

An Inconvenient Truth? Optimization of Carotid Stenting Is Dependent on the Approach and Method of Embolic Protection

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Carotid artery disease remains one of the major contributors to ischemic stroke, and treatment strategies have focused on either removing the culprit plaque with carotid endarterectomy (CEA) or ameliorating it with carotid artery stenting (CAS). Over time, less invasive approaches have been developed to achieve outcomes comparable to CEA while reducing perioperative risk. Traditional transfemoral CAS (TFCAS) is typically performed with distal embolic protection (DEP). This involves crossing the plaque in the internal carotid artery (ICA) to deploy a filter distal to the lesion, with the goal of capturing debris released during angioplasty and stent placement. However, navigating catheters through a diseased, elongated aortic arch and crossing the stenotic lesion to deploy the filter are critical steps in both TFCAS and transradial CAS (TRCAS) but risk embolic stroke. Novel alternatives that aim to address limitations in DEP, such as integrated stent systems, dual filter protection, or novel stent designs, face inherent design limitations due to navigating the aortic arch, a potent source of periprocedural stroke, including contralateral stroke,¹ and have yet to be proven under broad conditions of use.

Transcarotid artery revascularization (TCAR) was developed as an alternative to TFCAS, using direct access to the common carotid artery (CCA) without the need to traverse the aortic arch. TCAR is typically performed under dynamic flow reversal, which eliminates the need for crossing the lesion with a DEP filter. These two fundamental differences between TCAR and TFCAS translate into lower stroke risk with TCAR. However, there are other approaches to perform CAS, such as proximal balloon occlusion (PBO) during TFCAS, that attempt to mimic this protection.

Given the variety of neuroprotection strategies now in use, we aimed to provide a more comprehensive under-

KEY FINDINGS²

- Patients who underwent TFCAS-DEP had consistently higher rates of the primary outcomes as compared with those treated with TCAR.
- Compared with TCAR, TCAS-DEP patients had higher risks across most endpoints.
- TCAR maintained superior survival outcomes when flow arrest via PBO was used instead of DEP during transfemoral stenting.
- TCAR with flow reversal demonstrated improved safety and survival compared with CAS performed through the same carotid access using DEP for neuroprotection.

standing of their impact. To address these knowledge gaps, we conducted a study directly comparing CAS outcomes across four strategies: TCAR with flow reversal, TFCAS with DEP, TFCAS with PBO, and transcarotid stenting with DEP (TCAS-DEP). This allowed an evaluation of both the access route and the neuroprotection method, which could influence stroke risk and other complications after carotid stenting. The analysis comprised Vascular Quality Initiative (VQI) data to perform a retrospective analysis of all CAS procedures from September 2016 to August 2024.²

DATA SOURCE

Until October 2023, when the Centers for Medicare & Medicaid Services (CMS) reevaluated reimbursement for CAS (to include TCAR), agnostic to symptom

status and surgical risk designation, outcomes had to be reported in the VQI CAS module (housing TFCAS, TRCAS, and TCAR). The first TCAR after training and all subsequent TCAR outcomes were entered, covering a total of 95% of all United States TCAR experience since commercialization, an unprecedented milestone in medical device evaluations.³ The other 5% is represented by Veterans Affairs hospital systems that maintain federal databases. This is unique for endovascular or surgical procedures in the United States, and this program of reimbursement in exchange for data entry did not apply to either CEA or TFCAS/TRCAS, as their reimbursement was not contingent on data entry. The collected data demonstrate the outcomes of comparative carotid revascularization strategies under broad real-world conditions, showing the lowest stroke rates for TCAR compared with CEA and TFCAS in high-surgical-risk patients.⁴⁻⁷ In January 2021, the American College of Cardiology NCDR PVI (National Cardiovascular Diseases Registry Peripheral Vascular Interventions) database was merged with the Society for Vascular Surgery VQI CAS module. All TFCAS procedures performed by interventional cardiologists were included if the operator was so compelled.

Data entry is performed by a nurse or data extractor. All modules are equally hindered (CEA and CAS modules) because there is no independent neurologic assessment using the National Institutes of Health Stroke Scale and modified Rankin Scale evaluations by health care professionals certified to perform such assessments. However, it is essential to note that the results of the ROADSTER trials⁸⁻¹⁰ are remarkably similar to those of VQI analyses in the real world, particularly when there was independent adjudication of major adverse events and independent neurologic assessments, as these were FDA-directed trials.

