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Transcarotid Artery Revascularization versus Carotid Endarterectomy with and without High-Risk Criteria: A National Target Trial

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ABSTRACT

Objective:
We sought to evaluate outcomes associated with transcarotid artery revascularization with flow reversal(TCAR) versus carotid endarterectomy(CEA) for carotid artery stenosis(CAS), emulating a randomized controlled trial.

Summary Background Data:
The introduction of TCAR has revolutionized management of CAS. While this approach has been demonstrated to yield reduced morbidity relative to transfemoral carotid artery stenting, a comparison of outcomes with gold-standard CEA remains lacking.

Methods:
We identified all records entailing CEA or TCAR for CAS within the 2021-2022 Nationwide Readmissions Database. We conducted a target trial emulation using doubly robust inverse probability-weighted regression analysis to evaluate the adjusted hazard of 90-day composite morbidity, comprised of in-hospital stroke, myocardial infarction, or death. Patients were further stratified as high- or low-risk based on Centers for Medicare and Medicaid Services(CMS) criteria.

Results:
We identified 113,994 patients who received CEA, and 12,613 TCAR. The adjusted risk of composite morbidity over 90 days following revascularization was 4.1% (CI 3.6-4.6%) following TCAR compared with 4.1% (CI 4.0-4.3%) after CEA. The average treatment effect of TCAR was not found to be significant. Target trial emulation revealed TCAR to confer similar hazard of 90-day composite morbidity as CEA among low-risk patients (HR 0.85, CI 0.72-1.01), but reduced hazard of myocardial infarction among high-risk patients (HR 0.76, CI 0.58-0.98).

Conclusions:
Upon target trial emulation, receipt of TCAR was associated with comparable morbidity over 90 days following revascularization, relative to CEA. Altogether, our data support recent CMS approval of TCAR, and encourage broadened utilization among both standard and high-risk patients.

KEYWORDS
Carotid artery stenosis, transcarotid artery revascularization, TCAR, carotid endarterectomy, CEA

ABBREVIATIONS

AOR	Adjusted Odds Ratio
CAS	Carotid Artery Stenosis
CEA	Carotid Endarterectomy

CI	Confidence Interval
CMS	Centers for Medicare and Medicaid Services
HR	Hazard Ratio
ICD	International Classification of Diseases
IQR	Interquartile Range
MAE	Major Adverse Events
NRD	Nationwide Readmissions Database
RCT	Randomized Controlled Trial
TCAR	Transcarotid Artery Revascularization
TFCAS	Transfemoral Carotid Artery Stenting

INTRODUCTION

Approximately 20-25% of all ischemic strokes are attributable to significant carotid artery stenosis (CAS).[1] While two landmark trials in the 1990s established carotid endarterectomy (CEA) as the gold standard treatment for CAS,[2,3] evolution of stent technology has permitted the development and adoption of transfemoral carotid artery stenting (TFCAS). Despite initial optimism and promising early clinical trial data,[4,5] however, subsequent investigations have demonstrated TFCAS to be associated with significantly greater risk of postoperative stroke among both asymptomatic and symptomatic CAS patients.[6–8]

More recently, the introduction of transcarotid artery revascularization (TCAR), employing flow reversal to reduce distal embolization, has revolutionized the field.[9] Elimination of the need to navigate the aortic arch with wires and catheters using direct carotid access, coupled with use of a simple pumpless flow reversal technique, have reduced the risk of cerebral embolization and yielded acceptable morbidity rates.[10] Indeed, several retrospective analyses of national registry data have reported TCAR to achieve comparable perioperative stroke and death rates as CEA, while maintaining the benefits of a less invasive approach.[11–15] Yet, with observational studies limited by underlying selection bias and confounding, the ultimate treatment effectiveness of TCAR, remains unclear. Regardless, based on initial evidence, the US Centers for Medicare and Medicaid Services (CMS) approved TCAR for both standard and high-risk patients.[16]

In the absence of a randomized controlled trial (RCT) comparing CEA versus TCAR, decision-making regarding the modality of revascularization, remains complex. Importantly, target trial emulation frameworks have achieved increasing recognition, through the opportunity to emulate

RCT using real-world data, while directly addressing the limitations of retrospective studies.[17] This methodology has not yet been applied in the context of carotid revascularization, but could provide actionable evidence regarding patient selection and optimal management of CAS.

Therefore, we sought to apply target trial emulation, to evaluate TCAR versus CEA among a national cohort of patients with CAS. We hypothesized patients undergoing TCAR to demonstrate comparable outcomes, but greater costs, to those receiving CEA. We further hypothesized this to persist even among sub-groups of high-risk, frail, and symptomatic patients.

METHODS

Data Source and Study Population

We queried the 2021-2022 Nationwide Readmissions Database (NRD) to ascertain all adult (≥18 years) hospitalizations entailing elective or emergent CEA or TCAR for asymptomatic or symptomatic CAS, using previously published *International Classification of Diseases, 10th Edition* (ICD-10) diagnosis and procedure codes.[18,19] The NRD represents the largest, all-payer national registry providing readmissions data, and provides accurate estimates for >60% of all hospitalizations, each year.[20] Records missing key data (<1%) were excluded, as were those indicating >1 recorded procedure (3%) (Figure 1).

