

Howard DPJ, Rothwell PM. Asymptomatic carotid stenosis and stroke risk - Authors' reply. *Lancet Neurol.* 2021;20(9):699

Anne Abbott highlights our finding that ipsilateral stroke risk is dependent on the degree of asymptomatic carotid artery stenosis. She states that this association was reported previously in the ACSRS Study, on which she was an author.¹ In fact, only a non-significant trend towards increased stroke risk with degree of stenosis was found in the ACSRS study, but as we showed in our systematic review other much earlier studies had already reported more convincing trends.²⁻³ However, confusion had subsequently been sown by the lack of any such associations in the randomised controlled trials of endarterectomy for asymptomatic carotid stenosis. The purpose of our review was to highlight this discrepancy between cohorts studies and trials and to explain that although randomised controlled trials are the gold standard for quantifying the effects of an intervention, they are prone to selection biases that will undermine risk associations within treatment groups.

Abbott argues that any stenosis-stroke risk association in asymptomatic patients is difficult to validate due to stroke rates often being unreported or only partially reported in relation to degree of stenosis in published studies. We also highlighted this issue and performed multiple analyses including all relevant studies that provided both partial and complete stroke rates by degree of stenosis. Half of the 56 studies identified in the systematic review provided data on ipsilateral stroke risk fully stratified by degree of asymptomatic stenosis (8419 patients), and we added our own data from the first such population-based cohort study.

Abbott questions the implication of a 3% annual ipsilateral stroke risk for patients with high-grade asymptomatic carotid stenosis on medical therapy alone, arguing that this risk is too low to identify those who may benefit from carotid intervention. However, many patients and clinicians will regard a 15% 5-year stroke risk on medical therapy as being worthy of reduction. Indeed, the ACST trial and the smaller ACAS and VA trials⁴⁻⁶ each showed a modest but significant benefit from endarterectomy vs medical therapy alone in patients with annual risks of stroke on medical treatment that were slightly below 3%.

Abbott suggests that best medical therapy might further reduce stroke risks, but admits that no one has yet defined best medical treatment or measured its impact. In the Oxford Vascular Study, we achieved much higher rates of uptake and compliance with contemporary medical therapy than are reported in routine clinical practice, with 89% of patients on high-dose statin therapy and antihypertensive agents at one-year follow-up, and 95% on an antiplatelet agent or anticoagulant. Better control of all risk factors might be possible in an animal model, but real-world studies of human beings, particularly population-based studies inclusive of all patients irrespective of age, frailty, drug allergies, or psychiatric co-morbidity, are more likely to be generalizable to the clinical practice of most clinicians.

References

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