

# Commentary on: Carotid Endarterectomy or Stenting or Best Medical Treatment Alone for Moderate-to-Severe Asymptomatic Carotid Artery Stenosis: 5-Year Results of a Multicentre, Randomised Controlled Trial

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Reiff et al. have recently published the results from the SPACE-2 trial [1] which compared carotid endarterectomy (CEA), stenting (CAS) or best medical treatment (BMT) alone for moderate-to-severe asymptomatic carotid artery stenosis. They presented the 5-year results. The trial was multicentre, prospective and randomised.

It is of note that this trial was conducted with patients with asymptomatic carotid artery stenosis only, who had at least 70% (using European Carotid Surgery Trial criteria) stenosis and were 50–85 years of age.

Initially the study was intended to be a three-arm trial, but as a result of slow recruitment was amended to become two sub-studies – SPACE-2a (CEA plus BMT v BMT alone) and SPACE-2b (CAS plus BMT v BMT alone). The primary efficacy endpoint was the cumulative incidence of any stroke or death from any cause within 30 days or any ipsilateral ischaemic stroke within 5 years. The primary safety endpoint was any stroke or death from any cause within 30 days of CEA or CAS.

Recruitment was intended to be for 3640 patients; however, the study was stopped at 513 patients, due to insufficient recruitment. Two hundred and three patients were allocated to CEA + BMT, 197 to CAS + BMT and 113 to BMT alone. The authors looked for superiority of an intervention to BMT alone and to assess for non-inferiority of CAS to CEA.

Mean follow-up was excellent 59.9 months and the cumulative incidence of any stroke or death within 30 days

or any ipsilateral ischaemic stroke within 5 years was 2.5% for CEA + BMT, 4.4% CAS + BMT and 3.1% for BMT alone. Ultimately CEA + BMT or CAS + BMT was not found to be superior to BMT alone, but caution was advised due to the small sample size.

The Trialists are to be congratulated on their diligence in setting up the trial, continuing to carefully follow up those who entered the trial to its conclusion and ensuring that the outcome data are published. The Trialists note that there were 12,453 CEA and 2801 CAS procedures performed in 2020 alone in Germany for asymptomatic carotid stenosis. Failure to recruit to the study was considered to be a combination of economics and expectations.

The SPACE-2a and SPACE-2b subsets were unlikely to be directly comparable, as the intervention was decided prior to randomisation (between the chosen intervention or BMT alone).

The duplex assessment following randomisation showed a trend to more restenosis in the CAS group. Despite the known limitations of duplex following CAS [2], this study concurs with the findings of the International Carotid Stenting Study (ICSS) [3] in that restenosis following CAS is not directly related to recurrent neurological events.

An interesting observation in follow-up was that in both CAS + BMT and the BMT alone groups there were further ipsilateral strokes, but in the CEA group there were none. The numbers again were small.

A further area of uncertainty that this study could have shed light upon is whether an asymptomatic carotid stenosis is progressive, and does progression result in an increased risk of stroke? In SPACE-2 there was a progression of the stenosis in 15% of the population treated by BMT alone, but this translated to only 1 event. The numbers were again too small to draw reliable conclusions.

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It is unfortunate that SPACE-2 could not progress to completion. Currently there remains much debate as to the benefit, or otherwise, of intervention in asymptomatic carotid stenosis [4]. SPACE-2 supports the notion that without other mitigating factors, modern BMT is not improved by additional intervention, but has not been able to deliver a certain message.

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**Declarations**

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**Ethical Approval** None.

**Informed Consent** None.

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