

LETTER TO THE EDITOR**To THE EDITOR****Current Scientific Evidence Regarding Use of Carotid Stenting and Endarterectomy**

A recent review by Pelz et al. has provided an excellent opportunity to clarify the current scientific evidence regarding the role of carotid endarterectomy and stenting in clinical practice.¹ First, in the prevention of arterial disease complications, medical intervention (lifestyle coaching and appropriate medication) is the basis and very effective. Medical intervention is non-invasive and protects the whole arterial tree. For these reasons, medical intervention is the gold standard by which invasive procedures should be compared.

For example, improvements in medical intervention have seen at least a 65% fall in the average annual ipsilateral stroke rate associated with $\geq 50\%$ (advanced) asymptomatic carotid stenosis since the 1980s.^{2,3} The latest reliable known measurements of the average annual ipsilateral stroke rate with medical intervention alone were published around 2013 and approximate 0.8–1.0%.^{2,3} This is lower than that seen with endarterectomy or stenting in past randomised trials and 56% lower than that achieved with medical intervention alone in the Asymptomatic Carotid Atherosclerosis Study (ACAS).⁴

ACAS, published in 1995, has been the only randomised trial showing a statistically significant stroke prevention benefit from endarterectomy with respect to advanced asymptomatic carotid stenosis. Although the Asymptomatic Carotid Surgery Trial (ACST) is sometimes cited in this context, it was not a trial of medical intervention alone. Rather, ACST was a trial of early versus delayed endarterectomy.⁵ In ACAS, an overall ipsilateral stroke prevention benefit was only seen in highly selected men aged <80 years. For these men, the overall benefit was small (estimated from projections to be 1.6%/year over the first 5 years).⁴

In ACST, it was only highly selected men aged <75 years who were among those who received a statistically significant overall stroke prevention benefit from early endarterectomy. However, for them the benefit was small and diminished over time (1.3%/year over the first 5 years, 0.6%/year over the first 10 years).⁵ Women did not benefit from carotid endarterectomy in ACAS.⁴ Women coming closest to a benefit from early endarterectomy in ACST were aged <75 years. However, the result just failed to reach statistical significance.⁵

Given this information, now no more than about 5% of individuals with advanced asymptomatic carotid stenosis will have a stroke from the carotid lesion during life and could possibly benefit from a carotid procedure if they are receiving good quality medical intervention.³ This 5% figure assumes that the procedural risk is always and everywhere zero, which is not possible. In addition, individuals with advanced ACS who now benefit from a carotid procedure remain unidentified.³

Proposed markers of high ipsilateral stroke rate despite medical intervention (including those published in some recent guidelines) have not been tested in the context of current best medical

intervention or randomised trials and are far too common.³ Furthermore, medical intervention continues to improve. Even better stroke prevention is expected with current best medical intervention. This all means that we have passed the era in which carotid procedures are likely to produce an overall benefit with respect to asymptomatic carotid stenosis, particularly with respect to the populations represented in trials such as ACAS and ACST.³

Regarding symptomatic individuals with advanced carotid stenosis, randomised trials in the 1980s and 1990s showed an overall and very time-sensitive stroke prevention benefit from endarterectomy for highly selected men and, to a lesser extent, highly selected women.⁶ However, outcomes are also improving for symptomatic individuals with carotid stenosis as medical intervention improves. Therefore, the potential stroke prevention value of carotid endarterectomy in symptomatic individuals requires re-evaluation.

Meanwhile, numerous randomised trials have shown that trans-aortic carotid stenting is associated with nearly twice as many 30-day peri-procedural strokes and deaths compared to endarterectomy in both asymptomatic and symptomatic individuals.^{7,8} This excess peri-procedural harm from trans-aortic stenting is not compensated by the peri-procedural rate of myocardial infarction. In the randomised trials of carotid endarterectomy versus stenting, stenting was associated with 1.6 times as many peri-procedural strokes, deaths and myocardial infarctions compared to endarterectomy.³ Where comparisons were adequately powered, stenting was associated with worse outcomes than endarterectomy.

The excess stroke rate associated with trans-aortic carotid stenting is durable. It is measurable for as long as we followed up individuals in randomised trials.^{9,10} It should be kept in mind that, by definition, all strokes represent at least some disability, and past randomised trials were not powered sufficiently to exclude clinically significant differences in the rate of the most severe or fatal strokes.^{3,9,10}

In addition, procedural outcomes are often worse outside randomised trials, negating any benefit and, instead, causing net harm.^{3,11} Many centres eventually caught up with 30-day peri-procedural stroke and death rates seen in past randomised trials.¹¹ However, the procedural standards derived from randomised trials have been increasingly outdated and excessive due to advances in medical intervention since they were published.³ New techniques, such as trans-carotid arterial revascularisation (TCAR), are promised to be even better than previous strategies.¹² However, a clinical indication for any procedure cannot be established without appropriate trials involving current best medical intervention alone.

In summary, current best medical intervention is indicated for all people with carotid arterial disease. There is no proven indication for any carotid artery procedure compared to current standards of medical intervention, only evidence of harm and cost. However, it is clear that trans-aortic carotid stenting is associated with a higher risk of stroke and death and other serious

adverse events than endarterectomy. Meanwhile, new procedural interventions, such as TCAR, cannot have a clinical indication without us first measuring what can be achieved with current best medical intervention alone.

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