# Quantification of new intracerebral lesions on diffusion-weighted magnetic resonance imaging after transcarotid artery revascularization for treatment of carotid artery stenosis

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## ABSTRACT

**Objective:** Transcarotid artery revascularization (TCAR) has been used with increasing prevalence for treatment of carotid artery stenosis. TCAR holds potential benefits over traditional carotid endarterectomy (CEA) or transfemoral carotid artery stenting by its nature of being less invasive than CEA but more neuroprotective than transfemoral carotid artery stenting. The purpose of this pilot study is to evaluate the effectiveness of the neuroprotection system of TCAR with flow reversal by quantifying the incidence and degree of new intracerebral lesions using diffusion-weighted magnetic resonance imaging (DW-MRI). This study is the first to evaluate these findings in a real-world, high-risk cohort, who would have been excluded from the ROADSTER and ENROUTE transcarotid neuroprotection system DW-MRI studies.

**Methods:** Patients undergoing unilateral TCAR for symptomatic or asymptomatic severe internal carotid artery disease were eligible and prospectively enrolled in the study. All patients had high risk features, including comorbidities or medications, which excluded them from industry-sponsored DW-MRI trials. Patients underwent a preoperative DW-MRI to obtain a baseline intracerebral evaluation within 1 week of the scheduled surgery. The follow-up DW-MRI occurred within 48 hours postoperatively. The primary outcome was new, acute postoperative lesion(s) identified on DW-MRI. Secondary outcomes include any major stroke, myocardial infarction, or death during hospitalization.

**Results:** Five consecutive patients underwent TCAR with preoperative and postoperative imaging. All five patients were on dual antiplatelet therapy before their procedure and verified to be therapeutic on these agents. All patients underwent a right-sided TCAR and three were symptomatic as the indication for their procedure. All five patients demonstrated chronic lesions on the preoperative DW-MRI. Technical success was achieved in all five patients, with one operative complication involving a dissection of the common carotid at the access site, which was stented using the TCAR system. Postoperative DW-MRI did not identify any new intracerebral lesions in any patient following the procedure. No patient had a stroke, myocardial infarction, or death during hospitalization.

**Conclusions:** In this real-world, high-risk cohort, TCAR was completed with no evidence of new, postoperative DW-MRI lesions. These data further demonstrate that TCAR with flow reversal is an effective neuroprotective strategy for carotid revascularization. Further study is warranted to evaluate DW-MRI differences between TCAR and CEA. (J Vasc Surg Cases Innov Tech 2023;9:1-6.)

**Keywords:** TCAR; MRI; Carotid stenosis; Carotid stent; Flow reversal

Atherosclerosis and plaque buildup within the walls of the carotid arteries is a common occurrence that has a multifactorial etiology. As the plaque develops, the carotid lumen can become stenotic with associated transient ischemic attacks (TIAs) or blood clotting if the plaque ulcerates. The most feared outcome of carotid artery disease is ischemic stroke, which has been associated with symptomatic and asymptomatic carotid artery stenosis and constitutes up to 20% of all ischemic strokes.[1] For these reasons, the management of carotid

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artery stenosis has revolved around practices that would result in the best likelihood of preventing a stroke while also having the fewest complications.

Carotid endarterectomy (CEA) is the traditional gold standard for surgical intervention of severe carotid stenosis in symptomatic patients. In the 2000s, carotid artery stenting (CAS) was suggested as a less invasive competing with CEA in treating stenosis. However, several studies including The Carotid Revascularization Endarterectomy vs Stenting Trial (CREST) have demonstrated a greater risk of stroke at four years after CAS in patients more than 70 years old.[2] A systematic review of carotid revascularization studies by Schnaudigel et al[3] involving more than 1000 CAS and more than 700 CEA procedures found new brain lesions measured by diffusion-weighted magnetic resonance imaging (DW-MRI) at 37% and 10%, respectively.

