Prevalence and Prognostic Impact of Carotid Artery Disease in Patients Undergoing Transcatheter Aortic Valve Implantation

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Background: To assess the prevalence of atherosclerotic carotid artery disease (ACAD) in patients undergoing transcatheter aortic valve implantation (TAVI) and postoperative cerebrovascular accidents (CVAs) and evaluate its prognostic impact on postoperative CVAs.
Methods: A retrospective review of all consecutive patients with severe symptomatic aortic valve stenosis (AVS) who underwent TAVI was conducted at a single tertiary university hospital (January 2008−December 2018). Patients with AVS scheduled for TAVI and concomitant carotid stenosis were evaluated for prophylactic carotid revascularization (carotid endarterectomy [CEA] or carotid artery stenting [CAS]).
Results: Seven hundred and seventy one consecutive patients (mean age: 80 years, 52% males) were treated by TAVI procedures. Carotid stenosis > 70% was detected in 69 patients (9%); it was unilateral in 47 (68%) and bilateral in 22 (32%) patients. Prophylactic carotid revascularization was performed before TAVI in 45 patients (31%): in 63.1% of patients (30/47) with unilateral carotid stenosis > 70% and in 68.1% (15/22) with bilateral carotid stenosis > 70%. Postoperative CVA following TAVI procedures were recorded in 25 patients (3.2%): 22 cases of stroke (2.8%) and 3 cases of transient ischemic attack (0.4%). At a multiple logistic regression, only bilateral carotid stenosis > 70% (odds ratio [OR] 1.16, confidence interval [CI] 95% 1.03−1.31; $P = 0.0009$) was found as independent predictors of periprocedural CVA.
Conclusions: In patients with severe symptomatic AVS undergoing TAVI, carotid stenosis was frequently observed. Unilateral carotid stenosis > 70% did not show a significant association with early CVA following TAVI. However, in the cohort of patients with bilateral carotid stenosis > 70%, a significant association with postoperative CVA was observed.

INTRODUCTION

The treatment of aortic valve stenosis (AVS) has dramatically changed in the last 15 years owing to the introduction of minimally invasive endovascular alternatives to a conventional surgical aortic valve replacement (SAVR). Transcatheter aortic valve implantation (TAVI) has now become the treatment of choice for high-risk and intermediate-risk elderly patients with severe

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symptomatic AVS.[1,2] Cerebrovascular ischemic events are serious complications of TAVI procedures and often associated to severe disability and high mortality.[3] In a pooled analysis, the reported overall stroke rate after TAVI was dependent on the surgical risk of the TAVI treated patients, and rates of 30-day stroke after TAVI were not significantly different in the high-risk and intermediate-risk groups.[4] To note, the mean age of latter patients was more than 80 years. Although the presence of extracranial atherosclerotic carotid artery disease (ACAD) has been associated with an increased risk of neurologic complications following cardiac surgery, including SAVR,[5] the association between ACAD and cerebrovascular accidents after TAVI is unsettled also in clinical practice guidelines and expert consensus documents from the United States of America and Europe.[1,6–8] Accordingly, we aimed to evaluate the prevalence of ACAD in patients undergoing TAVI and to assess its prognostic impact on postoperative cerebrovascular accidents (CVAs).

METHODS

Study Design

A retrospective chart review of all consecutive patients who underwent TAVI at a single tertiary university hospital over a 10-year period (January 1, 2008—December 31, 2018) was carried out. All diagnostic and therapeutic procedures followed institutional guidelines and the study did not interfere with patients' treatment. The institutional ethical committee approved the study; it complies with the Helsinki Declaration or comparable latter amendments. Patients consented for participation in minimal risk studies.

Evaluation and Treatment of Carotid Disease

All patients evaluated for TAVI underwent systematic screening for ACAD. The severity of carotid stenosis was defined based on duplex ultrasound (DUS) with the North American Symptomatic Carotid Endarterectomy Trial method.[9] Carotid stenosis was classified as $< 50\%$, 50—69%, 70—99%, and occlusion. If significant carotid stenosis (i.e., $\geq 50\%$) was identified, a subsequent computed tomography angiography of the supra-aortic and intracranial vessels was obtained to corroborate DUS findings. The definition of asymptomatic ACAD was the absence of any previous neurologic symptoms in the preceding 6 months.

