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Authors

Solomon, Yoel
Rastogi, Vinamr
Marcaccio, Christina
et al.

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Outcomes after Transcarotid Artery Revascularization Stratified by Pre-procedural Symptom Status

Yoel Solomon, MD^{1,2}, Vinamr Rastogi, MD^{1,3}, Christina L. Marcaccio, MD MPH¹, Priya B. Patel, MD MPH¹, Grace J. Wang, MD MSCE⁴, Mahmoud B. Malas, MD MHS⁵, Raghu L. Motaganahalli, MD⁶, Brian W. Nolan, MD⁷, Hence J.M. Verhagen, MD PhD³, Gert J. de Borst, MD PhD², Marc L. Schermerhorn, MD¹

¹Department of Surgery, Division of Vascular and Endovascular Surgery, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston

²Department of Vascular Surgery, University Medical Center Utrecht, Utrecht, The Netherlands

³Department of Vascular Surgery, Erasmus University Medical Center, Rotterdam, The Netherlands

⁴Division of Vascular Surgery and Endovascular Therapy, Department of Surgery, Hospital of the University of Pennsylvania, Philadelphia

⁵Division of Vascular and Endovascular Surgery, Department of Surgery, University of California San Diego Health System, San Diego

⁶Division of Vascular Surgery, Department of Surgery, Indiana University School of Medicine, Indianapolis

⁷Division of Vascular and Endovascular Therapy, Department of Surgery, Maine Medical Center, Portland

Abstract

Objective: Previous studies on carotid endarterectomy and transfemoral carotid artery stenting demonstrated that perioperative outcomes differed according to pre-operative neurologic injury severity, but this has not been assessed in transcarotid artery revascularization (TCAR). In this study, we examined contemporary perioperative outcomes in patients who underwent TCAR stratified by specific pre-procedural symptom status.

Methods: Patients who underwent TCAR between 2016–2021 in the Vascular Quality Initiative were included. We stratified patients into the following groups based on pre-procedural symptoms: asymptomatic, recent (symptoms occurring <180 days before TCAR) ocular transient ischemic

CORRESPONDING AUTHOR FULL NAME AND ADDRESS: Marc L. Schermerhorn, MD, FACS, Beth Israel Deaconess Medical Center, 110 Francis Street, Suite 5B, Boston, MA 02215, *Telephone:* 617-632-9971, mscherm@bidmc.harvard.edu.

CONFLICTS OF INTEREST:

R.L.M. was a U.S. national P.I. for the DW-MRI TCAR study. H.J.M.V. is a consultant for Medtronic, WL Gore, Terumo, Endologix, Philips. Y.S., V.R., C.L.M., P.B.P., G.J.W., M.B.M., B.W.N., G.J.D.B. and M.L.S. have no conflicts of interest.

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attack (TIA), recent hemispheric TIA, recent stroke, or formerly symptomatic (symptoms occurring >180 days before TCAR). First, we used trend tests to assess outcomes in asymptomatic patients vs those with increasing severity of recent neurologic injury (recent ocular TIA vs recent hemispheric TIA vs recent stroke). Then, we compared outcomes between asymptomatic and formerly symptomatic patients. Our primary outcome was in-hospital stroke/death. Multivariable logistic regression was used to adjust for demographics and comorbidities across groups.

Results: We identified 18,477 TCAR patients of whom 62% were asymptomatic, 3.2% had recent ocular TIA, 7.6% had recent hemispheric TIA, 18% had recent stroke, and 9.2% were formerly symptomatic. In patients with recent symptoms, we observed higher rates of stroke/death with increasing neurologic injury severity: asymptomatic 1.1% vs. recent ocular TIA 0.8% vs. recent hemispheric TIA 2.1% vs. recent stroke 3.1% ($P_{\text{trend}} < .01$). In formerly symptomatic patients, the rate of stroke/death was higher compared with asymptomatic patients, but this difference was not statistically significant (1.7% vs. 1.1%; $P = .06$). After risk adjustment, compared with asymptomatic patients, there was a higher odds of stroke/death in patients with recent stroke (Odds Ratio [OR], 2.8; 95% confidence interval [CI] 2.1–3.7; $P < .01$), recent hemispheric TIA (OR, 2.0; 95% CI, 1.3–3.0; $P < .01$), and former symptoms (OR, 1.6; 95% CI, 1.1–2.5; $P = .02$), but there was no difference in stroke/death in patients with recent ocular TIA (OR, 0.9; 95% CI, 0.4–2.2; $P = .78$).

