A History of Carotid Stenting and its Evolution: TCAR Innovation in the Context of Expanding Coverage

Sumaira MacDonald, MD, PhD, Executive Medical Director, Silk Road Medical, Inc.

August 1st, 2023

Upon the request of a select group of physicians largely comprised of neurologists, neuroradiologists, neurosurgeons, interventional radiologists, and interventional cardiologists named "The Multispecialty Carotid Alliance" (MSCA), the Center for Medicare Services (CMS) reopened the standing policy for treatment of carotid artery disease (CAD) through carotid artery stenting (CAS) techniques. Following an initial comment period, CMS released their proposal to extend broad coverage of carotid artery stenting (CAS) to both high and standard surgical risk patients that are asymptomatic with 70% stenosis or symptomatic patients with >50% stenosis. CMS also proposed to remove its own facility standards and approval requirements in favor of allowing society guidelines, quality incentives, hospital credentialing committees, and other forces to govern. Importantly, CMS proposed new guardrails required for coverage, including pre and post independent neurological assessment, advanced imaging requirements, and formal shared decision-making with the patient. A 2nd 30-day comment period is underway, with a final decision expected on October 9th.

While CMS' reconsideration has resurfaced debate concerning the best treatment modality for individuals with carotid artery disease, the optimal treatment technique has been an ongoing discussion for decades. Understanding the history of the debate and the evolution of treatment options is critical to contextualizing the recent reconsideration.

Carotid disease as a source of stroke and carotid endarterectomy (CEA) as an open surgical technique to remove the offending plaque was first described and performed in the 1950's. As the procedure grew in popularity, so did the surgical complications at an unacceptably high rate, until a series of clinical trials were performed to formally study CEA vs best medical therapy and define the appropriate patient populations for treatment. Trials run in the 1980's and 1990's led to Level I evidence and guidelines supporting CEA with best medical therapy as superior to medical therapy alone in patients with severe carotid stenosis. [1-9]

As surgical technique and patient selection improved, serious complications were further reduced but never eliminated, and CEA was and still is conservatively applied. The 1990's and 2000's gave rise to the endovascular revolution in other parts of the arterial tree throughout the body and given the still high risk of adverse events from CEA, it was presumed minimally invasive, endovascular therapies would take over carotid intervention just as percutaneous coronary intervention (PCI) did over coronary artery bypass graft surgery (CABG), amongst other open to endo examples. At that time, transfemoral carotid artery stenting (TF-CAS) was developed and began to expand in use as an alternative to CEA.

What was not well understood at the time was how exquisitely sensitive the end organ of the brain was, and despite lowering surgical complications like heart attacks, cranial nerve injuries, and wound-related complications, TF-CAS revealed an unacceptably high risk of peri-procedural stroke. Certainly counter-productive on the mission to prevent a future stroke. This led first to the development of embolic

protection devices, and later to significantly better understanding of patient selection and operator experience required to reduce peri-procedural stroke risk.

Clinical trials of TF-CAS vs CEA throughout the 2000's and 2010's led to an even better understanding of each modality, and the risks of surgical complications from CEA and excess stroke from TF-CAS became firmly understood but hotly debated as to which set of risks was worth taking.[10-19] The market spoke, and the answer was CEA complications were the less offending set of risks as measured by its still dominant market share, even in the patient population that TF-CAS has always had outright CMS coverage in, namely high surgical risk symptomatic patients.

Enter Trans Carotid Artery Revascularization (TCAR), born out of this debate and designed to leverage the best of what each intervention offered while mitigating their key risks. TCAR allows physicians to employ a similar mechanism of action to protect the brain as CEA, while leveraging endovascular technologies and techniques to yield a more patient-friendly, minimally invasive approach. Specifically, TCAR employs a neuroprotection device that prevents embolic debris from flowing to the brain during carotid revascularization by reversing blood flow away from the brain, before lesion manipulation, allowing a stent to be placed through direct incision above the collar bone. This lies in contrast to the technique employed through TF-CAS, which necessitates distal placement of an embolic protection device (EPD) which is navigated through the carotid stenosis while the flow to the brain is antegrade. The increased risk of cerebral embolization with TF-CAS has been attributed to the need to cross the lesion to place an EPD (an unprotected procedural step), tortuous and diseased aortic arch anatomy, and catheter manipulation within the atherosclerotic arch or target vessel.