Variable Definitions and Study Outcomes

The Healthcare Cost and Utilization Project data dictionary was utilized to define relevant patient, procedure, and hospital factors.[21] Patient burden of chronic disease was numerically represented using the van Walraven modification of the Elixhauser Comorbidity Index.[22]

Symptomatic CAS was defined as concurrent amaurosis fugax, transient vision loss, retinal vascular occlusion, retinal ischemia, cerebral infarction, or other cerebral ischemia, in line with previously published work.[23] High risk patients were identified using criteria designated by the CMS, and included those >80 years or with comorbid renal failure, congestive heart failure, unstable angina, severe chronic lung disease, recent myocardial infarction, or requiring coronary artery bypass grafting or valve operations.[24] Patient frailty was recorded using well-validated administrative codes, as described elsewhere.[25]

Our primary endpoint was a composite of major adverse events (MAE), encompassing in-hospital mortality, perioperative stroke, or myocardial infarction, at index hospitalization and over 90 days following revascularization. Secondary endpoints included in-hospital mortality, death, or myocardial infarction during index admission. Finally, we considered secondary composite adverse events at index hospitalization, including thromboembolism, respiratory failure, endotracheal intubation, mechanical ventilation, seizure, or acute kidney injury.[7] Institutional cost-to-charge ratios were applied to compute total hospitalization expenditures, which were then adjusted for inflation using the 2022 Personal Healthcare Price Index.[26]

While our main analysis considered all patients, we performed several rigorous, pre-specified subgroup analyses, evaluating patients >80 years versus ≤80 years, of high versus low risk, frail versus non-frail, women versus men, symptomatic versus asymptomatic disease, and in elective versus non-elective settings. The goal of these stratified subgroup analyses was to assess

potential heterogeneity of treatment effect, while limiting the potential for violations of the positivity assumption by restricting comparisons to clinically relevant subpopulations.

Statistical Analysis

Data are represented as medians with interquartile range (IQR) if continuous or as group proportion (%) if categorical. Subsequently, multivariable models were developed to consider the independent association of TCAR with key study endpoints. Covariates were selected for model inclusion using elastic net regularization, which reduces bias and optimizes model fit.[27] Factors selected for multivariable adjustment included patient age, sex, comorbidity burden, symptomatic CAS, frailty, high risk designation, median household income, insurance coverage, hospital teaching status, and annual center carotid procedure volume. Model goodness of fit was evaluated using the coefficient of determination or the receiver-operating characteristics, as appropriate. Logistic model estimates are delineated as adjusted odds ratio (AOR), while linear outputs are reported as β-coefficient, both with 95% confidence intervals (CI).

To consider the average treatment effect of TCAR, we utilized doubly robust inverse probability-weighted regression adjustment. Briefly, this method first predicts the likelihood of receiving TCAR versus CEA, and then computes inverse-probability weights. Using these weights, a regression model was fit to consider the predicted risk of 30-day MAE. Finally, treatment-specific outcomes are averaged, and the contrast is calculated to represent the average treatment effect.[28]

Finally, to comprehensively evaluate the impact of TCAR versus CEA on MAE, we used clone-censor-weight methodology and performed a target trial emulation. Target trial methods have been demonstrated to accurately and effectively replicate corresponding randomized controlled trials.[17,29] Guidelines regarding the target trial and our emulation are reported in *Supplementary Table S1*, Supplemental Digital Content 1, http://links.lww.com/SLA/F532. The present trial emulation was designed as an open-label trial of patients with asymptomatic or symptomatic carotid disease, who were randomized to receive TCAR or CEA. The primary endpoint was considered the difference in composite morbidity (death, stroke, MI) at 90 days following the procedure. First, records were duplicated at the date of hospitalization for carotid revascularization. One copy was assigned to the *TCAR* protocol and the other to the *CEA* group. Cases assigned to *TCAR* were censored if they received CEA, while those assigned to *CEA* were censored if they had TCAR. Acknowledging that treatment is not randomized, inverse probability weighting was applied to account for the likelihood of protocol censoring. Covariate balance was assessed using standardized mean differences before and after weighting, to ensure adequate treatment of potential confounders, and is reported in *Supplementary Table S2*, Supplemental Digital Content 1, http://links.lww.com/SLA/F532 and *Supplementary Table S3*, Supplemental Digital Content 1, http://links.lww.com/SLA/F532. Freedom from 90-day MAE was assessed using Kaplan-Meier time-to-event estimators and Cox proportional hazard models. Cox model outputs are detailed as hazard ratios (HR) with CI. CI were computed using bootstrapping, with 200 repetitions.

Statistical significance was defined at $\alpha=0.05$. All statistical analyses were performed using Stata 18.0 (StataCorp, LLC, College Station, TX). As the NIS is fully deidentified, the Institutional

Review Board at the University of California, Los Angeles, exempted this study from full review.

RESULTS

We tabulated 126,608 hospitalizations from the NRD, of which 12,613 (10%) entailed TCAR and 113,994 (90%) CEA. The proportion of patients undergoing TCAR increased from 7% in 2021, to 13% in 2022 (P for trend<0.001).

Cohort characteristics are comprehensively reported in Table 1. On average, the *TCAR* group was older (74 [67-80] vs 72 years [65-78], P<0.001), more often of male sex (63 vs 60%, P<0.001) and more frequently admitted electively (82 vs 79%, P=0.02), relative to *CEA*. Further, *TCAR* was more commonly designated higher risk (55 vs 49%, P<0.001), although the proportion of patients with symptomatic disease was similar across groups (8 vs 8%, P=0.16). Additionally, *TCAR* was more often treated at metropolitan teaching hospitals (86 vs 79%, P<0.001).

Unadjusted and adjusted outcomes are detailed in Table 2. Upon bivariate comparison, *TCAR* demonstrated similar incidence of 30-day (2.9 vs 3.2%, P=0.36) and 90-day MAE (4.0 vs 4.1%, P=0.78), compared to *CEA.* Considering outcomes at index hospitalization, rates of in-hospital mortality (0.4 vs 0.4%, P=0.71) and acute stroke (0.4 vs 0.6%, P=0.21) were comparable across cohorts, as was the incidence of composite adverse events (7.0 vs 7.3%, P=0.61). However, *TCAR* less frequently experienced acute MI (0.7 vs 1.0%, P=0.03).

Following comprehensive adjustment, receipt of TCAR remained associated with comparable likelihood of 30-day (AOR 0.92, CI 0.78-1.08, P=0.31) and 90-day MAE (AOR 0.97, CI 0.84-1.11, P=0.63) (Figure 2A). Specifically, the overall adjusted risk of MAE was found to be 3.2% (CI 3.0-3.3%) at 30 days and 4.1% (CI 4.0-4.3%) at 90 days. TCAR did not have a significant treatment effect at either time point, relative to CEA (30 days -0.1%, CI -0.6, 0.3%, P=0.58; 90 days < -0.1%, CI -0.6, 0.5%, P=0.92).

