Safety and Effectiveness of TCAR in Standard-Risk Patients

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Since gaining Food and Drug Administration (FDA) approval in 2015, transcarotid artery revascularization (TCAR) has become an increasingly utilized operative technique to treat patients with significant carotid stenosis. This hybrid procedure utilizes a common carotid artery cutdown with 8-French arterial sheath access, which is then connected to an 8-French sheath in the common femoral vein to establish cerebral flow reversal. This provides distal embolic protection during carotid stent placement. (See Fig. 1 and reference the Spring 2019 issue of *JLGH* for an article further detailing this procedure.[1])

Because the TCAR procedure — including the neuroprotection system and stent used for the procedure — had not undergone rigorous evaluation in the form of a randomized-controlled trial, there remained stipulations regarding the type of patients for which it could be used and how to obtain institutional reimbursement.

Initially, the Centers for Medicare and Medicaid Services (CMS) required patients to have at least one anatomic and/or physiologic criteria putting them at high surgical risk for carotid endarterectomy (CEA). Additionally, all patient outcome data had to be entered into a national database of vascular surgical procedures, called the Vascular Quality Initiative-TCAR Surveillance Project.

Using this data, a large review was published in the *Journal of Vascular Surgery* in 2021 looking solely at patients deemed standard risk for surgery who underwent either CEA or TCAR.[2]

The authors performed a 3:1 propensity-matched analysis of nearly 15,000 patients who had CEA and 5,000 patients who had TCAR. There was no statistically significant difference between stroke rates at 30 days. The TCAR stroke rate was notably 1.4%. This publication helped support the FDA label expansion to include standard-risk patients in April 2022.

Following suit, in October 2023, CMS changed its stance in National Coverage Determination 20.7 to state that any patient with ≥50% symptomatic or ≥70% asymptomatic stenosis, regardless of surgical risk, could obtain reimbursement for CEA, TCAR, or transfemoral carotid stenting. While there are stipulations, this now allows specialists to offer any revascularization modality to patients with significant carotid stenosis.

PRIOR TCAR CLINICAL TRIALS

When obtaining informed consent, vascular surgeons must discuss the perioperative stroke risk associated with carotid revascularization. The typical quoted rate is based on the largest randomized-controlled trial published on carotid interventions, CREST,[3] which demonstrated that patients undergoing CEA had a post-procedure stroke risk of 2.3%. Thus, this rate has remained the standard against which other interventions have been compared.

The ROADSTER study was the original investigative device exemption trial of TCAR, which enrolled 141 patients considered high risk for surgery.[4] The overall stroke rate was 1.4% at 30 days in the patients who followed through on the protocol, the so-called "intention-to-treat" (ITT) population.

While the ROADSTER study was underpowered, and thus the stroke rate in patients who stayed on protocol was not considered statistically significant, TCAR was preliminarily considered at least as safe as CEA. The FDA approved it for use in high-risk patients in 2015.

Although there has been strong interest regarding whether TCAR can be used in standard-risk patients, conducting an adequately powered randomized-controlled trial would require enrolling at least 100,000 patients, and thus this prospect has remained unfeasible. Yet, in 2020, the results of the ROADSTER 2 clinical trial demonstrated a 30-day stroke rate of 1.9% in the ITT population.[5] In this study of 692 patients, all considered high risk for surgery, a subset analysis of 632 patients who followed the prescribed dual antiplatelet and statin protocol showed the stroke

rate was 0.6%. This is the lowest stroke rate ever reported for any carotid revascularization trial.

Once the FDA approved TCAR for use in standard-risk patients, another clinical trial was required to prove its safety and efficacy in this patient population. Given our early adoption of TCAR at Lancaster General Hospital (LGH), our excellent patient outcomes, and our well-established research infrastructure, LGH was selected as a site for enrollment into ROADSTER 3.[6] As a national co-principal investigator, I had the privilege of presenting the 30-day outcomes of ROADSTER 3 at the Vascular InterVentional Advances conference in November 2024.[7]

METHODS

ROADSTER 3 is a prospective, single-arm, multicenter, post-approval study that enrolled 344 patients over 48 sites in the United States between September 2022 and June 2024. Patients had to be considered standard risk for surgery and have anatomy suitable for TCAR. Octogenarians were therefore excluded.

The study's primary endpoint was the composite rate of stroke, death, and myocardial infarction (S/D/MI) through 30 days post-procedure plus the ipsilateral stroke rate from days 31 through 365. The incidence of cranial nerve injury (CNI) within 30 days was a powered secondary endpoint. Events were adjudicated by an independent clinical events committee.

Patients had a National Institutes of Health Stroke Scale assessment and medication review performed by a study coordinator independent to the clinical team; this was completed within 24 hours of TCAR, again at 30 days, and at one year. If a CNI was detected, a six-month assessment was also performed.