Conclusion: After TCAR, compared with asymptomatic status, recent stroke and recent hemispheric TIA were associated with higher stroke/death, while recent ocular TIA was associated with similar stroke/death. In addition, a formerly symptomatic status was associated with higher stroke/death compared with an asymptomatic status. Overall, our findings suggest that classifying TCAR patients as symptomatic versus asymptomatic may be an oversimplification and that patients' specific pre-operative neurologic symptoms should instead be used in risk assessment and outcome reporting for TCAR.

TABLE OF CONTENTS SUMMARY

In this retrospective analysis of TCAR patients, we found that in-hospital outcomes varied by severity of pre-procedural neurologic symptoms, and even patients with remote neurologic symptoms had worse outcomes than asymptomatic patients. Overall, our findings suggest that patients' specific neurologic symptoms should be used in pre-operative risk assessment.

Keywords

Carotid artery stenosis; Transcarotid artery revascularization; Carotid artery stenting; Cerebrovascular disease; Stroke

INTRODUCTION

Various studies have shown that patients undergoing carotid revascularization for symptomatic carotid artery disease have worse perioperative outcomes compared with asymptomatic patients.^{1,2} Because of these findings, pre-operative symptom status is an important consideration in risk stratification and clinical trials reporting standards.^{3–9} However, patients with symptomatic carotid artery disease present with various degrees of

neurological injury such as stroke, hemispheric transient ischemic attack (TIA), and ocular TIA, which may differentially impact outcomes.

Two studies investigating carotid endarterectomy (CEA) and transfemoral carotid stenting (tfCAS) have shown that patients with pre-operative stroke had higher post-operative stroke/death rates compared with patients who experienced pre-operative hemispheric or ocular TIA.^{10,11} Therefore, these studies suggested that the current method in which all symptomatic patients are grouped together should be avoided to allow for a more accurate pre-operative risk assessment of outcomes following CEA or tfCAS, although this has not been assessed for transcarotid artery revascularization (TCAR).

Furthermore, within the current carotid revascularization literature and guidelines, patients with carotid artery disease are considered to be symptomatic only if a cerebrovascular event has occurred within 6 months of revascularization.¹²⁻¹⁴ This however, would imply that patients experiencing cerebrovascular events over 6 months prior to revascularization (formerly symptomatic patients) are considered to be asymptomatic and often are stratified that way in trials.^{1,12,13} Nevertheless, the appropriateness of grouping the formerly symptomatic and asymptomatic cohorts together has not been validated within the context of TCAR.

Thus, in this study we examined contemporary perioperative outcomes in patients who underwent TCAR stratified by their specific pre-procedural symptom status.

METHODS

Registry

We used data from the Vascular Quality Initiative (VQI) carotid stenting registry, which includes data from over 600 centers in the United States. The VQI consists of regional quality care groups who prospectively collect clinical data of vascular procedures to improve patient care (<https://www.vqi.org>). Data on patient characteristics, procedure information, and in-hospital outcomes are captured in over 200 variables. The Institutional Review Board at Beth Israel Deaconess Medical Center approved this study and waived the need for informed consent due to the retrospective, de-identified nature of the data.

Patient cohorts

We included patients who underwent TCAR between January 2016 and August 2021 (N=22,881). We excluded patients with inadequate data on ipsilateral pre-procedural symptom status and timing thereof (N = 4,229), patients with traumatic, dissection, or fibromuscular dysplasia lesions (N = 154), patients with planned concomitant intracranial procedures (N = 10), and patients under the age of 18 years (N = 11).

We stratified TCAR patients into the following groups based on pre-procedural carotid symptom status: asymptomatic, recent (meaning: having experienced symptoms <180 days before TCAR) ocular TIA, recent hemispheric TIA, recent stroke, or formerly symptomatic (prior stroke and/or TIA occurring >180 days before TCAR) in accordance with current guidelines.^{14,15} Recent stroke was defined as ocular or cortical symptoms lasting more than

24 hours. Recent hemispheric TIA was defined as cortical symptoms lasting a maximum of 24 hours. Recent ocular TIA was defined as solely having a full or partial visual loss due to a retinal embolism lasting a maximum of 24 hours. Patients with multiple types of symptoms were grouped according to their most severe symptom in the following order of severity: stroke, hemispheric TIA, ocular TIA.