Evaluating outcomes at index hospitalization, treatment with TCAR was associated with similar odds of in-hospital mortality (AOR 0.94, CI 0.62-1.42, P=0.77) and acute stroke (AOR 0.81, CI 0.56-1.19), but lower adjusted risk of MI (AOR 0.69, CI 0.49-0.97, P=0.03). The *TCAR* and *CEA* cohorts demonstrated similar likelihood of secondary composite adverse events (AOR 0.95, CI 0.84-1.08, P=0.45) (Figure 2B). While LOS was similar, *TCAR* faced a $4,880 per-patient increase in hospitalization expenditures (CI $4,120-5,640, P<0.001).

We conducted six pre-specified sensitivity analyses, with results detailed in *Supplementary Table S4*, Supplemental Digital Content 1, http://links.lww.com/SLA/F532. Receipt of TCAR remained associated with similar hazard of 90-day MAE among patients <80 and ≥80 years, of male versus female sex, high or low risk strata, frail or non-frail status, and elective versus emergent case designation. Interestingly, TCAR was found to confer similar hazard of 90-day MAE among asymptomatic patients, but greater risk of MAE relative to CEA, among those with symptomatic disease.

Finally, we performed a target trial emulation. Following cohort cloning and weighting, adequate covariate balance was achieved (*Supplementary Table S2*, Supplemental Digital Content 1, http://links.lww.com/SLA/F532*, Supplementary Table S3*, Supplemental Digital Content 1, http://links.lww.com/SLA/F532). Among low-risk patients, 90-day incidence of MAE was 2.7% in the TCAR protocol and 2.6% in the CEA protocol (log-rank P=0.71). Following doubly robust risk-adjustment, the TCAR protocol remained associated with comparable hazard of 90-day MAE as the CEA protocol (HR 1.05, CI 0.83-1.31). Specifically, the TCAR protocol was linked with similar hazard of stroke (HR 1.08, CI 0.81-1.44), MI (HR 1.14, CI 0.75-1.73), and mortality within 90-days (HR 0.90, CI 0.53-1.52). Considering high-risk patients, the TCAR protocol was associated with reduced hazard of 90-day MI (HR 0.76, CI 0.58-0.98), but similar likelihood of stroke (HR 1.05, CI 0.82-1.36) and mortality (HR 1.02, CI 0.74-1.41) (Figure 3).

DISCUSSION

The advent of minimally invasive, transcatheter-based technology has transformed outcomes across various cardiovascular procedures but remained limited in the context of carotid revascularization. Recently, TCAR has emerged as a promising new modality, that allows surgeons to access the carotid artery and establish cerebral protection before stent deployment. While prior work has noted TCAR to confer superior outcomes to TFCAS,[30] a contemporary comparison between TCAR and CEA, the standard of care, remains lacking. Evaluating a real-world database, this national analysis reports TCAR to confer largely comparable acute outcomes as CEA in the treatment of carotid artery stenosis among a general population. Specifically, TCAR was found to yield reduced rates of acute MI, but similar incidence of stroke or death. Importantly, to move beyond retrospective analysis alone, we then performed a target

trial emulation and found TCAR to be linked with a 24% relative reduction in hazards of acute MI among high-risk patients. In the absence of gold-standard, RCT evidence, our work represents the most statistically advanced analysis of TCAR versus CEA to date. With implications towards the management of CAS patients, several of these findings merit further discussion.

In this study, we found treatment with TCAR to be linked with similar likelihood of in-hospital mortality and stroke, but lower odds of MI, during the revascularization hospitalization. Moreover, TCAR was associated with comparable likelihood of composite mortality, stroke, and MI, over 90-days following revascularization. These results remained true following comprehensive risk-adjustment, including for symptomatic disease, high-risk designation, patient frailty, and elective case status, and across several rigorous sensitivity analysis. Our work builds upon limited retrospective studies of older datasets and meta-analyses that suggest similar perioperative endpoints between TCAR and CEA.[14,15,31–33] Taken together, we conclude that TCAR is non-inferior to CEA in modern practice, and may indeed confer patient benefit through reduction in periprocedural MI rates.

There are several crucial factors that may underlie these associations. First, by allowing initial direct access to the carotid, TCAR avoids initial catheter interactions with diseased, atherosclerotic aortic vessels – significantly reducing embolization risk.[34,35] TCAR also relies on an ENROUTE system, which uses a supraclavicular cutdown to avoid crossing the carotid lesion without cerebral protection, and provides continuous flow reversal across the procedure.[36] This approach substantially reduces the embolic risk associated with carotid stenting,[37,38] with recent

studies reporting similar incidence between TCAR and CEA of ischemic brain lesions on diffusion-weighted magnetic resonance imaging.[39] Additionally, others have also indicated TCAR to require shorter operative times, relative to CEA, and to more commonly be performed under local or regional anesthesia.[13,14] Reduced exposure to anesthesia and associated hemodynamic stress may contribute to lower MI rates following TCAR, relative to CEA, as noted in our study.

However, in the absence of a RCT, existing literature examining TCAR versus CEA has been restricted to retrospective studies. These investigations have been limited by non-random allocation, the persistent potential for confounding, and an inability to draw causal inference. Despite this sharp lack of level 1 evidence, TCAR now comprises nearly 25% of all revascularization procedures at some centers; this already widespread utilization may actually make a dedicated RCT less likely.[40] Therefore, to directly address these points, we applied a target trial emulation framework, to accurately estimate the causal effect of TCAR on the risk of composite mortality, stroke, and MI, in both low- and high-risk cohorts. Notably, we found comparable hazard of 90-day MAE in the TCAR and CEA protocols among low-risk patients, but reduced hazard of acute MI with the TCAR protocol among high-risk patients. These data encourage strong consideration of TCAR for such patients, while calling for further study of this subgroup. Altogether, our work echoes prior studies demonstrating the baseline non-inferiority of TCAR, but stands as the closest analysis to a gold-standard RCT.