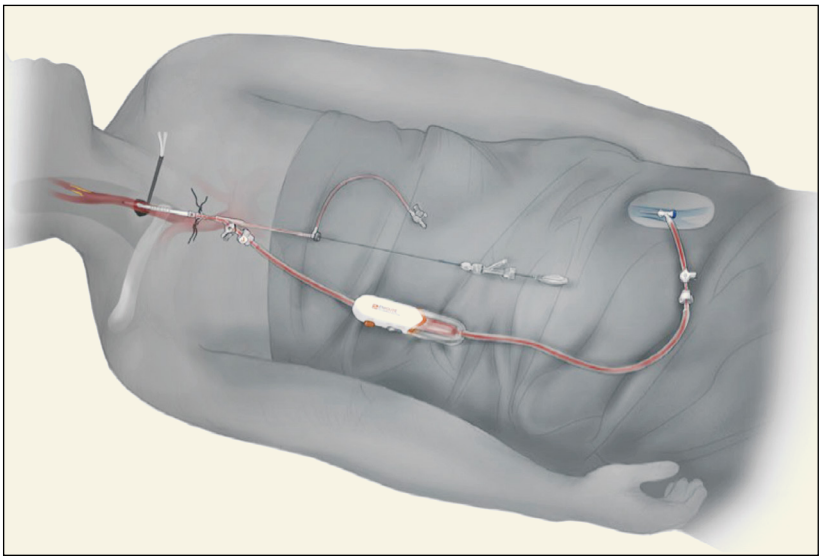

Fig. 1. With sheath access in the common carotid artery and femoral vein, a filter device is connected to each during the TCAR procedure to create an arteriovenous shunt with reversal of flow from the brain. This eliminates the possibility of plaque or thrombotic debris from entering the brain while crossing the lesion with a wire, performing angioplasty, and placing a stent.

RESULTS

A total of 344 patients enrolled in the study. Of these, 24 patients deviated from the protocol, 16 due to medication non-compliance, leaving 320 patients in the per protocol (PP) cohort. Most of the patients (55.1%) were between 70-79 years old; 42.8% were female. The majority of patients were asymptomatic, but of the 15.7% who were symptomatic, 23.5% had experienced their neurologic event within two weeks of having the procedure done.

A majority of patients (75.3%) had a baseline stenosis of 70% to 89%. The mean lesion length was 23.3 mm, and 64.2% of lesions had calcification. Most cases (85.2%) were performed under general anesthesia. The average procedure time was 56.6 minutes, and average flow reversal time was 9.0 minutes. There were no reported episodes of intolerance to flow reversal.

In the intention-to-treat population, the composite rate of S/D/MI at 30 days was 0.9%. There were no deaths or cardiac events. Thus, the 30-day stroke rate was also 0.9%. Three individuals undergoing TCAR experienced a post-procedure stroke; one of these was considered major ischemic, one minor ischemic, and one major hemorrhagic. All stroke events occurred in patients who had been asymptomatic before having the TCAR performed.

The patient who experienced a major ischemic stroke had stent thrombosis on post-operative day 1. This patient was taken back to the operating room for open thrombectomy and balloon angioplasty of the stent, which remained patent at 30 days.

The major hemorrhagic event occurred in a patient who presented on post-operative day 9 with intracranial hemorrhage. Dual antiplatelet medications were held which moved the patient off protocol. Table 1 on page 6 shows the 30-day outcomes in both the ITT and PP populations.

Two patients experienced voice hoarseness post-TCAR. Both cases of CNI resolved within six months. Only

seven access site complications occurred, three of which self-resolved without intervention. Four patients had an access site dissection requiring repair with either additional stent or balloon angioplasty. None of these access site complications resulted in a stroke or CNI.

CONCLUSION

While TCAR is already considered an appropriate option for patients deemed to be at high risk for carotid artery-associated ischemic stroke, in the first-ever, independently adjudicated, prospective study evaluating TCAR in standard-risk patients, we have found it safe and effective at treating stenosis without incurring increased risk of stroke.

The composite S/D/MI rate of 0.9% is lower than in our high-risk population, as we'd expect. When looking at the subset of patients who were able to complete their postprocedural medication protocol, that rate drops to 0.6%, which is the lowest stroke rate ever reported in the literature.

We are over halfway through completion of one-year follow-up; final data are expected in late 2025. We have also started enrolling patients in a five-year follow-up arm to determine stent patency and neurologic events over time.[8]

It is prudent to keep this data in mind when having shared decision-making discussions with patients being offered carotid revascularization. TCAR is now an appropriate option to consider for both high-risk and standard-risk patients here in Lancaster.

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Table 1. 30-Day Outcomes of the ROADSTER 3 Trial

Parameter	ITT (n = 344)	PP (n = 320)
Stroke	0.9% (3)	0.6% (2)
Death	None	None
Myocardial Infarction	None	None
Stroke/Death/Myocardial Infarction	0.9% (3)	0.6% (2)

ITT = intention-to-treat cohort; PP = per protocol cohort