Variable definitions

Patients were defined as Non-Hispanic White, Black, Asian, Hispanic, or other, and race/ethnicity data were either self-reported or determined from chart review. Body mass index (BMI) was calculated according to the weight(kg)/height(m)² formula. Underweight was defined as a BMI <18.5 kg/m² and obesity was defined as a BMI >30 kg/m². Pre-operative degree of ipsilateral stenosis was measured by carotid duplex, CT angiography, magnetic resonance angiography, and/or arteriogram. To calculate the estimated glomerular filtration rates (eGFR), the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula was used.¹⁶ We specified time to intervention after symptom onset as 0–2 days, 3–14 days, and >14 days per current guidelines.¹⁴ High risk for CEA criteria were defined per the Centers for Medicare and Medicaid Services (CMS) decision memo as medical or anatomic high risk criteria.¹⁷ Medical high risk criteria included: age ≥ 80 years old, congestive heart failure class III/IV according to the New York Heart Association Functional Classification, unstable angina, prior myocardial infarction in the prior 6 months, or a severe pulmonary disease. Anatomic high risk criteria were defined as one of the following: a history of ipsilateral CEA, contralateral carotid occlusion, a lesion below the clavicle, prior neck radiation, neck stoma, laryngeal nerve palsy, or prior neck surgery. We calculated annual TCAR volume by using unique numbers in VQI assigned to participating centers and physicians performing TCARs. We categorized the annual volume into quintiles and then defined low volume as the lowest quintile. The lowest quintile of performed TCARs was 3 TCARs for centers and <1 TCARs for physicians.

Outcomes

Our primary outcome was a composite endpoint of any in-hospital ipsilateral or contralateral stroke or death (stroke/death). Secondary outcomes included any in-hospital ipsilateral or contralateral stroke, death, myocardial infarction (MI), and length of hospital stay of over two days (prolonged LOS). Post-operative myocardial infarction was defined in the VQI as a rise and/or fall of cardiac biomarkers with at least one of the values in the abnormal range for that laboratory with clinical symptoms or electrocardiogram changes indicative for new ischemia.

Statistical analysis

First, we compared post-operative outcomes in asymptomatic patients versus those with increasing severity of recent neurologic injury: asymptomatic vs recent ocular TIA vs recent hemispheric TIA vs recent stroke. Then, we compared outcomes between asymptomatic and formerly symptomatic patients. Furthermore, we stratified the formerly symptomatic cohort by specific symptom status to examine the sample sizes and in-hospital stroke/death rates. Finally, within the recently symptomatic patient cohort, we compared the primary outcome by specific symptom status and time to repair (<2 days vs. 3–14 days vs. 14–180 days).

Categorical variables were presented as numbers and percentages, and continuous variables were presented as mean \pm standard deviation for normally distributed variables or as median and interquartile range (IQR) for non-normally distributed variables. Cuzick's extension of the Wilcoxon rank-sum test to assess trends was used to examine outcome trends by increasing symptom severity.¹⁸ Univariate comparisons were performed using the Wilcoxon rank-sum test or Kruskal-Wallis test for continuous variables, and the χ^2 or Fisher's exact tests for bicategorical or multicategorical variables, respectively.

We used multivariable logistic regression to assess the risk-adjusted association between pre-procedural symptom status and in-hospital stroke/death. Previously identified risk factors were selected in the model *a priori*, and included the following: age, sex, race, ethnicity, hypertension, diabetes mellitus, congestive heart failure, coronary artery disease, current smoking status, chronic obstructive pulmonary disease (COPD), dialysis status, eGFR < 30 mL/min, low TCAR volume by center, low TCAR volume by physician, and pre-operative use of: aspirin, statin, P2Y12 inhibitors, anticoagulants. We used asymptomatic status as the reference group for all comparisons *a priori* because asymptomatic patients tend to have the lowest frequency of complications.

All variables had <3% missing data. All tests were two-sided, and $\alpha < .05$ was considered statistically significant. All analyses were performed using Stata version 14.2 (StataCorp LP, College Station, TX).