An indication for carotid intervention was in accordance with the Society for Vascular Surgery/European Society for Vascular Surgery clinical practice guidelines based on stenosis severity and symptoms present.[10,11] Patients with significant ACAD and AVS scheduled for TAVI were evaluated for decision-making on prophylactic carotid revascularization (carotid endarterectomy [CEA] or carotid artery stenting [CAS]) before TAVI in multidisciplinary meetings.[12] Briefly, CEA was considered the procedure of choice unless specific surgical (e.g., prior neck radiation) or medical conditions (e.g., unstable cardiac angina) were present. Details of CEA/CAS procedures were previously published.[13,14] Technical success was defined as an uneventful CEA/CAS without immediate neurologic events (INE) or the need for additional procedures during surgery/intervention or on waking.

Transcatheter Aortic Valve Implantation Procedure

The TAVI procedure was performed using either self-expanding or balloon-expandable devices. The transfemoral approach was routinely used as a first-line option when suitable; the transaxillary or transapical approaches were used as a second-line option in case of hostile iliofemoral anatomy. All procedural data and outcomes of TAVI interventions were defined as per the VARC-2 criteria.[15] Porcelain aorta was defined as heavy circumferential calcification or severe atheromatous plaques of the entire ascending aorta extending to the aortic arch such that aortic cross-clamping would not be feasible. Procedural success of TAVI was defined as a valve implanted in the intended location, aortic regurgitation $<$ grade 3, mean aortic gradient < 20 mm Hg, effective orifice area (EOA) ≥ 1.0 cm^2, no valve-in-valve or conversion to surgery, and no intraprocedural mortality. Device success of TAVI was defined as a valve implanted in the intended location, aortic regurgitation $<$ grade 3, mean aortic gradient < 20 mm Hg, EOA ≥ 1.0 cm^2, no valve-in-valve or conversion to surgery, no impingement of the mitral valve, and normal coronary blood flow. All patients were under best medical therapy (BMT) at the time of index TAVI procedure, being at least on single antiplatelet therapy (unless fully anticoagulated for concomitant medical reasons or under dual antiplatelet therapy after CAS) and taking a statin if they had concomitant dyslipidemia. Blood pressure control was ensured by referral physicians, as was glycometabolic control for those with diabetes mellitus who were managed by referral diabetologists.

Table I. Demographics, cardiovascular risk factors, and procedural data

Variable	*n* (%)/mean ± SD
Demographics	
Gender, male	402 (52.1)
Age	80.1 ± 6.8
Cardiovascular risk factors	
Diabetes	207 (26.8)
BMI	26.3 ± 5.8
Dyslipidemia	453 (58.8)
Hypertension	639 (82.8)
CRI	339 (43.9)
Dialysis	10 (14.0)
COPD	172 (22.3)
Active smoker	155 (20.1)
AF	250 (32.4)
NYHA class	
0	9 (1.1)
I	70 (9.1)
II	263 (34.1)
III	362 (46.9)
IV	67 (8.6)
Logistic euroSCORE, points	11.5 ± 8.4
Carotid arteries status	
Stenosis >50%	145 (18.8)
Unilateral	96 (12.5)
Bilateral	49 (6.4)
Stenosis >70%	69 (8.9)
Unilateral	47 (6.1)
Bilateral	22 (2.9)
Occlusion	7 (0.9)
Procedural data	
Procedural time, min	87.1 ± 38.4
General anesthesia	184 (23.8)
Access, transfemoral	445 (57.7)
Type of valve, balloon-expandable	424 (54.9)
Predilatation	419 (54.3)
Mean procedural BP, mm Hg	89.2 ± 15.1
Hospital LOS, days	15 ± 11

BMI, body mass index; COPD, chronic obstructive pulmonary disease; CRI, chronic renal insufficiency; AF, atrial fibrillation; BP, blood pressure; CVA, cerebrovascular accident; NYHA, New York heart association; TIA, transient ischemic attack; MI, myocardial infarction.

