

DEBATE: INTERVENTION VS. BEST MEDICAL THERAPY IN ASYMPTOMATIC CAROTID STENOSIS - BEST MEDICAL THERAPY

J. David Spence

Stroke Prevention & Atherosclerosis Research Centre, Robarts Research Institute, London, Canada

In the United States, 90% of carotid intervention (endarterectomy and stenting) is now for asymptomatic carotid stenosis. This inappropriate practice is being justified on the basis of comparing the results from the CREST¹ trial (a modern study with no medical arm, with the medical arms of two studies that were done before intensive statin therapy (ACAS² and ACST³). Such comparisons across studies are not legitimate.

The risks in CREST for asymptomatic patients – a procedural (30-day) risk of stroke or death of 2.5% for stenting and 1.4% for endarterectomy, and a 4-year risk of 4.5% with stenting and 2.7% with endarterectomy may seem reasonable compared to the 10% 5-year risk (or 2% per year) in ACAS and ACST.

However, with modern medical therapy, the risk of stroke or death has markedly declined since 2005. A prospective population-based study⁴ in the UK, a Canadian study of patients attending a stroke prevention clinic⁵ and a meta-analysis⁶ all showed that the risk of stroke or death in asymptomatic patients is now 0.5% per year. Concerns that the earlier meta-analysis did not take into account severity of stenosis were answered by Naylor in a later meta-analysis⁷.

Cardiologists, who account for 30% of those performing carotid stenting, account for more than half the procedures. They seem to think, perhaps based on coronary anatomy, that opening up arteries to restore blood flow is a good thing. However, the brain is protected by the Circle of Willis; carotid endarterectomy and stenting are not about restoring blood flow; they are about preventing embolization from the proximal stenosis. Shoving a stent into a narrow carotid artery produces a shower of emboli into the brain, frequently resulting in small diffusion-weighted lesions in the brain on MRI. Stenting carries twice the risk of stroke compared to endarterectomy.

It is possible to identify, among patients with asymptomatic carotid stenosis, the 10% of patients who have a high enough risk to benefit from intervention. The best supported method is transcranial Doppler embolus detection^{8;9}. Other promising approaches include ulceration on 3-dimensional ultrasound¹⁰, and echolucency on ultrasound¹¹. Additional methods for imaging vulnerable plaque, including MRI plaque composition and plaque inflammation on PET/CT scans, are under investigation¹². For now, however, it must be understood that 90% of patients with asymptomatic stenosis would be better off with intensive medical therapy.

Lifestyle changes are far more important than most physicians realize. Best medical therapy includes smoking cessation, a Mediterranean diet, and moderate exercise¹³. It also includes blood pressure control (including angiotensin converting enzyme inhibitors or angiotensin receptor blockers unless they are contraindicated), diabetes control, antiplatelet therapy, intensive statin therapy (and addition of ezetimibe for patients whose plaque burden is progressing despite statins^{14;15}).

Until a modern randomized trial comparing stenting, endarterectomy and best medical therapy is carried out, widespread endarterectomy or stenting of asymptomatic carotid stenosis for unselected patients with asymptomatic carotid stenosis should be regarded as malpractice. It is to be hoped that the proposed CREST-2 trial, which includes a medical arm, will be funded.

References

1. Brott, TG, Hobson, RW, II, Howard, G, Roubin, GS, Clark, WM, Brooks, W, Mackey, A, Hill, MD, Leimgruber, PP, Sheffet, AJ, Howard, VJ, Moore, WS, Voeks, JH, Hopkins, LN, Cutlip, DE, Cohen, DJ, Popma, JJ, Ferguson, RD, Cohen, SN, Blackshear, JL, Silver, FL, Mohr, JP, Lal, BK, Meschia, JF, and the CREST Investigators. Stenting versus Endarterectomy for Treatment of Carotid-Artery Stenosis. *N Engl J Med* 2010; 363:11-23.
2. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. Endarterectomy for asymptomatic carotid artery stenosis. *Journal of the American Medical Association* 1995; 272:1421-1428.

3. Halliday,A, Mansfield, A, Marro, J, Peto, C, Peto, R, Potter, J, and Thomas, D. Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: randomised controlled trial. *Lancet* 2004; 363:1491-1502.
4. Marquardt,L, Geraghty, OC, Mehta, Z, and Rothwell, PM. Low risk of ipsilateral stroke in patients with asymptomatic carotid stenosis on best medical treatment: a prospective, population-based study. *Stroke* 2010; 41:e11-e17.
5. Spence,JD, Coates, V, Li, H, Tamayo, A, Munoz, C, Hackam, DG, DiCicco, M, DesRoches, J, Bogiatzi, C, Klein, J, Madrenas, J, and Hegele, RA. Effects of Intensive medical therapy on microemboli and cardiovascular risk in asymptomatic carotid stenosis. *Arch Neurol* 2010; 67:180-186.
6. Abbott,AL. Medical (nonsurgical) intervention alone is now best for prevention of stroke associated with asymptomatic severe carotid stenosis: results of a systematic review and analysis. *Stroke* 2009; 40:e573-e583.
7. Naylor,AR. Time to rethink management strategies in asymptomatic carotid artery disease. *Nat. Rev. Cardiol* 2011.
88. Spence,JD, Tamayo, A, Lownie, SP, Ng, WP, and Ferguson, GG. Absence of microemboli on transcranial Doppler identifies low-risk patients with asymptomatic carotid stenosis. *Stroke* 2005; 36:2373-2378.
9. Markus,HS, King, A, Shipley, M, Topakian, R, Cullinane, M, Reihill, S, Bornstein, NM, and Schaafsma, A. Asymptomatic embolisation for prediction of stroke in the Asymptomatic Carotid Emboli Study (ACES): a prospective observational study. *Lancet Neurol* 2010; 9:663-671.
10. Madani,A, Beletsky, V, Tamayo, A, Munoz, C, and Spence, JD. High-risk asymptomatic carotid stenosis: ulceration on 3D ultrasound vs TCD microemboli. *Neurology* 2011; 77:744-750.
11. Topakian,R, King, A, Kwon, SU, Schaafsma, A, Shipley, M, and Markus, HS. Ultrasonic plaque echolucency and emboli signals predict stroke in asymptomatic carotid stenosis. *Neurology* 2011; 77:751-758.
12. Bogiatzi,C, Cocker, MS, Beanlands, R, and Spence, JD. Identifying high-risk asymptomatic carotids stenosis. *Expert Opin Med Diagnostics* 2012; 6:139-151.
13. Spence,JD and Barnett, HJM. *Stroke Prevention, Treatment and Rehabilitation*. 2012. McGraw-Hill Medical Publishers, New York.
14. Spence,JD and Hackam, DG. Treating Arteries Instead of Risk Factors. A Paradigm Change in Management of Atherosclerosis. *Stroke* 2010; 41:1193-1199.
15. Bogiatzi,C and Spence, JD. Ezetimibe and Regression of Carotid Atherosclerosis: Importance of Measuring Plaque Burden. *Stroke* 2012; 43:1153-1155.