The newest surgical addition to carotid stenosis management has been the increasing use of transcarotid artery revascularization (TCAR), which combines the open surgical exposure of the common carotid artery with carotid stenting. A benefit of TCAR to other strategies is its neuroprotective flow reversal design, by which an arteriovenous shunt between the carotid artery and femoral vein is created to allow distal flow of potential emboli to pass through a filter and then to the venous system instead of traveling to cerebral circulation. The Embolic PROtectiOn System: First-In-Man (PROOF) Study suggests that the TCAR procedure using the MICHI Neuroprotection system (Silk Road, LLC, Sunnyvale, CA) was a viable and safe method of carotid revascularization with none of their patients reaching a primary end point of major stroke, myocardial infarction (MI), or death within 30 days and only 16% of patients with detectable brain lesions by MRI.[4] There has been a relative paucity of research to strongly support the results of this study and there are no studies of a head-to-head trial between CEA and TCAR. This pilot study aims to evaluate the incidence of DW-MRI detectable lesions before and after TCAR in a real-world, nonstudy population.

## METHODS

This is a prospective, single-center, descriptive study. The Research Subjects Review Board approved this study at the University of Rochester. The research study discussed here was supported, in part, with a grant from Silk Road Medical. Silk Road Medical was not involved in the planning, execution, data collection, analysis, or interpretation of the study. Five consecutive patients who underwent TCAR for carotid artery revascularization were recruited into the study. These patients received the standard of care with regard to their perioperative management, with the addition of a preoperative and postoperative DW-MRI. The studies primary end point is the incidence of any new, postoperative lesion(s) on DW-MRI. Secondary end points include any major stroke, MI, or death within 30 days after the surgery. A stroke was defined as any new onset focal or generalized neurological change that persists for more than 24 hours and is unlikely to be related to any other cause other than deleterious changes in cerebral blood flow. MI was defined as elevated troponin with or without electrocardiogram changes. Troponins were only evaluated in the clinical context of chest pain or unexplained hypotension.

**Study population.** Patients were selected based on the need for carotid revascularization and TCAR as the preferred revascularization modality by the vascular surgeons in our practice. Inclusion criteria included being greater than 18 years old and being able to consent to the procedure. To be eligible for the TCAR procedure, patients must have met anatomic and physiological instructions for use criteria. Exclusion criteria included inability to undergo MRI (nonremovable metal implants, unable to lie still for MRI) and baseline dementia or other functional or neurological deficits that would preclude the assessment of new neurological changes.

Both asymptomatic and symptomatic patients were eligible for inclusion. Symptomatic carotid lesions were defined as a TIA and/or stroke within the past 6 months with greater than 50% internal carotid artery stenosis on carotid duplex (based on Strandness criteria) or computed tomographic angiography (CTA) of the neck. Asymptomatic patients were only offered revascularization if they had greater than 80% stenosis on carotid duplex imaging or CTA. All patients deemed to benefit from carotid revascularization underwent a preoperative CTA to assist with case planning. The choice for TCAR versus other revascularization modalities was individualized, based on surgeon preference, and dependent on patient anatomic and physiological factors. All patients included in the study were considered to have high-risk criteria, such as atrial fibrillation or hypercoagulability, which had prevented them from being included in industry sponsored DW-MRI clinical trials.

**TCAR procedure.** The TCAR procedures at the University of Rochester are performed in a standardized fashion, as previously described.[5] The choice of anesthesia for the procedure is an individualized decision among the surgeon, anesthesiologist, and patient to determine the safest and preferred anesthesia modality. We do not routinely perform intraoperative cerebral monitoring or complete cerebral angiography during TCAR cases. A representative for Silk Road Medical, LLC, is present for every case.

**DW-MRI protocol.** MRI is not a typical standard of care for our patients undergoing carotid revascularization. The assessment of cerebrovascular accident or compromise is made clinically through the use of serial neurological examinations before, during, and after the