RESULTS

A total of 18,477 patients undergoing TCAR were included in the analysis. Median age was 74 years (IQR: 67, 80) and 6,773 (37%) patients were female. Stratified by pre-procedural symptoms, 3,417 (18%) of patients had recent stroke, 1,408 (7.6%) had recent hemispheric TIA, 597 (3.2%) had recent ocular TIA, 5,422 (9.2%) were formerly symptomatic, and 11,363 (62%) were asymptomatic. Patient characteristics are presented in Table I.

Asymptomatic vs. recent ocular TIA vs. recent hemispheric TIA vs. recent stroke

Demographics—Compared with all other groups, patients with recent stroke were more likely to be Black, current smokers, have a history of diabetes, and to be treated with pre-procedural statin or anticoagulant therapy (Table I). In addition, recent stroke patients were less likely to have a history of coronary artery disease, to undergo intervention >14 days after symptom onset, or to be treated at low volume centers or by low volume physicians.

Unadjusted outcomes—We observed greater stroke/death rates with increasing severity of recent neurologic injury between asymptomatic vs. recent ocular TIA vs. recent hemispheric TIA vs. recent stroke patients (1.1% vs. 0.8% vs. 2.1% vs. 3.1%; $P_{\text{trend}} < .01$; Table II). Furthermore, with increasing neurologic injury, we observed greater rates of in-hospital stroke, death, and prolonged LOS. There were no significant trends in MI rates when comparing asymptomatic vs. recent ocular TIA vs. recent hemispheric TIA vs. recent stroke patients.

Asymptomatic vs. formerly symptomatic

Demographics—Compared with asymptomatic patients, formerly symptomatic patients were more likely to be Black, to have a lower median age, to have a history of hypertension, diabetes, COPD, or congestive heart failure, or to be treated with pre-procedural statin, P2Y12 inhibitor or anticoagulant therapy (Table I). Finally, formerly symptomatic patients were less likely to be underweight when compared with asymptomatic patients.

Unadjusted outcomes—Formerly symptomatic patients trended towards a higher stroke/death rate compared with asymptomatic patients (1.7% vs. 1.1%; $P = .06$), but had significantly higher rates of in-hospital stroke (1.5% vs. 0.9%; $P = .02$; Table III). There were no differences in rates of in-hospital death, MI, or prolonged LOS between asymptomatic and formerly symptomatic patients.

Formerly symptomatic – stratified by specific prior symptoms

When examining formerly symptomatic patients by their specific pre-procedural symptoms, 151 (9%) had prior ocular TIA, 384 (23%) had prior hemispheric TIA, and 1,157 (68%) patients had prior stroke (Table IV). In-hospital stroke/death rates among formerly symptomatic patients varied by increasing severity of neurologic injury: prior ocular TIA (0.7%), prior hemispheric TIA (1.6%), prior stroke (1.8%).

Recently symptomatic – stratified by time to repair

Within patients with recent ocular TIA, there was no significant trend of in-hospital stroke/death with increasing time to repair (< 2 days vs. 3–14 days vs. 14–180 days: 0.0% vs. 0.7% vs. 0.9%; $P_{\text{trend}} = .64$; Table V). Within patients with recent hemispheric TIA, we observed a non-significant trend of lower in-hospital stroke/death with increasing time to repair (4.3% vs. 2.2% vs. 1.6%; $P_{\text{trend}} = .08$). Finally, recent stroke patients displayed a significant trend of lower in-hospital stroke/death with increasing time to repair (5.6% vs. 3.6% vs. 2.4%; $P_{\text{trend}} < .01$).

Unadjusted outcomes - stratified by degree of stenosis

When evaluating in-hospital stroke/death stratified by specific pre-procedural symptoms and degree of stenosis, we observed greater stroke/death rates with increasing severity of recent neurologic injury between asymptomatic vs. recent ocular TIA vs. recent hemispheric TIA vs. recent stroke patients when they either had ipsilateral stenosis $\geq 80\%$ (1.2% vs. 1.0% vs. 1.9% vs. 3.2%; $P_{\text{trend}} < .01$) or ipsilateral stenosis $< 80\%$ (1.1% vs. 0.5% vs. 2.2% vs. 2.9%; $P_{\text{trend}} < .01$; Supplemental Table I).