Mitigating the procedural risks associated with TF-CAS fundamentally required and still requires highly skilled and carefully trained physicians with a large body of interventional experience. Given the aforementioned lack of TF-CAS market development, the skillset required to perform the procedure currently lies in the hands of a select few. Various studies seek to define and quantify site and operator characteristics required to perform TF-CAS, including Gray et. al, who concludes the need for surgeons to perform dozens of cases before consistently achieving a sub-3% risk of stroke.[21] Further evidence suggests that this is a conservative estimate of the TF-CAS learning curve.[22]

The clear influence of site and operator characteristics on patient outcomes for TF-CAS lies in direct contrast to TCAR. Since its inception, TCAR has shown reliably low risk of peri-operative stroke across the spectrum of site and operator characteristics. For TCAR, sub-3% stroke risk can be attained from the very first procedure regardless of an individual physician's position on the learning curve, their practice environment (community versus academic or teaching hospital), their annual carotid volume, or the involvement of trainees, [23-31] democratizing access to life-saving CAD intervention. TCAR's low barrier to entry for treating physicians is reflected in the rapid proliferation of the procedure as TF-CAS and CEA stagnate in utilization. Today, more than 70,00 TCAR procedures have been performed, with real-world data continuing to accrue.

Robust registry data, representing the embodiment of Real-World Evidence, formed the basis for TCAR's applicability beyond patients deemed to be at high risk of adverse events in the course of surgery. In

2022, TCAR stenting technology was deemed appropriate by the FDA for individuals considered to be of standard risk, further broadening the scope of applicability for TCAR.

Since the previous national coverage decision in 2012, new TF-CAS evidence has been generated. However, these randomized trial data continue to demonstrate the persistent excess periprocedural stroke risk incurred by TF-CAS.

Against the broader history of stenting techniques for CAD, the proposed decision issued by CMS holds a distinct intent. It is an explicit endorsement of the stent-based treatment of carotid artery disease but rather than endorsing a particular technique, the proposed policy seeks to open access to care for Medicare beneficiaries, including under-served and under-diagnosed patient populations, underwritten by the deep knowledge of the clear risks and benefits of differing treatment options and the market forces that will steer the patient to the best possible treatment decision for their unique circumstances.

Yet within this apparent panacea, the minimally invasive option of choice should contemplate the broader population of patients who warrant treatment. They should come to no harm when treated by all operators; the elderly, the females, the recently symptomatic, the obese and the ethnic minorities. When equitable access is granted, equitable outcomes must be guaranteed.[32-47]

References:

1. North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. N Engl J Med. 1991;325:445–453.
2. Barnett HJM, Taylor DW, Eliasziw M, Fox AJ, Ferguson GG, Haynes RB,Rankin RN, Clagett GP, Hachinski VC, Sackett DL, Thorpe KE, Meldrum HE, for the North American Symptomatic Carotid Endarterectomy Trial Collaborators. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. N Engl J Med. 1998;339:1415–1425.
3. European Carotid Surgery Trialists' Collaborative Group. MRC European Carotid Surgery Trial: interim results for symptomatic patients with severe (70–99%) or with mild (0–29%) carotid stenosis. Lancet. 1991;337: 1235–1243. European Carotid Surgery Trialists' Collaborative Group. Randomized trialof endarterectomy for recently symptomatic carotid stenosis: final results of the MRC European Carotid Surgery Trial (ECST). Lancet. 1998;351: 1379–1387.
4. Mayberg MR, Wilson SE, Yatsu F, Weiss DG, Messina L, Hershey LA,Colling C, Eskridge J, Deykin D, Winn HR, for the Veterans Affairs Cooperative Studies Program 309 Trialist Group. Carotid endarterectomy and prevention of cerebral ischemia in symptomatic carotid stenosis. JAMA. 1991;266:3289–3294.
5. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. Endarterectomy for asymptomatic carotid artery stenosis. JAMA. 1995;273: 1421–1428.
6. Mayo Asymptomatic Carotid Endarterectomy Study Group. Results of a randomized controlled trial of carotid endarterectomy for asymptomatic carotid stenosis. Mayo Clin Proc. 1992;67:513–518.