**Table I.** Patient demographics

| | |
|---|---|
| Age (n = 5) (mean (SD)) | 72 (11.85) |
| Sex (n = 5) | |
| Male | 2 (40) |
| Female | 3 (60) |
| Comorbidities | |
| Hypertension | 3 (60) |
| Coronary artery disease | 4 (60) |
| Congestive heart failure | 1 (20) |
| MI | 2 (40) |
| Hyperlipidemia | 3 (60) |
| Cancer | 1 (20) |
| Atrial fibrillation | 2 (40) |
| Deep vein thrombosis | 2 (40) |
| Pulmonary embolism | 1 (20) |
| Prior CEA | 1 (20) |
| Prior cerebrovascular accident | 2 (40) |
| TIA | 1 (20) |
| Smoking | |
| Current | 1 (20) |
| Never | 0 (0) |
| Former smoker | 4 (80) |
| Preoperative medications | |
| Dual antiplatelet | 5 (100) |
| Aspirin | 5 (100) |
| Clopidogrel | 5 (100) |
| Anticoagulant | 2 (40) |
| Apixaban | 1 (50) |
| Warfarin | 1 (50) |
| Beta-blocker | 1 (20) |
| Statin | 5 (100) |
| Angiotensin-converting enzyme inhibitor | 2 (40) |
| Diuretic | 3 (60) |
| Lesion side | n = 5 |
| Right | 5 (100) |
| Left | 0 (0) |
| Average percent stenosis | 77.80 ± 0.14% |
| Symptomatic | 3 (60) |
| Amaurosis fugax | 2 (40) |
| Contralateral weakness | 2 (40) |
| Acute preoperative lesions | 1 (20) |
| Chronic preoperative lesions | 5 (100) |

*CEA*, Carotid endarterectomy; *MI*, myocardial infarction; *TIA*, transient ischemic attack.
Values are mean ± standard deviation or number (%).

procedure. An MRI screening questionnaire is conducted as a part of standard clinical practice for any patient undergoing an MRI.

Study participants underwent DW-MRI scans using changes in water diffusion as a marker for acute ischemic stroke and cerebral damage. This imaging included sagittal T1 sequences, T2 weighted axial, fluid-attenuated inversion recovery axial, and apparent diffusion coefficient modalities. Susceptibility-weighted imaging was also used in each scan, which is used to look for hemorrhagic transformation. Slice thickness was 4 mm or thinner for every scan. The MRI sequences obtained for this study were the standard-of-care protocols used at our institution for evaluating patients with stroke or concern for stroke. These images were interpreted by board-certified neuroradiologists who were not blinded to procedural details or clinical status. All studies were reviewed by a second neuroradiologist after the fact. If there were disagreements with any of the initial interpretations, the case would have been brought to a group of neuroradiologists for consensus. There were no disagreements between reads for any patient in the study.

A total of two imaging sessions were conducted for each patient in the study. The first occurred within 1 week before the subject's scheduled surgery, and the second imaging session occurred within 48 hours after the surgery, either inpatient or outpatient. The 48-hour time frame was chosen because we wanted to identify strokes related to implantation of the stent during TCAR and acute strokes are best identified within 48 hours of occurrence. The MRI scans were performed at an imaging center run by the University of Rochester.

**Statistical analyses.** Patients were evaluated for a variety of factors. Preoperative patient characteristics, procedural details, and postoperative outcomes were all recorded. Descriptive statistics were used to categorize patient demographics and results.

## RESULTS

Five consecutive patients were enrolled in the study. All eligible participants completed the study. Patient demographics and comorbidities can be seen in Table I. Three of the five patients were women. Additionally, 60% of patients had hypertension, hyperlipidemia, and coronary artery disease. All patients had a history of smoking, with only one patient being an active smoker at the time of study. All five patients were maintained on dual antiplatelet medications and all were verified to be responders to this antiplatelet regimen based on preoperative antiplatelet inhibition assay testing. Two patients were also on therapeutic anticoagulation for a prior history of deep vein thrombosis. Both of these patients had their anticoagulation held for 2 days before the intervention and had their anticoagulation resumed after a 1-week follow-up to ensure a hematoma-free surgical site, according to our standard practice.

All five patients had right-sided carotid lesions and three patients were symptomatic at the time of revascularization. One patient had amaurosis fugax as a presenting symptoms, one had a contralateral weakness, and