PRIMARY ANALYSIS²

Only patients treated via femoral or carotid access were included, excluding procedures via alternative routes (ie, brachial or radial access). Patients with carotid stenosis caused by trauma, dissection, fibromuscular dysplasia, or uncharacterized lesions were not included. We focused exclusively on cases of atherosclerotic disease or intimal hyperplasia after prior ipsilateral CEA or carotid stenting. We also excluded patients who underwent CAS in combination with intracranial procedures, patients missing information on symptom status, access route or protection method, and those with tandem lesions. To maintain uniformity, we only analyzed cases where a neuroprotection device was successfully used. The primary outcomes were in-hospital stroke, death, the composite of stroke or death, and 30-day mortality.

Secondary outcomes included transient ischemic attack (TIA), stroke/death/myocardial infarction (MI), postoperative congestive heart failure (CHF), prolonged hospital stay longer than 1 day, and reperfusion symptoms. Inverse probability of treatment weighting was the primary statistical analysis employed.²

In total, 99,030 patients were included. TCAR was by far the most common procedure, accounting for 67.3% of cases, followed by TFCAS-DEP at 31%, TCAS-DEP at 0.9%, and TFCAS-PBO at 0.8%. Compared with the other groups, TCAR patients were the oldest on average and more likely to be female and Medicare insured. Diabetes and CHF rates were similar across groups, but TFCAS-PBO patients had the lowest prevalence of coronary artery disease. TCAR patients were more likely to be on statins and P2Y inhibitors at the time of the procedure.

RESULTS

TFCAS-DEP Versus TCAR

On univariate analysis, patients who underwent TFCAS-DEP had consistently higher rates of the primary outcomes compared with those treated with TCAR. Stroke occurred in nearly 2% of TFCAS-DEP cases versus 1.3% of TCAR cases, while in-hospital death was more than triple (1.08% vs 0.36%). The combined endpoint of stroke or death was also higher with TFCAS-DEP (2.70% vs 1.51%), and 30-day mortality was more than twice as high (1.80% vs 0.75%, $P < .001$ for all). These differences remained significant after inverse probability weighting. TFCAS-DEP carried more than double the odds of both in-hospital mortality (odds ratio [OR], 2.68; 95% CI, 2.25-3.19; $P < .001$) and 30-day mortality (OR, 2.39; 95% CI, 2.08-2.74; $P < .001$). Stroke risk was 34% higher (OR, 1.34; 95% CI, 1.18-1.53; $P < .001$), and stroke or death was 62% higher (OR, 1.62; 95% CI, 1.45-1.81; $P < .001$). Secondary outcomes followed the same pattern, with higher rates of TIA (OR, 1.30; $P = .017$), postoperative CHF (OR, 1.53; $P = .001$), reperfusion syndrome (OR, 3.38; $P < .001$), and prolonged hospital stay (OR, 1.31; $P < .001$) in the TFCAS-DEP group compared with TCAR.

Assessing the Relative Value of Protection Method From a Direct CCA Approach: TCAS-DEP Versus TCAR

When comparing TCAS-DEP with TCAR, TCAR again showed superior outcomes. Although in-hospital mortality and reperfusion syndrome did not differ significantly, TCAS-DEP patients had higher risks across most endpoints. Stroke was 58% more likely with TCAS-DEP (OR, 1.58; 95% CI, 1.04-2.38; $P = .031$), and the combined outcome of stroke or death was 66% higher (OR, 1.66; 95% CI, 1.15-2.39; $P = .006$). Thirty-day mortality was almost double with TCAS-DEP (OR, 2.00; 95% CI, 1.13-3.53; $P = .016$). Secondary outcomes also favored

TCAR, as TCAS-DEP patients had more than twice the odds of TIA (OR, 2.33; $P = .016$), nearly triple the odds of postoperative CHF (OR, 2.92; $P = .002$), and over 50% increased risk of prolonged hospital stay (OR, 1.52; $P < .001$).

Assessing the Relative Value of PBO Versus Flow Reversal: TFCAS-PBO Versus TCAR

The comparison between TFCAS-PBO and TCAR showed a different pattern. There was no significant difference in neurologic outcomes such as stroke, TIA, or the combined endpoint of stroke, death, and MI. CHF and prolonged hospital stay also did not differ significantly. However, mortality outcomes favored TCAR. In-hospital death with TFCAS-PBO was more than double that of TCAR (OR, 2.47; 95% CI, 1.22-5.00; $P = .012$), and 30-day mortality was nearly twice as high (OR, 1.85; 95% CI, 1.03-3.30; $P = .038$). TFCAS-PBO also had a markedly higher risk of reperfusion syndrome, almost five times greater than TCAR (OR, 4.72; 95% CI, 2.49-8.94; $P < .001$).