7. Hobson RW, Weiss DG, Fields WS, Goldstone J, Moore WS, Towne JB, Wright CB, for the Veterans Affairs Cooperative Study Group. Efficacy of carotid endarterectomy for asymptomatic carotid stenosis. N Engl J Med.
8. Mayo Asymptomatic Carotid Endarterectomy Study Group. Results of a randomized controlled trial of carotid endarterectomy for asymptomatic carotid stenosis. Mayo Clin Proc. 1992;67:513–518.
9. Hobson RW, Weiss DG, Fields WS, Goldstone J, Moore WS, Towne JB, Wright CB, for the Veterans Affairs Cooperative Study Group. Efficacy of carotid endarterectomy for asymptomatic carotid stenosis. N Engl J Med. 1993;328:221–227.
10. Naylor AR, Bolia A, Annott RJ, Pye IF, Smith J, Lennard N et al (2000) Randomized study of carotid angioplasty and stenting versus carotid endarterectomy: a stopped trial. J Vasc Surg 28:326–334
11. Alberts M (2001) Results of a multicentre prospective randomized trial of carotid artery stenting versus carotid endarterectomy. Stroke 32:325 Endovascular versus surgical treatment in patients with carotid stenosis in the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS): a randomised trial (2001) Lancet 357:1729–1737
12. Brooks WH, McClure RR, Jones MR, Coleman TC, Breathitt L (2001) Carotid angioplasty and stenting versus carotid endarterectomy: randomized trial in a community hospital. J Am Coll Cardiol 38:1589–1595
13. Brooks WH, McClure RR, Jones MR, Coleman TL, Breathitt L (2004) Carotid angioplasty and stenting versus carotid endarterectomy for treatment of asymptomatic carotid stenosis: a randomized trial in a community hospital. Neurosurgery 54:318–324
14. Yadav JS, Wholey MH, Kuntz RE, Fayad P, Katzen BT, Mishkel GJ et al (2004) Protected carotid-artery stenting versus endarterectomy in high-risk patients. N Engl J Med 351:1493–150
15. Mas JL, Chatellier G, Beyssen B, Branchereau A, Moulin T, Becquemin JP et al (2006) Endarterectomy versus stenting in patients with symptomatic severe carotid stenosis. N Engl J Med 355:1660–1671
16. Ringleb PA, Allenberg J, Bruckmann H, Eckstein HH, Fraederich G, Hartmann M et al (2006) 30 day results from the SPACE trial of stent-protected angioplasty versus carotid endarterectomy in symptomatic patients: a randomised non-inferiority trial. Lancet 368:1239–1247
17. International Carotid Stenting Study Investigators (2010) Carotid artery stenting compared with endarterectomy in patients with symptomatic carotid stenosis (International Carotid Stenting Study): an interim analysis of a randomized controlled trial. Lancet 375:985–99
18. Brott TG, Hobson RW 2nd, Howard G, Roubin GS, Clark WM, Brooks W et al (2010) Stenting versus endarterectomy for treatment of carotid-artery stenosis. N Engl J Med 363:11–23
19. Long-term outcomes after stenting versus endarterectomy for treatment of symptomatic carotid stenosis: the International Carotid Stenting Study (ICSS) randomised trial Leo H Bonati, Joanna Dobson, Roland L Featherstone, Jörg Ederle, H Bart van der Worp, Gert J de Borst, Willem P Th M Mali, Jonathan D Beard, Trevor Cleveland, Stefan T Engelter, Philippe A Lyrer, Gary A Ford, Paul J Dorman, Martin M Brown, for the International Carotid Stenting Study investigators* Lancet. 2015 Feb 7;385(9967):529-38
20. Randomized Trial of Stent versus Surgery for Asymptomatic Carotid Stenosis Kenneth Rosenfield , Jon S Matsumura, Seemant Chaturvedi, Tom Riles, Gary M Ansel, D Chris