Formerly symptomatic patients trended towards a higher stroke/death rate compared with asymptomatic patients when they had ipsilateral stenosis $< 80\%$ (2.0% vs. 1.1%; $P = .06$; Supplemental Table II). There were no differences in stroke/death rate between asymptomatic and formerly symptomatic patients with ipsilateral stenosis $\geq 80\%$.

Multivariable analysis

After risk-adjustment, compared with an asymptomatic status, we observed higher odds of stroke/death with recent stroke (odds ratio [OR] OR 2.8; 95% confidence interval [CI] 2.1–3.7; $P < .01$), recent hemispheric TIA (OR 2.0; 95% CI 1.3–3.0; $P < .01$), and a formerly symptomatic status (OR 1.6; 95% CI 1.1–2.5; $P = .02$; Table VI). Meanwhile, recent ocular TIA was associated with similar stroke/death when compared with an asymptomatic status (OR 0.9; 95% CI 0.4–2.2; $P = .78$).

DISCUSSION

In this retrospective observational study of 18,477 patients who underwent TCAR, we demonstrated that perioperative outcomes varied based on patients' specific pre-procedural symptom status. After risk-adjustment, patients with recent stroke or recent hemispheric TIA had higher in-hospital stroke/death compared with asymptomatic patients, while those with recent ocular TIA had similar stroke/death compared with asymptomatic patients. Furthermore, formerly symptomatic patients (with neurologic symptoms >180 days pre-procedure) had higher stroke/death compared with an asymptomatic patients. These findings support stratifying patients based on specific neurologic symptoms to improve pre-operative risk assessment.

Our finding that increasing severity of recent neurologic injury was associated with higher in-hospital stroke/death after TCAR is consistent with current evidence in other methods of carotid revascularization. A study examining contemporary perioperative outcomes after CEA suggested that a history of recent stroke was associated with a higher risk of adverse outcomes compared with a history of recent ocular TIA or an asymptomatic status.¹⁰ Furthermore, a recent study investigating outcomes after tFCAS stratified by specific symptom status reported higher stroke/death after recent stroke when compared with recent hemispheric TIA (OR, 2.6; 95% CI, 1.6–4.3; $P < .01$), and a trend towards higher stroke/death after recent stroke when compared with recent ocular TIA (OR, 2.0; 95% CI, 1.0–3.9; $P = .06$).¹¹ In addition, when stratifying outcomes in our study by degree of stenosis and specific symptom status, the trend of higher stroke/death with increasing recent symptom severity remained significant. This suggests that degree of stenosis did not explain differences in outcome between patient cohorts stratified by prior symptom status. Collectively, these findings suggest that patients undergoing carotid revascularization for recent neurologic symptoms should be stratified based on their specific pre-procedural symptoms, rather than being grouped together as “symptomatic”. This granularity may improve pre-operative risk assessment and accuracy of outcome reporting in future trials.

We observed a similar rate of stroke/death in patients with ocular TIA when compared with patients with an asymptomatic status (0.8% vs 1.1%; $P = .52$). Although not always significantly different, previous studies have shown that an asymptomatic status is more benign than ocular TIA.^{10,11} Otherwise, our findings may reflect differences in outcomes with TCAR compared with other carotid revascularization techniques, or our findings may be a result of low statistical power due to low event rates in the recent ocular TIA cohort. Nonetheless, perioperative stroke/death in recent ocular TIA patients was not significantly

different compared with stroke/death in asymptomatic patients after TCAR or CEA, which further supports stratification by specific pre-procedure symptom status.

Compared with an asymptomatic status, we found higher odds of stroke/death with a formerly symptomatic status (symptoms >180 days prior to TCAR), primarily amongst those with prior hemispheric TIA or prior stroke. Our findings on this front were similar to findings in a previous analysis of outcomes after tfCAS, in which a significantly lower stroke/death association was demonstrated in patients with an asymptomatic status compared with patients who were formerly symptomatic (OR, 0.4; 95% CI 0.2–0.6; $P < .01$).¹¹ When grouping formerly symptomatic and asymptomatic patients, a high proportion of formerly symptomatic patients defined as asymptomatic may result in inflated adverse outcome rates for the asymptomatic patient cohort. Nevertheless, although our findings suggest that grouping formerly symptomatic patients and asymptomatic patients may lead to skewed results, multiple previous and ongoing trials investigating carotid stenting have defined formerly symptomatic patients as asymptomatic.^{1,12,13,19} Thus, our findings advocate for regarding formerly symptomatic patients as higher at risk for perioperative stroke/death compared with asymptomatic patients, and for stratification between these groups to improve veracity in outcome reporting in future TCAR trials.

