752 (4.8%) GA and 80/1771 (4.5%) LA patients. This difference is not statistically significant with 3 events prevented/1000 LA patients (95% confidence interval −11, +17); risk ratio 0.94 (95% CI 0.70, 1.27). Similarly, when primary outcome events are considered individually no significant differences were identified: stroke 70 (4.0%) GA patients versus 66 (3.7%) LA patients (3 strokes prevented/1000 LA patients (95% CI −10 to +16)), risk ratio 0.93 (95% CI 0.67–1.30); death 26 (1.5%) GA patients versus 19 (1.1%) LA patients (4 events prevented per 1000 (95% CI −3 to +12); risk ratio 0.72 (95% CI 0.40–1.30)); fatal and non-fatal myocardial infarctions LA 9 (0.5%) versus GA 4 (0.2%) patients (3 more events/1000 LA patients (95% CI −2 to +8)). Even if recruitment had continued until the target of 5000 patients had been reached the findings almost certainly would have been the same.

Similarly there were no differences between LA and GA for patients aged > or <75 years or for those considered at higher risk from surgery using a previously defined algorithm. A third pre-defined sub-group for analysis were patients with a contralateral carotid occlusion. In 310 patients with contralateral carotid occlusion there were 23 primary outcome events (15/150 (10%) GA versus 8/160 (5%) LA, P for interaction 0.098). Further, neurological events were more likely to occur contralateral to the operated artery (i.e. on the same side as the occlusion) in the GA group (54% versus 29%). Thus LA may offer an advantage for patients with a contralateral occlusion although this requires further confirmation.

Although GALA was not powered detect a difference between LA and GA for peri-operative death alone, when our data is combined with that from randomised trials in the Cochrane Review the impact of LA ranges from a 64% reduction to a 7% increase for this end-point. Further one-year survival data for GALA patients suggests fewer subsequent events (stroke, death, MI) in LA patients (log rank
test \( P = 0.094 \). Additional follow-up is required to establish the validity of this trend. Although the findings might question the validity of the original hypothesis, there are a number of reasons why they are not surprising. In particular the overall results for CEA were significantly better than those reported in all previous trials which included independent peer review for outcome assessment. With fewer primary outcome events it is much more difficult to show a difference between the two "treatments". It also seems likely that the reflex rise in systolic blood pressure following application of the carotid clamps with LA (the mechanism by which LA facilitates autoregulation) became recognised by anaesthetists who mimicked this pharmacologically during GA surgery. Thus, blood pressure was manipulated "up" in 43% of GA patients compared to 17% of LA patients.

Finally carotid patches were used in fewer patients in the LA group (42% versus 50%) which, given the evidence from a previous Cochrane Review might have had some influence on outcomes in this group.

A potential criticism of the Trial is that these differences in blood pressure manipulation and patching rates would have been avoided by a more prescriptive study protocol. This might also be considered the case for other variables (indicators for surgery, diagnostic methods, anaesthetic drugs and techniques, heparin dose, antiplatelet therapy, endarterectomy technique). Such a rigid approach would almost certainly have had a detrimental effect upon recruitment in an international multicentre study. Equally a more pragmatic approach should improve the generalisability of the results.

A further potential criticism of the trial design is that clinicians might not have randomised higher risk patients who were considered better suited to one or the other types of anaesthetic. A prospective log of non-randomised patients in each centre might have answered this question but was not considered practical.

Potentially important secondary end-points of time spent in high dependency or intensive care and total hospital stay were also similar in both arms of the trial. That there was no difference between the groups might reflect adherence to pre-existing care pathways rather than adopting an individual management plan based on each patient's specific requirements. Finally there was no difference in post-operative quality of life data collected 4–6 weeks after surgery. It is conceivable that any advantage to LA would only have been identified if this information had been collected earlier.

In summary the GALA Trial has clearly shown that outcomes for carotid endarterectomy have improved since publication of the ECST and NASCET trials with a reduction in primary outcome events of more than a third. The Trial also shows that both methods of anaesthesia are safe and that the anaesthetist and surgeon, in consultation with the patient, should probably determine the method of anaesthesia. However, for patients with a contralateral carotid occlusion it is tempting to suggest that LA might offer some benefit, presumably related to its effect on preserving autoregulation and therefore blood flow to the contralateral hemisphere. Similarly, the trends suggesting fewer peri-operative deaths and improved one-year survival following LA surgery require further analysis.

References


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