Metzger, Lawrence Wechsler, Michael R Jaff, William Gray ACT I Investigators N Engl J Medicine 2016 Mar 17;374(11):1011-20.
21. Gray WA, Rosenfield KA, Jaff MR, Chaturvedi S, Peng L, Verta P; CAPTURE 2 Investigators and Executive Committee Influence of site and operator characteristics on carotid artery stent outcomes: analysis of the CAPTURE 2 (Carotid ACCULINK/ACCUNET Post Approval Trial to Uncover Rare Events) clinical study JACC Cardiovasc Interv. 2011 Feb;4(2):235-46.
22. Smout J, Macdonald S, Weir G, Stansby G Carotid artery stenting: relationship between experience and complication rate Int J Stroke. 2010 Dec;5(6):477-82.
23. Kashyap VS, King AH, Liang P, et al. Learning Curve for Surgeons Adopting Transcarotid Artery Revascularization Based on the Vascular Quality Initiative-Transcarotid Artery Revascularization Surveillance Project. J Am Coll Surg. 2020;230(1):113-120. doi:10.1016/j.jamcollsurg.2019.09.020. PMID 31672680
24. King AH, Kumins NH, Foteh MI, Jim J, Apple JM, Kashyap VS. The learning curve of transcarotid artery revascularization. J Vasc Surg. 2019;70(2):516-521. Doi:10.1016/j.jvs.2018.10.115
25. Alfawaz AA, Rossi MJ, Kiguchi MM, et al. Transcarotid Arterial Revascularization Adoption Should not Be Hindered by a Concern for a Long Learning Curve. Ann Vasc Surg. 2022;78:45-51. doi:10.1016/j.avsg.2021.05.068. PMID 34481884
26. Lal BK, Mayorga-Carlin M, Kashyap V, et al. Learning curve and proficiency metrics for transcarotid artery revascularization. J Vasc Surg. 2022;75(6):1966-1976.e1. doi:10.1016/j.jvs.2021.12.073. PMID 35063612
27. Husman R, Tanaka A, Saqib NU, Mirza A, George MJ, Keyhani A, Keyhani K, Wang SK. Adverse events are not increased with trainee participation in transcarotid revascularization Vascular. 2022 Nov 15:17085381221140158. Doi: 10.1177/17085381221140158. Online ahead of print. PMID 36377465
28. Lal BK, Cambria R, Moore W, Mayorga-Carlin M, Shutze W, Stout CL, Broussard H, Garrett HE Jr, Nelson W, Titus JM, Macdonald S, Lake R, Sorkin JD. Evaluating the optimal training paradigm for transcarotid artery revascularization based on worldwide experience J Vasc Surg. 2022 Feb;75(2):581-589.e1. doi: 10.1016/j.jvs.2021.08.085. Epub 2021 Sep 23. PMID 34562569
29. Lal BK, Jordan W, Kashyap VS, Kwolek CJ, Moore WS, Mukherjee D, Schermerhorn ML. Clinical competence statement of the Society for Vascular Surgery on training and credentialing for transcarotid artery revascularization. J Vasc Surg. 2020 Sep;72(3):779-789. doi: 10.1016/j.jvs.2020.05.053. Epub 2020 Jun 20. PMID 32569715
30. Evaluation of the optimal training paradigm for TCAR: Lal BK, Cambria R, Moore W, Mayorga-Carlin M, Shutze W, Stout CL, Broussard H, Garrett HE Jr, Nelson W, Titus JM, Macdonald S, Lake R, Sorkin JD. Evaluating the optimal training paradigm for transcarotid artery revascularization based on worldwide experience J Vasc Surg. 2022 Feb;75(2):581-589.e1. doi: 10.1016/j.jvs.2021.08.085. Epub 2021 Sep 23. PMID 34562569
31. Zebolsky AL, Chou J, Key P, et al. Safety and efficacy of transcarotid artery revascularization in a community hospital. J Vasc Surg. 2021;74(1):203-208. doi:10.1016/j.jvs.2020.12.066. PMID 33348008
32. Dias CG, Fajardo A, Martin GH, Tanaka A, Motaganahalli RL, Keyhani A, Keyhani K, Wang SK. Transcarotid Revascularization Results in Patients Over 70 Years of Age Vasc Endovascular Surg. 2022 Sep 27:15385744221130867. doi: 10.1177/15385744221130867. Online ahead of print. PMID 36168186