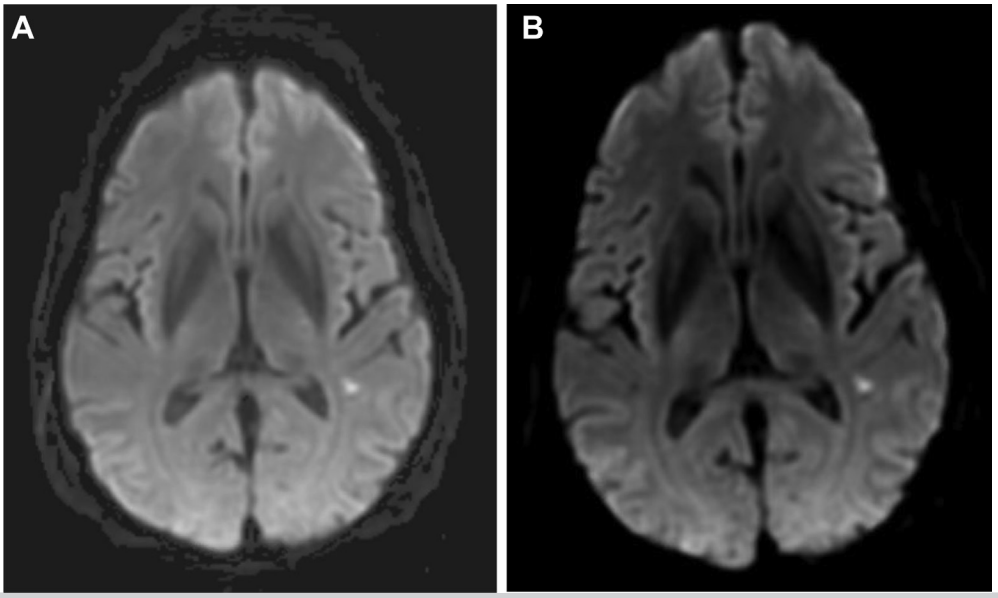


**Fig. A,** Preoperative diffusion-weighted magnetic resonance imaging (DW-MRI) demonstrating acute preoperative lesion in the left temporoparietal lobe. **B,** Postoperative DW-MRI redemonstrating the same preoperative lesion, without any new intracerebral lesions.

one patient had both amaurosis and contralateral weakness. Two patients had a modified Rankin score of 1, and the remaining patients had modified Rankin scores of 0 at the time of revascularization. The average percent stenosis among the participants was 77.8% with a range of 50.0% to 99.0%. All five patients underwent a preoperative MRI. One patient (Fig) was found to have an acute lesion; all five patients had chronic lesions on the preoperative MRI. The patient with an acute lesion was symptomatic; however, the lesion location on MRI did not correlate with the patient's presenting symptoms.

Procedural details can be found in Table II. Sixty percent of the cases were performed under local anesthesia. Mean flow reversal time was 18 minutes ranging from 3 to 64 minutes. Technical success was achieved in all cases with one intraoperative complication—a dissection of the common carotid artery at the access site that occurred during interventional sheath insertion. This event was managed by clamping the proximal common carotid artery to minimize embolization risk before the initial access site was closed. The common carotid artery was reaccessed proximal to the previous access site and dissection. The case was completed in standard fashion and the dissection was corrected by using a longer stent than previously planned and bringing the stent into the common carotid artery at the site of initial access to cover the dissection.

Patient outcomes are detailed in Table III. No patient experienced a new, postoperative lesion on DW-MRI. No postoperative complications were experienced in any of the study participants. No patient experienced a TIA, stroke, MI, or death within 30 days of the procedure. There were no postoperative changes in the modified Rankin score compared with the preoperative baseline. All patients were discharged on postoperative day 1.

## DISCUSSION

This study looked at new intracerebral ischemic lesions following TCAR with DW-MRI. We found no acute postoperative changes in any of our patients. The sample size is small; however, our cohort included high-risk patients who would not have been included in any previous trials. In addition, one patient experienced a significant intraoperative dissection, which placed them at a much higher risk for an acute neurological event. These preliminary data further expand the literature regarding the low stroke risk associated with the TCAR procedure.

The results of our study demonstrate low rates of neurological events after TCAR, similar to other studies. The ROADSTER trial demonstrated a 30-day stroke rate of 1.4% after TCAR.[6] Recent reports of one-year data from ROADSTER 2 show no ipsilateral stroke up to 1 year after TCAR.[7] These data from ROADSTER 2 also included high anatomic or physiological risk patients, similar to our study. Multiple other studies support the safety and efficacy of the TCAR procedure.[8-10]

Other previous MRI studies have looked at postoperative cerebral ischemic events following carotid revascularization. The International Carotid Stenting Study (ICSS) substudy evaluated MRI findings before and after carotid stenting from a transfemoral approach or CEA. The ICSS investigators found 50% of carotid stenting patients to have new ischemic cerebral lesions on postoperative MRI, compared with 17% of patients after CEA.[11] The