We argue there are several advantages to our analytical method, that move beyond existing retrospective studies. Causal estimates rely on three main assumptions of exchangeability,

consistency, and positivity. To achieve exchangeability, we balanced patients based on relevant patient, disease, and hospital characteristics. While functional status was not available but could influence choice of and outcomes following revascularization, we adjusted for patient frailty as a proxy. We utilized well-defined exposures – receipt of TCAR or CEA – to achieve consistency. Lastly, to achieve positivity, we applied cloning methodology to randomize records to each protocol arm, and utilized inverse probability of censoring weighting to address informative censoring.[41] While we could not specifically ensure that each patient was dually eligible for TCAR and CEA, we performed several subgroup analyses further stratifying patients by symptomatic disease, frailty, and procedural risk to address positivity beyond matching alone. Altogether, these statistical strategies permitted us to directly address the selection bias and confounding present in observational, retrospective studies. We believe this approach is of particular relevance for a comparison between TCAR and CEA; although CMS criteria now reimburse for TCAR among both high- and standard-risk patients, patient profiles may expectedly differ between the two groups. It is particularly encouraging, therefore, that while retrospective studies have often reported lower rates of periprocedural stroke, MI, or death, compared to the single-arm Safety and Efficacy Study for Reverse Flow Used During Carotid Artery Stenting Procedure (ROADSTER) trial, we report comparable rates.[10,42] Finally, while a true RCT considers only select patients at select participating centers, our investigation assessed a pragmatic sample, based on real-world evidence outside of controlled clinical trial settings. Therefore, our work provides the framework, preliminary evidence, and a real-world perspective, for a RCT evaluating these two revascularization modalities.

Finally, we found TCAR to confer a $5,000 incremental increase in per-patient expenditures compared to CEA, across both index hospitalization and over the first 90 days following revascularization. These added TCAR cost requirements expectedly stem from both the stent, valued at ~$2,500, and the premium ENROUTE neuroprotection flow reversal system, priced at $~3,000.[43–45] While prior single center studies have reported TCAR to yield over two fold higher expenditures relative to CEA,[43] our work promisingly identifies a more modest cost differential that appears to be limited to established materials expenses. Although limited by pricing set by manufacturers, it is certainly possible that upfront revascularization costs will continue to decrease with expanded adoption, market penetration, and surgeon experience.[46] Moreover, beyond cost-effectiveness in the acute setting, TCAR has been suggested to contribute to greater quality adjusted life-years in the longer term.[47] Given recent CMS expansion of TCAR eligibility criteria, future studies should consider both cost-effectiveness and quality of life benefit, among the various age, risk, and symptom-stratified subgroups, now eligible for this procedure.

We acknowledge several limitations. Our analysis only considered admissions through calendar year 2022, representing the most contemporary available dataset provided by the Healthcare Cost and Utilization Project. As more data becomes available, future studies should explore potential differences in acute and longer-term endpoints between TCAR and CEA. While a widely utilized administrative dataset that captures a nationally representative sample, the NRD relies on billing practices, which may vary across hospitals or regions. Radiographic and laboratory data is not documented. We could not parse prescription for or adherence to antiplatelet therapy. Symptom onset or severity was also not detailed, nor was extent of plaque. Time to treatment was not reported, yet could impact outcomes, particularly among symptomatic patients. We could not

determine if patients were candidates for both CEA and TCAR. Yet, certain patients may have presented with high carotid lesions or hostile neck anatomy that would have made them ineligible for CEA. As such, while we sought to adjust for known comorbidities, patient frailty, and CMS high risk criteria, we could not exclude the possibility of positivity violations. Therefore, the generalizability of our causal estimates may be limited to those with genuine equipoise between TCAR and CEA. Among CEA cases, we could not ascertain if intraoperative shunting was used; however, we recognize such an approach may be linked with higher rates of stroke or mortality.[48] As TCAR becomes more widely adopted, outcomes may vary by operator experience and hospital familiarity. Moreover, while target trial emulation allows us to estimate a causal effect using observational data, the potential for unmeasured confounders and selection bias stemming from lack of true randomization remains. Finally, future work is needed to consider long-term results, including restenosis, stroke recurrence, and durability of revascularization. Despite these limitations, we applied advanced statistical methods and target trial emulation to consider the independent association of TCAR with 90-day endpoints.

In conclusion, we found TCAR to yield overall similar outcomes as CEA in a general population treated for asymptomatic or symptomatic CAS. Our target trial emulation confirmed non-inferiority of TCAR relative to CEA, and further suggested TCAR to confer reduced rates of MI among a high-risk cohort. Altogether, our data support recent CMS approval of TCAR, and encourage broadened utilization among both standard and high-risk patients. Yet, in this new era of revascularization potential, additional regulation and supervision is needed, to ensure either strategy is performed by clinicians and hospitals with sufficient experience, and patients continue to receive effective and high-quality care.

