EDITORIAL

Carotid Stenosis Management: Getting the Genie Back in the Bottle

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In the recently published 5-year results of the Stent-Protected Angioplasty in Asymptomatic Carotid Artery Stenosis vs Endarterectomy Trial (SPACE-2), Reiff et al explain how 25,000 carotid artery 'revascularisation' procedures are done in Germany each year.[1] They also explained how there is no current evidence of patient benefit from these procedures and the need for new trials which include study of outcomes with current best practice non-invasive intervention alone (ie, lifestyle coaching and medication). Yet, very disappointingly, they could only recruit 513 patients with 50-99% carotid stenosis into SPACE-2 and it took approximately 10 years. SPACE-2 subjects had no referrable ipsilateral stroke symptoms in the previous 180 days.[1] SPACE-2 was the first randomized trial comparing carotid endarterectomy (CEA) and carotid stenting (CAS) with non-invasive medical intervention alone and it was stopped prematurely due to slow recruitment.[1,2]

Meanwhile, traditionally a genie is not the benevolent wish-granter as portrayed in some modern pop culture.[3] The overuse of carotid procedures, in both asymptomatic and symptomatic patients, is a powerful, nonbenevolent 'genie' of the contemporary medical industry.[4] Carotid artery procedures have become very common in many countries, with wide variation in indication despite access to the same evidence base.[5] This is a multibillion dollar per year industry driven by outdated and over-reaching, procedurally biased guidelines and 'fee for service' reimbursement practices.[4-6] Misdirected reimbursement practices include non-randomized comparison 'studies' (registries) of procedures such as CEA, CAS and now 'transcarotid arterial revascularisation' (TCAR), without studies of current best practice non-invasive medical-intervention alone.[7,8]

SPACE-2 was underpowered to compare outcomes with CEA, CAS and non-invasive intervention. However, SPACE-2 adds to evidence of procedural overuse and improved non-invasive medical intervention.[1,2,4] In SPACE-2, the average annual rate of ipsilateral ischemic stroke was only 0.6% in the 113 individuals managed non-invasively. SPACE-2 adds to quality studies that show that the average annual rate of ipsilateral ischemic stroke fallen by at least 67% over the last 3-4 decades and since the Asymptomatic Carotid Atherosclerosis Study (ACAS) was commenced.[4] ACAS is still the only randomized trial showing an overall stroke risk reduction benefit from a carotid 'revascularisation' procedure (i.e., CEA) for individuals with asymptomatic carotid stenosis compared to non-invasive intervention alone.[4] Only highly selected 'average surgical risk' men aged <80 years and with a life expectancy of at least 3-5 years benefited and that benefit was marginal (1%/year stroke risk reduction).[4]

Meanwhile, outcomes in 'high CEA risk' patients with non-invasive medical intervention alone have not been measured and CAS is more dangerous than CEA in the short and long term.[4] Further, we can expect even lower ipsilateral stroke rates than 0.6%/year as outcomes with current best non-invasive intervention have still not been measured. Current best practice was not used in SPACE-2 or in previously published studies. For example, outdated, excessively high targets for lowering low density lipoprotein (<130mg/dL [<3·37 mmol/L]) were used in SPACE-2 and many participants did not reach treatment goals.[1]

So how do we get the 'carotid "revascularisation" procedure genie' back in the bottle and create systematic methods to prevent other such harmful genies? This must be done for the health and economic survival of societies globally. The solutions are in plain sight, as illustrated by SPACE-2, and summarised below:[1,2]

i. Fund an intervention only when there is a sufficient current body of evidence that there is a clinically significant benefit that outweighs the risk of serious complications and in absence of a more cost-effective treatment. Sci-