**Table II.** Procedural characteristics

| Patient | Symptomatic status | Lesion length, mm | Internal carotid artery diameter, mm | Common carotid artery diameter, mm | Predilation balloon size, mm | Stent size, mm | Flow reversal time, minutes | Anesthesia type | Stenosis by angiography, % |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Asymptomatic | 16 | 4.5 | 7 | 4.5 × 20.0 | 7 × 30 | 7 | Local | 99 |
| 2 | Symptomatic | 20 | 5 | 7.8 | 5 × 30 | 10 × 40 | 5 | Local | 80 |
| 3 | Asymptomatic | 20 | 6 | 8.9 | 6 × 20 | 10 × 30 | 11 | Local | 80 |
| 4 | Symptomatic | 10 | 5 | 7.9 | 5 × 20 | 10 × 30 | 3 | General | 50 |
| 5 | Symptomatic | 23 | 4.6 | 7.1 | 4.5 × 30.0 | 9 × 40 | 64 | General | 80 |

**Table III.** Patient outcomes

| Outcome | No. (%) |
|---|---|
| New white matter lesions | 0 (0) |
| Modified Rankin score change from preoperatively | 0 (0) |
| New TIA or stroke | 0 (0) |
| Postoperative complications | 0 (0) |

*TIA*, Transient ischemic attack.

Embolic PROtectiOn System: First-In-Man (PROOF) Study first evaluated MRI-based neurological changes after TCAR.[4] Their results demonstrated that 16% of patients undergoing the procedure were found to have new intracerebral lesions on MRI. However, none of the patients had any clinical sequelae from the procedure and these lesions were considered silent.

Our results are congruent with this study; we did not observe clinical signs of TIA or stroke, or evidence of postoperative intracerebral ischemic events on MRI. In addition, symptomatic patients only made up 9% of the subjects in the PROOF study; 60% of the patients in our study had symptomatic carotid lesions, indicating a higher risk cohort. Although our study was small, the findings of no new intracerebral lesions after TCAR are starkly improved from the original PROOF study. The difference in results may be due to an evolution of technology and experience in performing the TCAR procedure. Other than the high outlier case with a technical complication, our flow reversal times are decreased compared with the mean flow reversal time of the PROOF study (18 minutes in the PROOF trial). The length of time under flow reversal is a surrogate for case complexity; therefore, longer flow reversal times, by being more complex cases, have an inherently higher risk of embolization during TCAR. However, it does not seem that the length of flow reversal impacted our DW-MRI findings. In addition, all of our patients were intervened upon under the high flow reversal setting. It does not seem that the high versus low setting for flow reversal impacts embolization risk, although the evidence for this assertion is lacking. Modern device technology and more experienced and efficient case conduct may partly account for our improved outcomes. In addition, each of our patients was taking and confirmed to be responders to dual antiplatelet therapy. There was no mention of antiplatelet therapy in the PROOF study. The importance of antiplatelet therapy in CAS has been well-documented and our confirmation of antiplatelet response may have contributed to our improved outcomes after TCAR.[12-14] Finally, it is possible that the small sample size of our study impacts the outcome and that, if this study included a larger sample size, more postoperative DW-MRI lesions may be identified, resulting in similar outcomes to the prior studies.

**Limitations.** The first and most obvious limitation to this study is the limited sample size. We limited the sample size to five patients owing to cost and logistical barriers encountered while organizing the study. Given these promising results, we have begun the process of recruiting more patients to further examine the neurological effects of TCAR. The small sample size limits the generalizability and applicability of our findings, but the results do set the stage for larger studies of this kind and further the understanding of the safety and efficacy of the TCAR procedure. In addition, although this study was prospective, its data are nonblinded and nonrandomized. Unintended bias may have been incorporated into the study process. We attempted to mitigate bias by adhering to our standard preoperative, intraoperative, and postoperative algorithms, other than the preoperative and postoperative DW-MRI. Our objective was to evaluate MRI-detected lesions after TCAR in our real-world, clinical patient population. We achieved this goal and accept the bias and limitations that come with current clinical practice.

## CONCLUSIONS

This study is the first to evaluate new intracerebral ischemic changes on DW-MRI after TCAR in a nonstudy, real-world cohort. We demonstrated no new intracerebral lesions after TCAR, even in one study participant who developed a significant intraoperative complication. These findings support other studies demonstrating a

low risk of acute TIA or stroke after TCAR. Further studies are needed to expand our results to a more extensive study population.

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