REFERENCES

1. Cheng SF, Brown MM, Simister RJ, Richards T. Contemporary prevalence of carotid stenosis in patients presenting with ischaemic stroke. *Br J Surg*. 2019;106(7):872-878. doi:10.1002/bjs.11136

2. Walker MD, Marler JR, Goldstein M, et al. Endarterectomy for Asymptomatic Carotid Artery Stenosis. *JAMA*. 1995;273(18):1421-1428. doi:10.1001/jama.1995.03520420037035

3. Ferguson GG, Eliasziw M, Barr HWK, et al. The North American Symptomatic Carotid Endarterectomy Trial. *Stroke*. 1999;30(9):1751-1758. doi:10.1161/01.STR.30.9.1751

4. Yadav JS, Wholey MH, Kuntz RE, et al. Protected Carotid-Artery Stenting versus Endarterectomy in High-Risk Patients. *N Engl J Med*. 2004;351(15):1493-1501. doi:10.1056/NEJMoa040127

5. Gurm HS, Yadav JS, Fayad P, et al. Long-Term Results of Carotid Stenting versus Endarterectomy in High-Risk Patients. *N Engl J Med*. 2008;358(15):1572-1579. doi:10.1056/NEJMoa0708028

6. Brott TG, Hobson RW, Howard G, et al. Stenting versus Endarterectomy for Treatment of Carotid-Artery Stenosis. *N Engl J Med*. 2010;363(1):11-23. doi:10.1056/NEJMoa0912321

7. Krittanawong C, Ang SP, Tangsrivimol JA, et al. Carotid artery stenting versus carotid endarterectomy for symptomatic or asymptomatic extracranial carotid stenosis: A national cohort study. *J Stroke Cerebrovasc Dis*. 2024;33(12):108094. doi:10.1016/j.jstrokecerebrovasdis.2024.108094

8. Mas JL, Arquizan C, Calvet D, et al. Long-Term Follow-Up Study of Endarterectomy Versus Angioplasty in Patients With Symptomatic Severe Carotid Stenosis Trial. *Stroke*. 2014;45(9):2750-2756. doi:10.1161/STROKEAHA.114.005671

9. Malas MB, Leal J, Kashyap V, Cambria RP, Kwolek CJ, Criado E. Technical aspects of transcarotid artery revascularization using the ENROUTE transcarotid neuroprotection and stent system. *J Vasc Surg*. 2017;65(3):916-920. doi:10.1016/j.jvs.2016.11.042

10. Kwolek CJ, Jaff MR, Leal JI, et al. Results of the ROADSTER multicenter trial of transcarotid stenting with dynamic flow reversal. *J Vasc Surg*. 2015;62(5):1227-1234.e1. doi:10.1016/j.jvs.2015.04.460

11. Motaganahalli RL, Jaff M, Kwoleck CJ, MacDonald S, Rudey R, Cambria RP. Pre- and Post-Transcarotid Artery Revascularization Characteristics of Common Carotid Artery: A Post Hoc Analysis of ROADSTER-1 Trial. *J Vasc Surg*. 2017;66(2):e34-e35. doi:10.1016/j.jvs.2017.06.038

12. Malas MB, Dakour-Aridi H, Wang GJ, et al. Transcarotid artery revascularization versus transfemoral carotid artery stenting in the Society for Vascular Surgery Vascular Quality Initiative. *J Vasc Surg*. 2019;69(1):92-103.e2. doi:10.1016/j.jvs.2018.05.011

13. Schermerhorn ML, Liang P, Dakour-Aridi H, et al. In-hospital outcomes of transcarotid artery revascularization and carotid endarterectomy in the Society for Vascular Surgery Vascular Quality Initiative. *J Vasc Surg*. 2020;71(1):87-95. doi:10.1016/j.jvs.2018.11.029

14. Malas MB, Dakour-Aridi H, Kashyap VS, et al. TransCarotid Revascularization With Dynamic Flow Reversal Versus Carotid Endarterectomy in the Vascular Quality Initiative Surveillance Project. *Ann Surg*. 2022;276(2):398. doi:10.1097/SLA.0000000000004496

15. Kashyap VS, King AH, Foteh MI, et al. A multi-institutional analysis of transcarotid artery revascularization compared to carotid endarterectomy. *J Vasc Surg*. 2019;70(1):123-129. doi:10.1016/j.jvs.2018.09.060

16. Malas MB. US Centers for Medicare and Medicaid Services Policy Shift. *JAMA Surg*. 2025;160(3):241-242. doi:10.1001/jamasurg.2024.4797

17. Hernán MA, Wang W, Leaf DE. Target Trial Emulation: A Framework for Causal Inference From Observational Data. *JAMA*. 2022;328(24):2446-2447. doi:10.1001/jama.2022.21383

18. Abbott. Carotid artery stenting coding guide. https://www.cardiovascular.abbott/content/dam/cv/cardiovascular/hcp/reimbursement/vascular/carotid/documents/carotid-artery-stenting-guide.pdf

19. Han JS, Rangwala SD, Liu KQ, et al. Association of carotid endarterectomy at low-volume centers with higher likelihood of major complications and nonroutine discharge. Published online November 24, 2023. doi:10.3171/2023.9.JNS231037

20. Healthcare Cost and Utilization Project. NRD Overview. Accessed March 1, 2022. https://www.hcup-us.ahrq.gov/nrdoverview.jsp

21. Healthcare Cost and Utilization Project. NRD Description of Data Elements. Accessed March 15, 2022. https://www.hcup-us.ahrq.gov/db/nation/nrd/nrddde.jsp

22. van Walraven C, Austin PC, Jennings A, Quan H, Forster AJ. A Modification of the Elixhauser comorbidity measures into a point system for hospital death using administrative data. *Med Care*. 2009;47(6):626-633.

23. Giles KA, Hamdan AD, Pomposelli FB, Wyers MC, Schermerhorn ML. Stroke and death after carotid endarterectomy and carotid artery stenting with and without high risk criteria. *J Vasc Surg*. 2010;52(6):1497-1504. doi:10.1016/j.jvs.2010.06.174

24. Centers for Medicare & Medicaid Services. *Decision Memo CAG-00085R8: Percutaneous Transluminal Angioplasty (PTA) of the Carotid Artery Concurrent with Stenting*.