When stratifying outcomes by time to repair, patients with recent stroke displayed a significant trend of lower stroke/death rates with increasing time to TCAR. This finding is in line with a recent study which found lower perioperative stroke/death rates when carotid revascularization was delayed beyond 14 days in patients with symptomatic carotid disease who underwent CEA.²⁰ Although these data might suggest that the risk of perioperative stroke/death decreases with increasing time to repair, this is only part of the story. In order to determine benefit after delayed TCAR, natural history risks of recurrent events, patients that were treated medically, and patients that died before intervention (and thus were not included in the VQI) need to be considered. Further population based studies are needed to determine the optimal time to repair for TCAR.

As we still are in the early years of TCAR, the SVS and European Society for Vascular Surgery (ESVS) guidelines for management of carotid disease do not make distinctions by specific pre-procedural neurologic symptoms within symptomatic patients or between asymptomatic and formerly symptomatic patients.^{14,15} The SVS and ESVS clinical practice guidelines recommend a perioperative stroke/death rate <6% in recently symptomatic patients and <3% in asymptomatic patients to ensure benefit after carotid revascularization.^{14,15,21} The most recent European Stroke Organisation guidelines even propose acceptable in-hospital stroke/death rate thresholds of <4% in recently symptomatic patients and <2% in asymptomatic patients.²² All recently symptomatic patient cohorts in our study had a stroke/death rate well below <4% which would meet guidelines recommendations based on the anticipated stroke/death rate. As for asymptomatic and formerly symptomatic patients, we found in-hospital stroke/death rates of 1.1% and 1.7%, respectively, which would qualify both asymptomatic and formerly symptomatic patients for treatment with TCAR according to guideline criteria. Although promising, future studies are needed to determine the full scope of utilization prospects for TCAR.

As this study was a retrospective review of prospectively collected data, the results of this study must be interpreted within the context of its design. Limitations that are inherent to large clinical registries have to be considered. Data in VQI are self-reported, though to curtail such limitations, the VQI conducts annual audits to review the submitted clinical data.²³ We could not include additional information on carotid lesion severity in our study due to limited data. However, a sensitivity analysis showed that the trend of outcomes in our study remained the same when including these variables on carotid lesion severity. Moreover, routine follow-up by a neurologist is not a requirement. Another limitation in our study is that the broad majority of patients who underwent TCAR were at high risk for CEA, which made it harder to put our findings in the context of patients with low surgical risk. This question should be addressed in future trials. Despite these limitations, this study provides a contemporary view of in-hospital outcomes after TCAR, stratified by specific pre-procedural symptom status.

Conclusion

Compared with asymptomatic status, recent stroke or recent hemispheric TIA were associated with higher in-hospital stroke/death, whereas recent ocular TIA was associated with similar in-hospital stroke/death. In addition, compared with asymptomatic status, a formerly symptomatic status was associated with higher in-hospital stroke/death. Our findings support that worse neurological injuries prior to TCAR are associated with higher in-hospital complications. Moreover, although our findings might suggest that delay of TCAR may benefit patients with recent stroke, these data need to be considered against the natural course outcome in the weeks after symptom onset and further population based studies are needed to determine the benefit of delayed TCAR. Adding specific stratification based on pre-procedural symptom status would improve clinical pre-operative risk assessment and accuracy of outcome reporting in future carotid revascularization trials.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ARTICLE HIGHLIGHTS**Type of Research:**

Retrospective cohort study of prospectively collected data from the Vascular Quality Initiative registry.

Key Findings:

Following transcarotid artery revascularization (TCAR) in symptomatic patients, increasing pre-procedural neurologic injury (prior ocular TIA vs. prior hemispheric TIA vs. prior stroke) was associated with higher in-hospital stroke/death. Furthermore, patients who experienced neurologic symptoms >180 days prior to TCAR had higher in-hospital stroke/death compared with asymptomatic patients.

