INVITED COMMENTARY

SPACE and EVA-3S Trials: The Need of Standards for Carotid Stenting

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Large randomized trials comparing endarterectomy (CEA) vs Best Medical Therapy (BMT) have convincingly demonstrated that surgery significantly reduces the long-term risk of subsequent stroke from severe carotid artery stenosis in symptomatic and asymptomatic patients.1–4 Nowadays surgery remains the standard of care for patients with severe obstructive carotid artery disease but carotid artery stenting (CAS) has progressed in recent years, and is now challenging CEA as an alternative for stroke prevention. During the last decade single center experiences have been collecting data on the efficacy of CAS, but only few randomized trials comparing CAS vs. CEA have been published. The Cochrane database reports a total of 1269 patients with carotid artery stenosis that were treated in five randomised trials (LEICESTER 2001, WALLSTENT 2001, CAVATAS 2001, KENTUCKY 2001, SAPPHIRE 2004), reporting a heterogeneity of outcome, no significant difference in the major risks of treatment, and the wide confidence intervals indicate that it is not possible to exclude a difference in favour of one treatment.5

At this moment there is a lot of interest in the results of the on-going trials, and two of these, EVA-3S6 and SPACE,7 have just published their data. These two trials enrolled a total of 1727 patients with symptomatic carotid stenosis but are not able to clarify the dilemma. Both trials were stopped: the EVA-3S for the high complication rate in the stenting arm, and the SPACE trial for the lack of adequate funding that made impossible to enrol 2500 patients, needed to have an 80% power statistical analysis.

The EVA-3S had already been stopped in 2003, because of the very high percentage of stroke (20%) of the unprotected procedure. The stroke-rate dropped after the re-start of the trial with an embolic-protection-device but still with a high rate of neurological complications (9.6%).

In the SPACE trial the results in patients treated with CAS were better (6.84%) but the difference of 0.51% (90% CI –1.89 to 2.91) between the two arms did not allow to confirm the non-inferiority hypothesis of CAS versus CEA.

Notably in the latter study only 27% of the CAS patients received a protection device.

A possible explanation for these results probably lies in the technical expertise required for interventional physicians to join the trials (EVA-3S: 12 CAS or 35 stenting procedures in the supra-aortic trunks, 5 of which had to be CAS; SPACE: 25 successful carotid percutaneous transluminal angioplasties or stent procedures).

Moreover, the EVA-3S protocol stated that interventional physicians who did not fill these requirements were nevertheless accepted, provided that the procedures were performed under the supervision of an “experienced tutor” defined as “a clinician who qualified to perform stenting in this study”.

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However can we consider as “experienced interventionalist” a physician with an expertise of either 12 CAS or 35 stenting procedures of the supra-aortic trunks, 5 of which CAS? Furthermore, is this interventionalist so experienced that he can act as a proctor for another physician willing to participate to a trial comparing CAS versus CEA in patients suffering from TIA or minor stroke due to severe carotid stenosis?

As difficult as it is to say, we must admit that both EVA 3S and SPACE didn’t match an acceptable level of physician training and credentialing. The consequences of this technical bias on the reported CAS results are left to the scientific community’s evaluation.

We strongly believe that at this moment the real applicability of CEA and CAS is very different. CEA has been widely performed during the last thirty years by experienced and fully trained vascular surgeons, while CAS is a recently emerged treatment, that cannot yet be generalized.

A correct learning curve for this procedure is mandatory and cannot be reached with 12 cases or with 35 generic PTA or stenting procedures of supraortic vessel as suggested by EVA 3S trial. Moreover, carotid stenting requires specific expertise that is not acquired with 25 procedures as reported in the SPACE trial.

To this regard, a recently published Consensus Document among all the specialists involved in the CAS scenario, suggested that the minimum recommended training to achieve competence is at least 150 procedures of supra-aortic vessel engagement (during diagnostic as well as interventional procedures), 100 of which as primary operator, or at least 75 carotid stenting procedures, 50 of which as primary operator within two-years.

We are far away from the resolution of the dilemma and up to now, the analysis of more than 2900 patients treated within the published trials have not shown a clear evidence of CAS inferiority to CEA.

This number will increase in the future years with the ongoing trials CREST, ACST 2, TACIT, ICSS, and hopefully when the results of these trials will be diffused we will reach a better knowledge of the value and efficacy of CAS.

The potential technical gap related to CAS has to be overcome by reliable programs for physician training and credentialing.

CAS is a procedure that can not be easily standardized: in clinical practice we have learned that a patient with a specific carotid plaque and supra-aortic anatomy needs a tailored procedure and additional expertise.

A randomized trial comparing CEA and CAS is needed, where both rigorous standard of practice and technical skills will be required and where the use of an embolic protection device will be mandatory.

References


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