Definitions and Outcomes

The primary outcomes of interest were mortality and CVA (at 30 days and 1 year). All postoperative CVA events were independently adjudicated by neurologists. Stroke was diagnosed if duration of the neurological deficit was $\geq$ 24 hr or $<$ 24 hr if available neuroimaging documented a new hemorrhage or infarct; transient ischemic attack (TIA) was diagnosed if duration of the neurological deficit was $<$ 24 hr and any variable neuroimaging did not demonstrate a new hemorrhage or infarct. Stroke was defined as disabling (if associated with a modified Rankin Scale (mRS) score of $\geq$ 2 at 90 days and an increase in at least 1 mRS category from an individual's prestroke baseline) or nondisabling (if associated with an mRS score of $<$ 2 at 90 days or one that does not result in an increase in at least 1 mRS category from an individual's prestroke baseline).

Statistical Analysis

Continuous data are presented as mean + standard deviation and categorical data are presented as numbers with percentage. Preoperative and procedural factors were evaluated for an association to postoperative CVA using multivariate logistic regression and expressed as odds ratio (OR) with 95% confidence intervals (CIs). A sensitivity analysis was performed by assessing predictors of CVA for the combined stroke/TIA outcome and for stroke alone. Freedom from CVA and mortality at one year were evaluated using Kaplan—Meier curves; the log-rank test was used to compare patients with unilateral and bilateral carotid stenosis $>$ 70%, and all estimates reported with a standard error $<$ 10%. A P value $<$ 0.05 was considered statistically significant. A data analysis was performed using the R software (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Study Cohort

During the study period, 771 consecutive patients (mean age: 80 years, 52% males) underwent TAVI. The mean logistic EuroSCORE was 11.5 ± 8.4 points (Table I). Carotid stenosis $>$ 50% was detected in 141 patients (18.3%), unilateral in 96 (66%), and bilateral in 45 (34%). Carotid stenosis $>$ 70% was detected in 69 patients (9%), unilateral in 47 (68%), and bilateral in 22 (32%). Seven patients (0.95%) presented with unilateral carotid occlusion. Four patients were symptomatic (0.5%); all had bilateral carotid stenosis $>$ 70%. Unilateral prophylactic carotid revascularization was performed before TAVI in 45 (31%) cases. A prophylactic carotid intervention was performed in 63.1% (30/47) of patients with unilateral carotid stenosis $>$ 70% and in 68.1% (15/22) with bilateral carotid stenosis $>$ 70%. Overall, 30 patients (66.7%) underwent CEA and 15 patients (33.3%) underwent CAS. Technical success of carotid revascularization was 100%; the rate of INE within 24 hr of prophylactic CEA or CAS was 0%. At the time of TAVI,

17 patients had untreated unilateral carotid stenosis > 70% and 7 patients had untreated bilateral carotid stenosis > 70%.

Details of TAVI and Periprocedural Morbidity

The mean procedural time of TAVI was 87.1 ± 38.4 min and 326 procedures (42.2%) were conducted under general anesthesia. Transfemoral access was used for 445 procedures (54.3%) and balloon-expandable valves were implanted in 424 cases (54.9%). Predilatation of the aortic valve was performed in 419 patients (54.3%). The mean procedural blood pressure recorded was 89.2 ± 15.1 mm Hg. Procedural success was achieved in 752 patients (98%) and device success in 746 cases (97%).

The mortality rate at 30 days was 2.5% (20 patients). Of these, 17 (2.2%) died of a cardiovascular cause (2.2%) and 3 (0.4%) died of a noncardiovascular cause (Table II). Postoperative CVA were recorded in 25 patients (3.2%): 22 cases of stroke (2.8%) and 3 cases of TIA (0.4%). Stroke was classified as ischemic in all cases and was disabling in 2. The postoperative (≤ 30 days) stroke/TIA rate was higher in patients with unilateral carotid stenosis > 70% (4.9% vs. 3.3%; $P = 0.465$) or with unilateral carotid occlusion (14.3% vs. 3.3%; $P = 0.082$), without reaching any statistical significance. However, the subgroup of patients with bilateral carotid stenosis > 70% (including occlusion on one side) had a significantly higher stroke/TIA rate (13.6% vs. 3.1%; $P = 0.036$). Cerebrovascular event rates were similar comparing patients (with unilateral and bilateral carotid stenosis > 70%) undergoing prophylactic carotid revascularization before TAVI and those with untreated carotid stenosis > 70% (4% vs. 6.6%; $P = 0.99$). Similarly, patients treated with CAS presented stroke/TIA rates comparable to patients treated with CEA (6.6% vs. 6.8%; $P = 0.99$). Patients with bilateral carotid stenosis > 70% undergoing treatment (CEA or CAS) on the most stenotic side before TAVI ($n = 15$) showed no advantage to those untreated ($n = 7$) who presented no neurological complications ($P = 0.99$).