Take home Message:

To improve pre-operative risk assessment for patients undergoing TCAR, and to increase accuracy in future TCAR studies, patients should be stratified by their specific pre-procedural symptom status. Additionally, patients with symptoms >180 days prior to TCAR should be distinguished from asymptomatic patients.

Univariable analysis of patient characteristics and procedural details stratified by specific pre-procedural symptom status

Table 1:

	Asymptomatic	Ocular TIA	Hemispheric TIA	Stroke	Formerly Symptomatic
N	11363	597	1408	3417	1692
Age, median (IQR)	74 (68, 80)	73 (66, 79)	75 (68, 81)	74 (66, 80)	73 (67, 79)
Female sex	4218 (37)	193 (32)	537 (38)	1224 (36)	601 (36)
Race/ethnicity					
White	10105 (91)	543 (93)	1251 (91)	2894 (87)	1464 (89)
Black	448 (4.0)	13 (2.2)	62 (4.5)	242 (7.3)	95 (5.7)
Asian	98 (0.9)	7 (1.2)	13 (0.9)	37 (1.1)	19 (1.1)
Hispanic	417 (3.8)	19 (3.3)	48 (3.5)	154 (4.6)	75 (4.5)
Other	60 (0.5)	7 (1.2)	7 (0.5)	16 (0.5)	10 (0.6)
Obese (BMI>30)	3734 (33)	195 (33)	491 (35)	1126 (33)	589 (35)
Underweight (BMI<18.5)	252 (2.2)	8 (1.3)	27 (1.9)	74 (2.2)	22 (1.3)
Hypertension	10310 (91)	535 (90)	1280 (91)	3097 (91)	1570 (93)
Any diabetes	4179 (37)	172 (29)	529 (38)	1450 (42)	676 (40)
Current smoker	2392 (21)	143 (24)	269 (19)	849 (25)	366 (22)
COPD	2899 (26)	164 (28)	340 (24)	839 (25)	488 (29)
CHF	1871 (17)	79 (13)	248 (18)	599 (18)	323 (19)
CAD	6247 (55)	270 (45)	664 (47)	1473 (43)	911 (54)
Ipsilateral stenosis 80%	7944 (71)	390 (66)	773 (55)	1793 (53)	1081 (64)
Pre-procedure renal function					

	Asymptomatic	Ocular TIA	Hemispheric TIA	Stroke	Formerly Symptomatic
eGFR >60 mL/min	6747 (60)	378 (64)	889 (63)	2244 (66)	1007 (60)
eGFR 30–60 mL/min	4015 (36)	190 (32)	452 (32)	1003 (30)	584 (35)
eGFR <30 mL/min	370 (3.3)	14 (2.4)	37 (2.6)	105 (3.1)	61 (3.6)
On dialysis	152 (1.3)	13 (2.2)	25 (1.8)	45 (1.3)	31 (1.8)
Procedure timing after symptom onset					
2 days		26 (4.4)	115 (8.2)	197 (5.8)	
3–14 days		135 (23)	550 (39)	1462 (43)	
>14 days		436 (73)	743 (53)	1758 (51)	
Pre-procedure medication					
Aspirin	10187 (90)	552 (93)	1288 (92)	3120 (91)	1509 (89)
Statin	10164 (90)	534 (89)	1237 (88)	3115 (91)	1544 (91)
Betablocker	6605 (58)	322 (54)	777 (55)	1808 (53)	1009 (60)
P2Y12 inhibitors	9957 (88)	530 (89)	1216 (86)	3015 (88)	1521 (90)
Anticoagulant	1494 (13)	67 (11)	211 (15)	516 (15)	310 (18)
ACE-inhibitor	6243 (55)	290 (49)	741 (53)	1660 (49)	914 (54)
High-Risk factors					
No factors	491 (4.3)	16 (2.7)	28 (2.0)	76 (2.2)	76 (4.5)
Anatomic	7209 (64)	404 (68)	845 (60)	2162 (63)	1085 (64)
Medical	271 (2.4)	14 (2.3)	19 (1.3)	52 (1.5)	47 (2.8)
Anatomic & Medical	3376 (30)	163 (27)	516 (37)	1126 (33)	484 (29)
Low volume center (3 cases)*	2466 (22)	127 (21)	246 (18)	579 (17)	374 (22)