To our knowledge, this was the largest multi-institutional study examining CAS outcomes with respect to both access type and the neuroprotection devices used. Our results show that TFCAS-DEP is associated with substantially higher risks of postoperative complications, including stroke, death, the composite of stroke or death, TIA, stroke/death/MI, postoperative CHF, reperfusion syndrome, and prolonged length of stay compared with TCAR. TCAR with flow reversal demonstrated improved safety and survival compared with CAS performed through the same carotid access using DEP for neuroprotection, with lower odds of stroke, 30-day mortality, stroke/death, CHF, and prolonged hospital stay. Additionally, when flow arrest via PBO was used instead of DEP during TFCAS, TCAR maintained superior survival outcomes, with lower odds of in-hospital and 30-day mortality and a significant reduction in reperfusion syndrome.

Previous studies have documented the improved perioperative outcomes of TCAR over TFCAS-DEP, particularly in reducing perioperative stroke, death, and TIA.^{11,12} In our 2019 study, we compared TCAR and TFCAS in patients undergoing treatment for carotid stenosis.¹¹ Analyses included propensity score-matched patients with similar baseline characteristics, and TCAR was associated with roughly half the risk of in-hospital stroke or death (1.6% vs 3.1%; absolute difference, -1.52% [95% CI, -2.29% to -0.75%]; relative risk [RR], 0.51 [95% CI, 0.37-0.72]; $P < .001$), stroke (1.3% vs 2.4%; RR, 0.54; [95% CI, 0.38-0.79]; $P = .001$), and death (0.4% vs 1.0%; absolute difference, -0.55% [95% CI, -0.98% to -0.11%]; RR, 0.44; [95% CI, 0.23-0.82]; $P = .008$) com-

pared to TCAR. At 1 year, the transcarotid approach continued to show a lower risk of ipsilateral stroke or death (5.1% vs 9.6%), demonstrating a clear advantage of TCAR over the transfemoral approach in reducing stroke and mortality.

In a prior meta-analysis by our group including nine studies, we found that the 30-day risk of stroke or death was low at 1.89%, with TCAR demonstrating similar perioperative stroke/death rates to CEA. Two of the included studies suggested that TCAR carried roughly half the risk of stroke and death compared with TFCAS.¹² More recently, a meta-analysis published in September 2025 that pooled 13 studies including 142,032 patients had confirmed that TCAR significantly reduced 30-day and in-hospital mortality, stroke, and the composite of stroke/death compared with TFCAS, while also reducing TIA, reperfusion injury, and hospital length of stay.¹³

Assessing the Additional Value of Flow Reversal From a Direct Carotid Approach

There is limited literature comparing a direct carotid approach and flow reversal and a direct carotid approach with a distal filter. One prior study from our group showed that TCAR is associated with lower risks of stroke and stroke/death compared with TCAS-DEP.¹⁴ This current analysis confirms those findings, showing significantly lower odds of stroke, TIA, CHF, and 30-day mortality with TCAR.² These results highlight the advantages of continuous procedural flow reversal over DEP for direct carotid access as well as the benefit of avoiding lesion crossing during filter deployment.

TCAR Outperforms TFCAS Regardless of Arch Type

The advantage of avoiding the aortic arch via direct transcarotid access was also a finding previously demonstrated by our team. We evaluated 20,114 patients with varying aortic arch types (type I, II, and III) and degrees of arch atherosclerosis (mild, moderate, severe) from the VQI CAS module.¹⁵ TCAR was found to be safer in terms of lowering the odds of stroke and death compared with TFCAS in patients with type I to II arch and any degree of atherosclerosis. Because TCAR by default eliminates the need for catheter manipulation in the arch, we believe this played a major role in achieving more favorable outcomes. Our results demonstrated that even in straightforward arch anatomy, such as type I arch, TCAR was superior to TFCAS.

CONCLUSION

- This is the largest series ever published on treatment of carotid artery disease with multiple stent-based strategies, with a total of 66,655 TCAR outcomes.

VQI COMPARATIVE ANALYSIS OF TCAR WITH THE ENROUTE® NPS AND ENROUTE® STENT VERSUS TFCAS

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- Comparing TCAR to TFCAS-DEP, TFCAS-PBO, and transcarotid CAS with distal filter, outcomes with TCAR are statistically superior (mortality, cerebrovascular accident).
- TCAR is superior to TFCAS, even in type I arches.
- This article also reviews comparative outcomes of TCAR versus CEA in multiple sizeable analyses, which consistently show that TCAR outperforms CEA in patients meeting CMS-defined high-surgical-risk criteria (the majority of patients with significant carotid disease).
- Dynamic flow reversal with direct carotid access with the Silk Road therapies has emerged as a mainstay of treatment for carotid artery disease. ■

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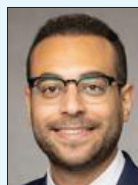


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