Presence of bilateral carotid stenosis > 70% was identified as a predictor of stroke/TIA rate at a univariate analysis (OR 7.81, 95% CI 1.69−26.80; $P = 0.002$, Supplementary Table I). Among the other variables, presence of porcelain aorta (OR 3.31, 95% CI 1.25−7.89; $P = 0.009$), valve predilatation (OR 4.17, 95% CI 1.18−26.43; $P = 0.046$), and mean blood pressure during the procedure < 90 mm Hg (OR 4.18, 95% CI 1.26−13.79; $P = 0.016$) were associated to stroke/TIA during TAVI. Preoperative carotid occlusion (OR 11.09, 95% CI 0.54−90.84; $P = 0.040$) and porcelain aorta (OR 3.16, 95% CI 1.10−7.95; $P = 0.020$) were specific predictors of early stroke. There was no evidence for the potential role of a learning curve effect on clinical outcomes (ref. first half of the study vs. second half of the study: OR 1.51, 95% CI 0.67−3.39; $P = 0.316$). At the multiple logistic regression, only bilateral carotid stenosis > 70% (OR 1.16, CI 95% 1.03−1.31; $P = 0.009$, Supplementary Table II) and mean blood pressure < 90 mm Hg (OR 1.05, 95% CI 1.01−1.11; $P = 0.014$) were confirmed to be independent predictors of periprocedural cerebrovascular events. Bilateral carotid stenosis was confirmed when the analysis was limited to stroke only (OR 1.17, 95% CI 1.05−1.30; $P = 0.003$).

One-Year Outcomes

Overall freedom from CVA was 95.6% (95% CI 94−97) one year after index TAVI. Freedom from stroke/TIA was 95.9% (95% CI 94−97) in patients without carotid stenosis, 95.6% (95% CI 90−100) in patients with unilateral carotid stenosis > 70%, and 86.4% (95% CI 73−100) in patients with bilateral carotid stenosis > 70%; the rate was significantly worse in patients with bilateral carotid stenosis > 70% ($P = 0.023$, Fig. 1). Overall survival at one year was 95.3% (95% CI 94−97), 95.7% (95% CI 94−97) in patients without carotid stenosis, 93.6% (95% CI 87−100) in patients with unilateral carotid stenosis > 70%, and 86.4% (95% CI 73−100) in patients with bilateral carotid stenosis > 70% ($P = 0.390$, Fig. 2).

DISCUSSION

Stroke following TAVI remains an important concern and its occurrence dramatically increases the 30-day mortality risk after the procedure.[16] In a large contemporary United States population registry ($n = 101,430$), the occurrence of stroke within 30 days was associated with a significant increase in 30-day mortality: 383 (16.7%) of 2,290 who had a stroke vs. 3,662 (3.7%) of 99,140 who did not have a stroke died ($P < 0.001$; risk-adjusted HR 6.1, 95% CI 5.4−6.8, $P < 0.001$).[17] Therefore, every effort should be made to identify potential predictors for stroke in the attempt to control the occurrence of postoperative cerebrovascular accidents to the extent possible. Several factors have been already identified as predictive of early stroke following TAVI. Using data from the STS/ACC Transcatheter Valve Therapy Registry on 97,600 TAVI procedures, a risk score for in-hospital stroke was created,