33. Kibrik P, Stonko DP, Alsheekh A, Holscher C, Zarkowsky D, Abularrage CJ, Hicks CW. Association of carotid revascularization approach with perioperative outcomes based on symptom status and degree of stenosis among octogenarians J Vasc Surg. 2022 Sep;76(3):769-777.e2. doi: 10.1016/j.jvs.2022.04.027. Epub 2022 May 25. PMID 35643202
34. Mayorga-Carlin M, Shaw P, Ozsvath K, Erben Y, Wang G, Sahoo S, Macdonald S, Kashyap VS, Sorkin JD, Lal BK. Transcarotid revascularization outcomes do not differ by patient age or sex J Vasc Surg. 2022 Jul;76(1):209-219.e2. doi: 10.1016/j.jvs.2022.01.141. Epub 2022 Mar 28. PMID 35358669
35. Mehta A, Patel PB, Bajakian D, et al. Transcarotid artery revascularization versus carotid endarterectomy and transfemoral stenting in octogenarians. J Vasc Surg. 2021;74(5):1602-1608. PMID 34082003
36. Ghamraoui AK, Ricotta JJ 2nd. Outcomes of Transcarotid Artery Revascularization (TCAR) in Octogenarians and Older. Ann Vasc Surg. 2020 Oct;68:151-158. Doi: 10.1016/j.avsg.2020.05.034. Epub 2020 May 29. PMID 32479873
37. Dakour-Aridi H, Kashyap VS, Wang GJ, Eldrup-Jorgensen J, Schermerhorn ML, Malas MB. The impact of age on in-hospital outcomes after transcarotid artery revascularization, transfemoral carotid artery stenting, and carotid endarterectomy. J Vasc Surg. 2020 Sep;72(3):931-942.e2. doi: 10.1016/j.jvs.2019.11.037. Epub 2020 Feb 5. PMID 32035784
38. Voeks JH, Howard G, Roubin GS, Malas MB, Cohen DJ, Sternbergh WC 3rd, Aronow HD, Eskandari MK, Sheffet AJ, Lal BK, Meschia JF, Brott TG; CREST Investigators. Age and outcomes after carotid stenting and endarterectomy: the carotid revascularization endarterectomy versus stenting trial. Stroke. 2011 Dec;42(12):3484-90
39. Nejim B, Alshwaily W, Dakour-Aridi H, Locham S, Goodney P, Malas MB. Age modifies the efficacy and safety of carotid artery revascularization procedures. Observational Study J Vasc Surg 2019 May;69(5):1490-1503.e3.
40. Bonati LH, Fraedrich G; Carotid Stenting Trialists' Collaboration. Age modifies the relative risk of stenting versus endarterectomy for symptomatic carotid stenosis--a pooled analysis of EVA-3S, SPACE and ICSS. Eur J Vasc Endovasc Surg. 2011 Feb;41(2):153-8
41. Howard G, Roubin GS, Jansen O, Hendrikse J, Halliday A, Fraedrich G, Eckstein HH, Calvet D, Bulbulia R, Bonati LH, Becquemin JP, Algra A, Brown MM, Ringleb PA, Brott TG, Mas JL; Carotid Stenting Trialists' Collaboration. Association between age and risk of stroke or death from carotid endarterectomy and carotid stenting: a meta-analysis of pooled patient data from four randomised trials. Lancet. 2016 Mar 26;387(10025):1305-11
42. Deery SE, Holscher CM, Nejim B, et al. In-hospital and one-year outcomes are similar for women and men following transcarotid artery revascularization in symptomatic and asymptomatic patients. J Vasc Surg. 2022;75(2):572-580.e3. doi:10.1016/j.jvs.2021.08.081. PMID 34560217
43. Cui CL, Zarrintan S, Marmor RA, Nichols J, Cajas-Monson L, Malas M. Performance of Carotid Revascularization Procedures as Modified by Sex. Ann Vasc Surg. 2022;81:171-182. doi:10.1016/j.avsg.2021.08.051. PMID 34752853
44. Howard VJ, Lutsep HL, Mackey A, Demaerschalk BM, Sam AD 2nd, Gonzales NR, Sheffet AJ, Voeks JH, Meschia JF, Brott TG; CREST investigators. Influence of sex on outcomes of stenting versus endarterectomy: a subgroup analysis of the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST). Lancet Neurol. 2011 Jun;10(6):530-7

45. Touzé E, Trinquart L, Felgueiras R, Rerkasem K, Bonati LH, Meliksetyan G, Ringleb PA, Mas JL, Brown MM, Rothwell PM; Carotid Stenting Trialists' Collaboration. A clinical rule (sex, contralateral occlusion, age, and restenosis) to select patients for stenting versus carotid endarterectomy: systematic review of observational studies with validation in randomized trials. Stroke. 2013 Dec;44(12):3394-400
46. Dansey KD, Pothof AB, Zettervall SL, Swerdlow NJ, Liang P, Schneider JR, Nolan BW, Schermerhorn ML. Clinical impact of sex on carotid revascularization. J Vasc Surg. 2020 May;71(5):1587-1594.e2
47. Dakour-Aridi H, Tanaka A, Mirza AK, Motaganahalli RL, Leckie KE, Keyhani A, Keyhani K, Wang SK. Transcarotid revascularization in obese patients Vascular. 2022 Jun 2:17085381221106326. doi: 10.1177/17085381221106326. Online ahead of print. PMID 35653693