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entific evidence may come from randomized procedural studies and/or from non-randomized studies demonstrating sufficiently low event rates with nonprocedural care such that procedures are not required.[4]

ii. Funding an intervention is dependent on regular, ongoing evidence review because populations and medicine evolve.[4] Funding is conditional and is stopped if an intervention becomes redundant or net harmful. Appropriate 'service' de-adoption and exnovation must be the norm.[9] The savings should feed back into effective interventions and new research.[4]

iii. Experimental interventions should not be funded a 'pseudo routine clinical practice' setting. For example, TCAR should not be funded in registries before establishing what can be achieved with current best practice non-invasive intervention alone and before appropriate randomized trials against the procedural gold standard (CEA) if a procedure is indicated. This approach is required to protect public safety and help direct patients into appropriate trials. This approach, for example, was critical in getting the Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands Trial (MR CLEAN) completed and in a timely fashion.[1,10]

iv. Scientific evidence must be easier to produce by combining the efforts of reporting in clinical practice and research and at the point-of-care. This resource-saving 'Brainy Medicine' capability will potentially enable the experience of every patient to improve health services. It will enable the critically needed switch from 'activity-based' to 'outcomes-based' health services.[4] It will help keep patients in a trial like setting, to optimise their outcomes.

v. Non-invasive medical intervention must be appropriately reimbursed if it is to be delivered and society is to reap the benefits. It is increasingly complicated (with an aging population with increasing comorbidities). It requires expertise and ongoing practitioner education, and it is time consuming.[1,2,4]

vi. Public education is required, starting from school age. Arterial disease is a multisystem disease requiring a holistic approach. Healthy lifestyle habits and appropriate medication are the best protection.[4] Further, there is no current evidence of a stroke protection benefit from any carotid artery procedure. However, there is ongoing significant risk and cost. Such procedures cannot compensate for neglecting our personal efforts to protect our own health.[4]

CONFLICT OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

REFERENCES

1 Reiff T, Eckstein HH, Mansmann U, Jansen O, Fraedrich G, Mudra H, Bockler D, Bohm M, Debus ES, Fiehler J, et al. 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. *Lancet Neurol*. 2022;21:877-888.

2 Eckstein HH, Reiff T, Ringleb P, Jansen O, Mansmann U, Hacke W, Investigators S. SPACE-2: A Missed Opportunity to Compare Carotid Endarterectomy, Carotid Stenting, and Best Medical Treatment in Patients with Asymptomatic Carotid Stenoses. *Eur J Vasc Endovasc Surg*. 2016;51:761-765.

3 Sagers A. A History of Genies in Folklore and PopCulture. *IGN.* May 25th, 2019: https://www.ign.com/articles/2019/05/25/a-history-of-genies-in-folklore-and-pop-culture

4 Abbott A. Extra-Cranial Carotid Artery Stenosis: An Objective Analysis of the Available Evidence. *Front Neurol.* 2022 Jun 21;13:739999

5 Venermo M, Wang G, Sedrakyan A, Mao J, Eldrup N, DeMartino R, Mani K, Altreuther M, Beiles B, Menyhei G, et al. Editor's Choice - Carotid Stenosis Treatment: Variation in International Practice Patterns. *Eur J Vasc Endovasc Surg*. 2017;53:511-519.

6 Abbott AL, Paraskevas KI, Kakkos SK, Golledge J, Eckstein HH, Diaz-Sandoval LJ, Cao L, Fu Q, Wijeratne T, Leung TW, et al. Systematic Review of Guidelines for the Management of Asymptomatic and Symptomatic Carotid Stenosis. *Stroke.* 2015;46:3288-3301.

7 Centers for Medicare & Medicaid Services. Carotid Artery Stenting (CAS) Investigational Studies: https://www.cms.gov/Medicare/Medicare-General-Information/MedicareApprovedFacilitie/Carotid-Artery-Stenting-CAS-Investigational-Studies

8 Society of Vascular Surgery Vascular Quality Initiative (VQI): TransCarotid Revascularization Surveillance Project (VQI-TCAR). ClinicalTrials.gov: https://clinicaltrials.gov/ct2/show/NCT02850588

9 Bekelis K, Skinner J, Gottlieb D, Goodney P. De-adoption and exnovation in the use of carotid revascularization: retrospective cohort study. *BMJ*. 2017;359:j4695.

10 Berkhemer OA, Fransen PS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, Schonewille WJ, Vos JA, Nederkoorn PJ, Wermer MJ, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. *New Eng J Med.* 2015;372:11-20.