	Asymptomatic	Ocular TIA	Hemispheric TIA	Stroke	Formerly Symptomatic
Low volume physician (<1 cases)*	2376 (21)	123 (21)	261 (19)	584 (17)	371 (22)

TIA, transient ischemic attack; IQR, interquartile range; BMI, body mass index; COPD, chronic obstructive pulmonary disease; CHF, congestive heart failure; CAD, coronary artery disease; eGFR, estimated glomerular filtration rate; HR, High-risk; TCAR, transcarotid artery revascularization. Variables are presented as numbers (%).

* TCARs performed by centers or physicians of whom the number of performed TCARs in the last 12 months was in the lowest quintile by volume

Unadjusted in-hospital outcomes after transcatheter aortic valve replacement stratified by specific pre-procedural symptom status

Table II:

	Asymptomatic	Ocular TIA	Hemispheric TIA	Stroke	P _{trend}
N	11363	597	1408	3417	
Stroke/death	127 (1.1)	5 (0.8)	29 (2.1)	105 (3.1)	<.01
Stroke	100 (0.9)	5 (0.8)	25 (1.8)	92 (2.7)	<.01
Mortality	34 (0.3)	1 (0.2)	5 (0.4)	26 (0.8)	<.01
MI	66 (0.6)	2 (0.3)	8 (0.6)	26 (0.8)	.30
LOS > 2 days	1180 (10)	68 (11)	257 (18)	948 (28)	<.01

TIA, transient ischemic attack; MI, myocardial infarction; LOS, hospital length of stay. Values are presented as numbers (%).

Unadjusted in-hospital outcomes after transcatheter aortic valve stenting stratified by pre-procedural symptom status

Table III:

In-hospital outcomes	Asymptomatic	Formerly Symptomatic	P-value
N	11363	1692	
Stroke/death	127 (1.1)	28 (1.7)	.06
Stroke	100 (0.9)	25 (1.5)	.02
Mortality	34 (0.3)	5 (0.3)	.98
MI	66 (0.6)	8 (0.5)	.58
LOS > 2 days	1180 (10)	194 (12)	.18

MI, myocardial infarction; LOS, hospital length of stay. Values are presented as numbers (%).

Formerly symptomatic patient cohort stratified by specific pre-procedural symptom status and unadjusted in-hospital stroke/death rates after transcatheter aortic valve replacement

Table IV:

	Sample size	In-hospital stroke/death
N	1692	
Prior stroke	1157 (68)	21 (1.8)
Prior hemispheric TIA	384 (23)	6 (1.6)
Prior ocular TIA	151 (8.9)	1 (0.7)

TIA, transient ischemic attack. Values are presented as numbers (%).

Unadjusted in-hospital stroke/death rates in the recently symptomatic patient cohort stratified by specific pre-procedural symptom status and time to repair after transcarotid artery revascularization

Table V:

	2 days	3–14 days	14–180 days	P_{trend}
Recent ocular TIA	0 (0.0)	1 (0.7)	4 (0.9)	.64
Recent hemispheric TIA	5 (4.3)	12 (2.2)	12 (1.6)	.08
Recent stroke	11 (5.6)	52 (3.6)	42 (2.4)	<.01

TIA, transient ischemic attack. Values are presented as numbers (%).

Association between pre-procedural symptom status and in-hospital stroke or death after transcatheter aortic valve replacement

Table VI:

	OR	95% CI	P-value
Asymptomatic		Reference	
Ocular TIA	0.9	0.4 – 2.1	.76
Hemispheric TIA	2.0	1.3 – 3.0	<.01
Stroke	2.8	2.1 – 3.8	<.01
Formerly symptomatic	1.6	1.1 – 2.5	.02

OR, odds ratio; CI, confidence interval; TIA, transient ischemic attack.

Adjusted for: age, sex, race, hypertension, current smoking status, any diabetes mellitus, congestive heart failure, coronary artery disease, COPD, dialysis status, eGFR < 30 mL/min, ipsilateral stenosis 80%, low TCAR volume by center, low TCAR volume by physician, pre-operative use of: aspirin, statin, P2Y12 inhibitors, anticoagulants.