25. Sakowitz S, Bakhtiyar SS, Curry J, et al. Off-Pump Coronary Artery Bypass Grafting Does Not Confer Superior Outcomes Among Frail Patients. *Am J Cardiol*. 2024;220:16-22. doi:10.1016/j.amjcard.2024.03.017

26. Agency for Healthcare Research and Quality. Using Appropriate Price Indices for Expenditure Comparisons. Accessed March 15, 2022. https://meps.ahrq.gov/about_meps/Price_Index.shtml

27. Zou H, Hastie T. Regularization and variable selection via the elastic net. *J R Stat Soc Ser B Stat Methodol*. 2005;67(2):301-320. doi:10.1111/j.1467-9868.2005.00503.x

28. StataCorp LLC. teffects ipwra- Inverse-probability-weighted regression adjustment. Published online 2023.

29. Hernán MA, Robins JM. Using Big Data to Emulate a Target Trial When a Randomized Trial Is Not Available. *Am J Epidemiol*. 2016;183(8):758-764. doi:10.1093/aje/kwv254

30. Schermerhorn ML, Liang P, Eldrup-Jorgensen J, et al. Association of Transcarotid Artery Revascularization vs Transfemoral Carotid Artery Stenting With Stroke or Death Among Patients With Carotid Artery Stenosis. *JAMA*. 2019;322(23):2313-2322. doi:10.1001/jama.2019.18441

31. Malas MB, Elsayed N, Naazie I, Dakour-Aridi H, Yei KS, Schermerhorn ML. Propensity score-matched analysis of 1-year outcomes of transcarotid revascularization with dynamic flow reversal, carotid endarterectomy, and transfemoral carotid artery stenting. *J Vasc Surg*. 2022;75(1):213-222.e1. doi:10.1016/j.jvs.2021.07.242

32. Wu H, Wang Z, Li M, et al. Outcomes of transcarotid artery revascularization: A systematic review. *Interv Neuroradiol*. 2024;30(3):396-403. doi:10.1177/15910199221123283

33. Gao J, Chen Z, Kou L, Zhang H, Yang Y. The Efficacy of Transcarotid Artery Revascularization With Flow Reversal System Compared to Carotid Endarterectomy: A Systematic Review and Meta-Analysis. *Front Cardiovasc Med*. 2021;8. doi:10.3389/fcvm.2021.695295

34. Ghannam M, AlMajali M, Khasiyev F, et al. Transcarotid Arterial Revascularization of Symptomatic Internal Carotid Artery Disease: A Systematic Review and Study-Level Meta-Analysis. *Stroke*. 2024;55(4):921-930. doi:10.1161/STROKEAHA.123.044246

35. Conway AM, Nguyen Tran NT, Qato K, et al. Complexity of Aortic Arch Anatomy Affects the Outcomes of Transcarotid Artery Revascularization Versus Transfemoral Carotid Artery Stenting. *Ann Vasc Surg*. 2020;67:78-89. doi:10.1016/j.avsg.2020.04.016

36. Alpaslan A, Wintermark M, Pintér L, Macdonald S, Ruedy R, Kolvenbach R. Transcarotid Artery Revascularization With Flow Reversal: The PROOF Study. *J Endovasc Ther*. 2017;24(2):265-270. doi:10.1177/1526602817693607

37. Miccichè E, Condello ,Francesco, Cao ,Davide, et al. Procedural embolic protection strategies for carotid artery stenting: current status and future prospects. *Expert Rev Med Devices*. 2023;20(5):373-391. doi:10.1080/17434440.2023.2198124

38. Naazie IN, Magee GA, Mathlouthi A, Elsayed N, Dakour-Aridi H, Malas MB. Primary mechanism of stroke reduction in transcarotid artery revascularization is dynamic flow reversal. *J Vasc Surg*. 2021;74(1):187-194. doi:10.1016/j.jvs.2020.10.082

39. Pinter L, Ribo M, Loh C, et al. Safety and feasibility of a novel transcervical access neuroprotection system for carotid artery stenting in the PROOF Study. *J Vasc Surg*. 2011;54(5):1317-1323. doi:10.1016/j.jvs.2011.04.040

40. Columbo JA, Stone DH, Martinez-Camblor P, Goodney PP, O'Malley AJ. Adoption and Diffusion of Transcarotid Artery Revascularization in Contemporary Practice. *Circ Cardiovasc Interv*. 2023;16(9):e012805. doi:10.1161/CIRCINTERVENTIONS.122.012805

41. Cole SR, Frangakis CE. The Consistency Statement in Causal Inference: A Definition or an Assumption? *Epidemiology*. 2009;20(1):3. doi:10.1097/EDE.0b013e31818ef366

42. Kashyap VS, Schneider PA, Foteh M, et al. Early Outcomes in the ROADSTER 2 Study of Transcarotid Artery Revascularization in Patients With Significant Carotid Artery Disease. *Stroke*. 2020;51(9):2620-2629. doi:10.1161/STROKEAHA.120.030550

43. Collins V, Adler LSF, Geller JE, et al. Carotid Endarterectomy is Less Expensive than Transcarotid Artery Revascularization. *J Vasc Surg*. Published online March 25, 2025. doi:10.1016/j.jvs.2025.03.192

44. Lajos PS, Bangiyev R, Eslami MH. Single-Center Cost Comparisons of Transcarotid Artery Revascularization, Carotid Endarterectomy and Transfemoral Carotid Stenting. *J Vasc Surg*. 2020;72(1):e204. doi:10.1016/j.jvs.2020.04.348

45. Obeid T, Alshaikh H, Nejim B, Arhuidese I, Locham S, Malas M. Fixed and variable cost of carotid endarterectomy and stenting in the United States: A comparative study. *J Vasc Surg*. 2017;65(5):1398-1406.e1. doi:10.1016/j.jvs.2016.11.062

46. Sridharan ND, Chaer RA, Smith K, Eslami MH. Carotid endarterectomy remains cost-effective for the surgical management of carotid stenosis. *J Vasc Surg*. 2022;75(4):1304-1310. doi:10.1016/j.jvs.2021.09.039

47. Cui C, Ramakrishnan G, Murphy J, Malas MB. Cost-effectiveness of transcarotid artery revascularization versus carotid endarterectomy. *J Vasc Surg*. 2021;74(6):1910-1918.e3. doi:10.1016/j.jvs.2021.05.051

48. Dakour-Aridi H, Gaber MG, Khalid M, Patterson R, Malas MB. Examination of the interaction between method of anesthesia and shunting with carotid endarterectomy. *J Vasc Surg*. 2020;71(6):1964-1971. doi:10.1016/j.jvs.2019.08.248

FIGURE 1: Study CONSORT Diagram
We tabulated 127,054 hospitalization records within the 2021-2022 Nationwide Readmissions Database (NRD). Of the 126,608 records that met study inclusion criteria, 113,004 (90%) received carotid endarterectomy (CEA) and 12,613 (10%) transcarotid artery revascularization (TCAR).

