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Therapeutic ultrasound during carotid endarterectomy

Intraoperative sonolysis reduces stroke complications

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Ultrasonography as a diagnostic modality for the diagnosis and surveillance of carotid stenosis has been a mainstay of clinical practice for decades.[1 2] Ultrasound is non-invasive, does not use ionizing radiation or contrast media, and remains low cost, making it an integral evidence based tool for patients with carotid disease.[3]

Carotid endarterectomy is the surgical therapeutic gold standard to reduce long term stroke risk in patients with severe carotid stenosis. In the linked study (doi:10.1136/bmj-2024-082750), investigators in the SONOBIRDIE trial have tested a new application for ultrasound: prevention of thromboembolic complications during carotid endarterectomy.[4] In a multicenter randomized trial of 1004 patients, investigators determined that intraoperative sonolysis with ultrasound at the time of carotid endarterectomy reduced the composite endpoint of transient ischemic attack, stroke, or death within 30 days from 7.6% to 2.2%, compared with sham sonolysis. These findings represent a potentially significant innovation in the application of ultrasound from its historical diagnostic role to now also as a therapeutic intervention. Given the well documented low risk of stroke associated with asymptomatic carotid endarterectomy, the observed absolute risk reduction of 5.4% seems to represent a substantial additive advance in carotid endarterectomy care.

The trial has several strengths. As noted by the authors, use of ultrasound for sonolysis is grounded in both animal models and studies of healthy control adults, giving biologic plausibility for the reduction in the risk of stroke seen in the trial. The use of sham sonolysis for the control group is a major strength of the study that enhances the internal validity of the intervention. Sham controlled interventions remain rare in surgery, because they are both costly and time intensive, but when conducted they often offer the most valid evaluation of a given intervention. In addition, outcomes in all patients were clinically adjudicated by a neurologist specializing in stroke both before and after their surgical procedure, which improves and standardizes the detection of the primary outcome across the treatment groups. The addition of a magnetic resonance imaging sub-study adds corroborating imaging data to support the findings of clinical stroke risk reduction in the main study, again enhancing the internal validity of the results.

However, some persistent questions surround the study design and results and should be considered before widespread adoption of this technique. Perhaps most importantly, the risk of the primary outcome in the control group is concerning. As noted above, the risk of the composite of 30 day transient ischemic attack, stroke, or death was 7.6% in the control arm. Post hoc analysis shows that the risk of the composite outcome was 6.9% in a control group of patients without symptoms and 8.5% in patients with symptoms. Although an 8.5% risk of this outcome in patients with symptoms might plausibly be justified, a 6.9% risk in patients with no symptoms seems high compared with societal guideline based safety benchmarks.[3 5] Specifically, this is more than double the risk of what can be expected in published randomized trials and large observational studies of carotid endarterectomy and remains above the threshold at which patients may fail to derive benefit from undergoing prophylactic surgery.[6 -11] Furthermore, symptomatic carotid stenosis was not a predictor of the primary outcome in the multivariable analysis, with similar risks of the primary outcome for patients with and without symptoms alike, once stratified by the treatment arm. This would seem to be inconsistent with historical surgical outcome norms in which elevated stroke risk among patients with symptoms compared with those without symptoms is a well established phenomenon, with patients with symptoms experiencing an increased risk of perioperative stroke.[12 -14] The unanticipated increased stroke risk observed in this trial among patients without symptoms, as well as the similarity in stroke risk for patients with versus without symptoms, calls into question the internal validity of the composite outcome assessment in this study.

Despite these inherent strengths and limitations, some important next steps seem to be justified. The ultrasound used in this study is non-invasive and did not seem to be associated with any safety risks. Given the low risk associated with the ultrasound, considering it for clinical use if the above questions of the internal validity of the study can be resolved may be reasonable. A formal cost effectiveness evaluation of routine use during carotid endarterectomy should be conducted, along with implications for implementation of this new treatment modality. Resolution of the above concerns, along with a cost effectiveness calculation, can then inform whether this exciting new application of an established technology can improve care for patients undergoing carotid endarterectomy.

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