

For the ICSS trial see <http://www.strokecenter.org/trials/TrialDetail.aspx?tid=86>

The excellent Seminar by Geoffrey Donnan and colleagues¹ provides a comprehensive review of the epidemiology, pathophysiology, prognosis, and treatment of stroke. An issue that might prove different from Donnan and colleagues' analysis is the place of carotid angioplasty with stenting (CAS) in the treatment of symptomatic carotid artery stenosis.

Donnan and colleagues suggest that "carotid angioplasty with stenting... will probably replace carotid endarterectomy as the treatment of choice in most patients". The first randomised trial comparing the long-term results of carotid endarterectomy with those of CAS (median observation time 64 vs 66 months, respectively) has now been published.² Compared with carotid endarterectomy, CAS was associated with a higher rate of post-procedural ipsilateral stroke (0 of 42 vs four of 42 patients, respectively; $p<0.05$), a higher rate of more than 70% restenosis (0 of 29 vs six of 32 patients, respectively; $p<0.05$), and a higher reintervention rate for more than 70% restenosis (0 of 29 vs five of 32 patients, respectively; $p<0.05$).²

Verification of the above results might question the place of CAS in the treatment of symptomatic carotid artery stenosis.

I declare that I have no conflict of interest.

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- 1 Donnan GA, Fisher M, Macleod M, Davis SM. Stroke. *Lancet* 2008; **371**: 1612–23.
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Authors' reply

Luca Mascitelli and colleagues suggest that the effect of statins in the secondary prevention of stroke is modest, associated with an increased risk of haemorrhagic stroke, and might protect mild strokes only. We would

argue against this at a number of levels.

First, the relative risk reduction of 16% on intention-to-treat analysis (not 13% as suggested) from the SPARCL trial¹ (NNT_{4.9} 45) is clinically important. Second, there was no difference in fatal haemorrhagic stroke between groups (17 in the treatment group, 18 placebo) and the absolute number overall was small at 55 in the atorvastatin group and 33 in the placebo group. Further, haemorrhagic strokes were included in the primary outcome measure of fatal and non-fatal stroke, so the net absolute benefit of 1.9% nicely takes the risks and benefits into account.

In other words, although we agree that there is an intriguing relation between low cholesterol and haemorrhagic stroke, this is more of academic than pragmatic interest since the benefits of cholesterol lowering with statins far outweigh the risks.²

Finally, the likelihood that statins protect only against mild stroke seems unlikely given that in the SPARCL trial there was a significant protection against fatal stroke (absolute risk reduction 0.7%, $p=0.04$), the most severe strokes of all.

Kosmas Paraskevas also addresses the very current and important issue in secondary stroke prevention of carotid angioplasty versus endarterectomy. We had quite conservatively suggested that angioplasty will probably replace endarterectomy in most patients but that further trials are awaited to confirm this view. With the exception of the EVA-3S trial,³ the periprocedural risk profiles of both procedures have been clinically similar.^{4,5} However, we do agree that long-term follow-up is important since comparative restenosis and vascular event rates are, as yet, poorly understood.

The study quoted by Paraskevas is an important initial contribution to this process although it should be noted that the sample size is somewhat small and the data come from a single centre. We await with interest for the results of follow-up

data from trials such as EVA-3S, SPACE, CREST, and the ongoing ICSS.

We declare that we have no conflict of interest.

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- 2 Thrift AG, McNeil JJ, Forbes A, et al, for the Melbourne Risk Factor Study (MERFS) Group. Risk factors for cerebral hemorrhage in the era of well-controlled hypertension. *Stroke* 1996; **27**: 2020–25.
- 3 EVA-3S Investigators. Endarterectomy vs. angioplasty in patients with symptomatic severe carotid stenosis (EVA-3S) trial. *Cerebrovasc Dis* 2004; **18**: 62–65.
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Hyperglycaemia as a cardiovascular risk factor in diabetes

In their Seminar (May 24, p 1790),¹ Ravi Retnakaran and Bernard Zinman argue, on the basis of the DCCT/EDIC Study,² that hyperglycaemia is an important cardiovascular risk factor, and that hyperglycaemia early in the disease course might exert particular harm through "metabolic imprinting/memory". Another study of intensive versus conventional treatment, in type 2 diabetic patients (Steno-2),³ has also shown continuing divergence of cardiovascular events during follow-up, despite converging glycaemia,