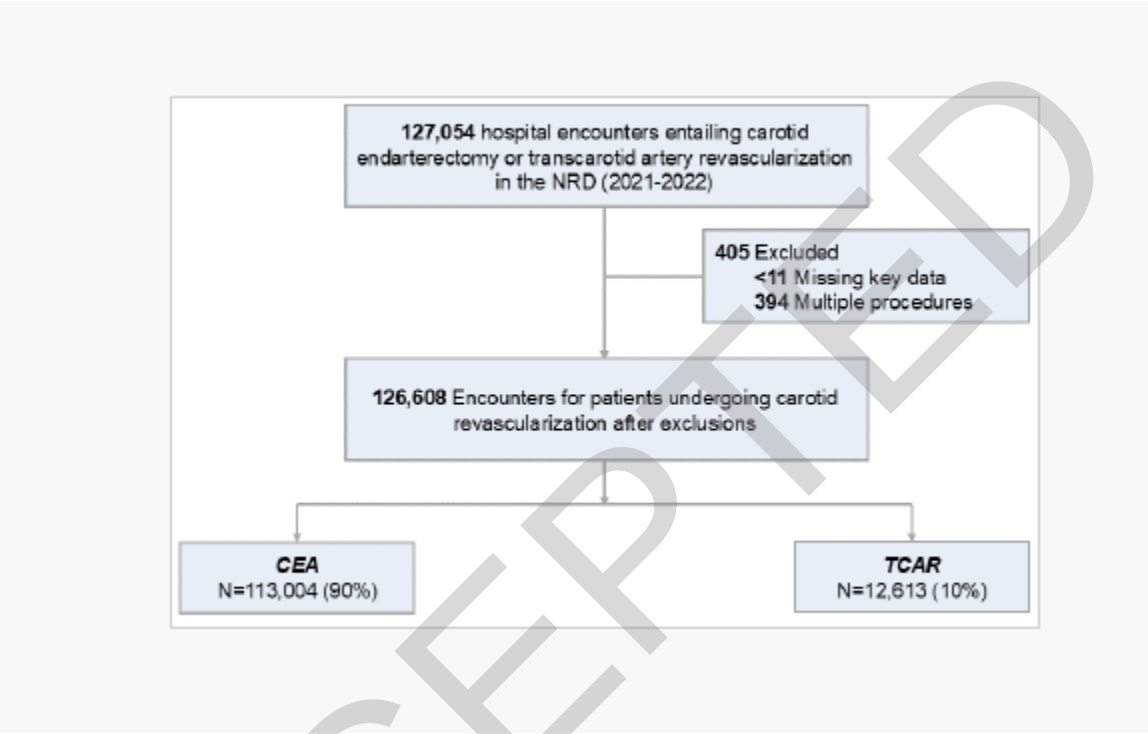

FIGURE 2: Association of TCAR with comparable outcomes as CEA
(A) Patients receiving transcarotid artery revascularization (TCAR) demonstrated comparable incidence of major adverse events (MAE) over 90 days, defined as a composite of death, stroke, and myocardial infarction (MI), relative to carotid endarterectomy (CEA). **(B)** Following comprehensive risk adjustment, receipt of TCAR remained associated with similar MAE at 30- and 90-day. Considering outcomes at index hospitalization, TCAR was linked with comparable in-hospital mortality, stroke, and composite events, but reduced likelihood of acute MI. Composite events comprised MAE, thromboembolism, respiratory failure, endotracheal intubation, mechanical ventilation, seizure, and acute kidney injury. Error bars represent 95% confidence intervals. Reference: CEA.

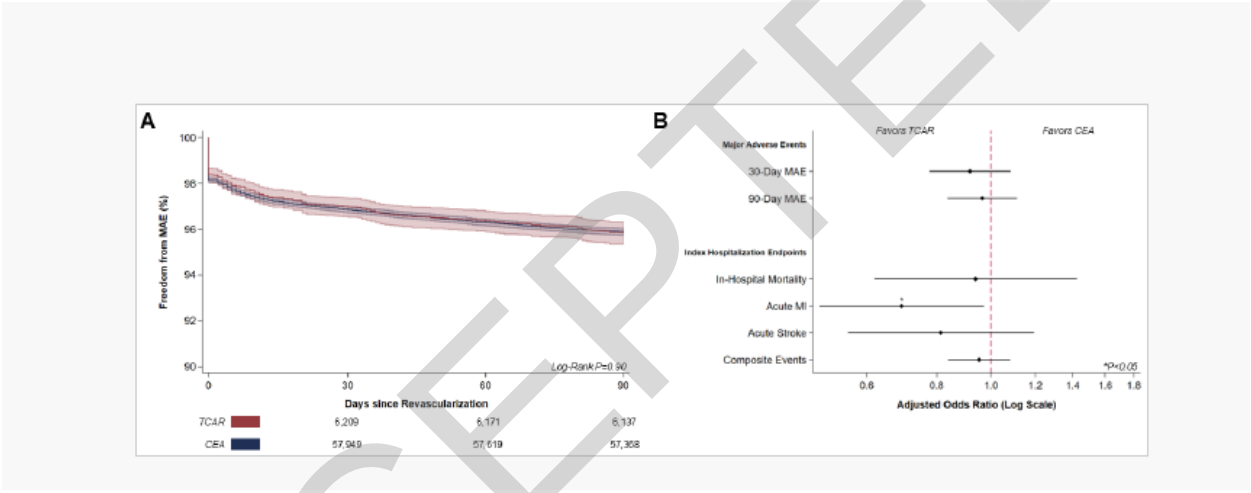

FIGURE 3: Freedom from major adverse events, stratified by high-risk designation
We emulated a target trial using clone-censor-weight methodology to consider the association of transcarotid artery revascularization (TCAR) or carotid endarterectomy (CEA), with major adverse events (MAE), including death, stroke, and acute myocardial infarction. We separately evaluated outcomes of low and high risk patients. High risk status was defined according to Centers for Medicare and Medicaid Services criteria for carotid artery stenosis reimbursement, and was considered >80 years, the presence of renal failure, severe chronic lung disease, recent myocardial infarction, concurrent aortocoronary bypass or cardiac valve surgery, unstable angina, or congestive heart failure. **(A)** Kaplan-Meier time-to-event analysis comparing freedom from MAE among the TCAR (red) and CEA (blue) cohorts among patients considered low risk. **(B)** Analysis evaluating patients considered high risk.

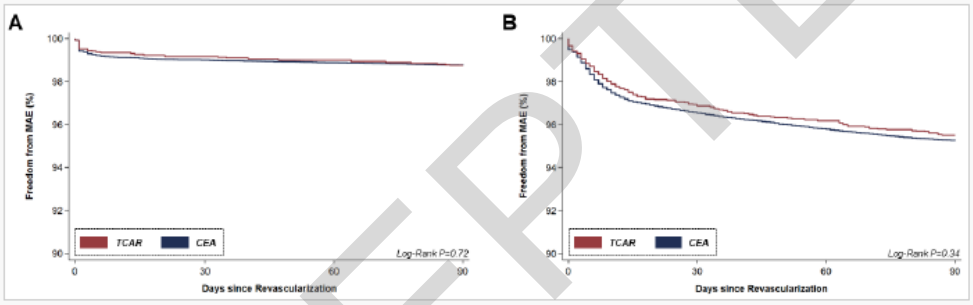

TABLE 1: Demographic, clinical, and hospital characteristics.

Reported as number with group proportions unless otherwise noted. Statistical significance was set at $\alpha = 0.05$.
** IQR*, inter-quartile range

	CEA (n = 113,994)	***TCAR*** (n = 12,613)	***P-value***
Age (years [IQR])	72 [65-78]	74 [67-80]	<0.001
Female sex	45,890 (40)	4,648 (37)	<0.001
Elixhauser Comorbidity Index (median [IQR])	3 [2-4]	3 [2-4]	<0.001
Elective case	89,760 (79)	10,299 (82)	0.02
Symptomatic carotid artery stenosis	9,685 (8)	979 (8)	0.16
High-risk	55,842 (49)	6,905 (55)	<0.001
Frail	4,886 (4)	630 (5)	0.03
Community income percentile			0.004
>75%	19,223 (17)	2,005 (16)	
51-75%	27,196 (24)	3,460 (28)	
26-50%	34,542 (31)	3,844 (31)	
0-25%	31,859 (28)	3,184 (25)	
Primary insurance			<0.001
Private	18,620 (16)	1,599 (13)	
Medicare	85,317 (75)	10,211 (81)	
Medicaid	5,447 (5)	465 (4)	
Other Payer	4,484 (4)	335 (3)	
Comorbidities			
Cardiac arrhythmias	23,822 (21)	3,284 (26)	<0.001
Coronary artery disease	47,450 (42)	5,711 (45)	<0.001
Chronic pulmonary disease	26,385 (23)	2,949 (23)	0.71
Coagulopathy	3,318 (3)	378 (3)	0.79
Congestive heart failure	15,623 (14)	2,176 (17)	<0.001
Diabetes	40,519 (36)	4,354 (35)	0.14
Liver disease	2,045 (2)	247 (2)	0.40
Peripheral vascular disease	22,160 (19)	2,711 (21)	0.002
Valvular disease	9,438 (8)	1,236 (10)	<0.001
Hospital teaching status			<0.001
Non-Metropolitan	5,714 (5)	210 (2)	
Metropolitan Non-Teaching	18,288 (16)	1,585 (13)	
Metropolitan Teaching	89,992 (79)	10,818 (86)	

TABLE 2: Unadjusted and adjusted outcomes among CEA and TCAR recipients
Outcomes reported as proportions or as Adjusted Odds Ratio (AOR) with 95% confidence intervals (95% CI). Major adverse events (MAE) comprised in-hospital death, stroke, or myocardial infarction. Costs are presented in USD. Reference: Non-Vulnerable.
**IQR*, interquartile range; *USD,* United States dollar

	Unadjusted			**Adjusted**		
	CEA	***TCAR***	***P***	***TCAR***	***95% CI***	***P***
Clinical outcomes						
30-day MAE	3.2	2.9	0.36	0.92	0.78-1.08	0.31
90-day MAE	4.1	4.0	0.78	0.97	0.84-1.11	0.63
Index Hospitalization Endpoints						
In-hospital mortality	0.4	0.4	0.71	0.94	0.62-1.42	0.77
Acute stroke	0.6	0.4	0.21	0.81	0.56-1.19	0.29
Acute MI	1.0	0.7	0.03	0.69	0.49-0.97	0.03
Secondary composite events	7.3	7.0	0.56	0.95	0.83-1.07	0.39
Resource utilization						
Duration of stay (days) [IQR]	1 [1-3]	1 [1-2]	<0.001	-0.15	-0.31, 0.005	0.06
Index Costs ($1,000s) [IQR]	13.2 [9.8-19.7]	18.9 [14.1-25.1]	<0.001	+4.88	+4.12, 5.64	<0.001
90-day Costs ($1,000s) [IQR]	14.7 [10.3-24.0]	20.6 [15.0-29.8]	<0.001	+5.39	+4.34, 6.45	<0.001
Non-home discharge	5.0	5.5	0.11	1.11	0.96-1.28	0.16
Readmission within 30 days	5.4	6.2	0.03	1.13	0.99-1.28	0.06