Table II. Postoperative ($\leq$ 30 days from index TAVI procedure) outcomes

Variable	*n* (%)/mean ± SD
Hemodynamic success	752 (97.5)
Device success	746 (96.8)
Death, all cause	20 (2.5)
Death, cardiovascular	17 (2.2)
Death, noncardiovascular	3 (0.4)
CVA	25 (3.2)
TIA	3 (0.4)
Stroke	22 (2.8)
Ischemic	22 (2.8)
Disabling	2 (0.3)
MI	17 (2.2)
AKI	74 (9.5)
Minor bleeding	102 (13.2)
Major or life-threatening bleeding	109 (14.1)
Major vascular complications	62 (8.0)
Minor vascular complications	127 (16.4)
New conduction abnormalities	
AF (or flutter)	111 (14.3)
Permanent pacemaker implantation	103 (13.4)
High-degree AV block	79 (10.2)

CVA, cerebrovascular accident; MI, myocardial infarction; AKI, acute kidney injury; AV, atrioventricular.

incorporating several preoperative and intraprocedural covariates.[18] However, the prognostic impact of carotid stenosis for neurologic outcomes following TAVI remains a relatively unexplored issue.

In accordance with prior studies,[19–22] using systematic carotid DUS evaluation we found that approximately one in 5 TAVI candidates presented a carotid stenosis > 50%, but only 9% of them presented with carotid stenosis > 70%. This high prevalence may be explained by a similar ''atherosclerosis-like'' pathogenesis of degenerative aortic stenosis, which may also justify the use of carotid ultrasound scan as a noninvasive method for screening in patients with aortic stenosis.[20] The overall 30-day risk of stroke/TIA following TAVI in the present series was 3.2%, in line with other published series (ranging from 0.5% to 6.8%).[20–22] We showed that the overall risk of early stroke/TIA was not significantly associated with the severity of carotid stenosis, although in the subgroup of patients with bilateral carotid stenosis > 70% (or occlusion) a significant association with postoperative cerebrovascular events was found. However, a formal causal relationship cannot be ascertained and it remains plausible that a more aggressive ACAD was a marker of more extensive atherosclerosis, thereby making these patients at a higher risk for cerebral embolic phenomena during endovascular maneuvers in the aortic arch.

Although published studies agree that unilateral carotid stenosis is not a predictor of postTAVI stroke, data for the subset of patients with severe bilateral carotid stenosis are either lacking or conflicting. Some of these studies did not specifically analyze the possible predictive role of bilateral ACAD.[21–23] Kochar et al. found no association between bilateral severe carotid artery stenosis and 30-day or one-year stroke or mortality.[19] In contrast, Thirumala et al. found that bilateral carotid stenosis was a significant predictor of stroke.[24] Even if these 2 retrospective studies analyzed quite large populations of patients, they both rely on administrative claims data, which suffer from several limitations and expose the analyses to the risk for coding errors affecting the results. Our study adds to the existing evidence that ACAD should not preclude AVS patients from undergoing TAVI. Indeed, clinical utility and cost-effectiveness of carotid DUS prior to cardiac surgery is a longstanding issue,[25,26] as it may alter the management of a minority of patients without translating into obvious reduction of a perioperative stroke risk.[27] Further studies are needed to identify those patients who may benefit the most from DUS screening before TAVI.

As it may happen in the setting of thoracic aorta endovascular repair (TEVAR),[28] cerebral embolization after TAVI might be mainly related to technical and procedural factors. Therefore, approaches to stroke prevention in TAVI are mainly focused on procedural mechanical neuroprotection and an interest has emerged in recent years toward the potential role of embolic protection devices (EPD) in this setting.[29] Two prior meta-analyses found that the use of EPD was associated with reductions in imaging markers of cerebral infarction but a risk for overt stroke and all-cause mortality was nonsignificantly lower in the EPD group.[30,31] However, in other studies, the observed risk of periprocedural all-stroke was significantly lower for protected procedures as compared with unprotected ones.[32,33] Therefore, larger trials specifically designed and adequately powered to detect differences in hard clinical endpoints with long-term neurocognitive assessments are warranted to provide conclusive evidence regarding the efficacy of EPD use during TAVI for stroke prevention.

In the present study, prophylactic carotid intervention (i.e., CEA or CAS) before TAVI did not reduce the risk of stroke/TIA within 30 days, in line with prior research.[19] Of note, the number of patients undergoing carotid revascularization was too small to perform a robust statistical analysis to determine the role of preTAVI revascularization, both in our study ($n = 45$) and in the one by Kochar

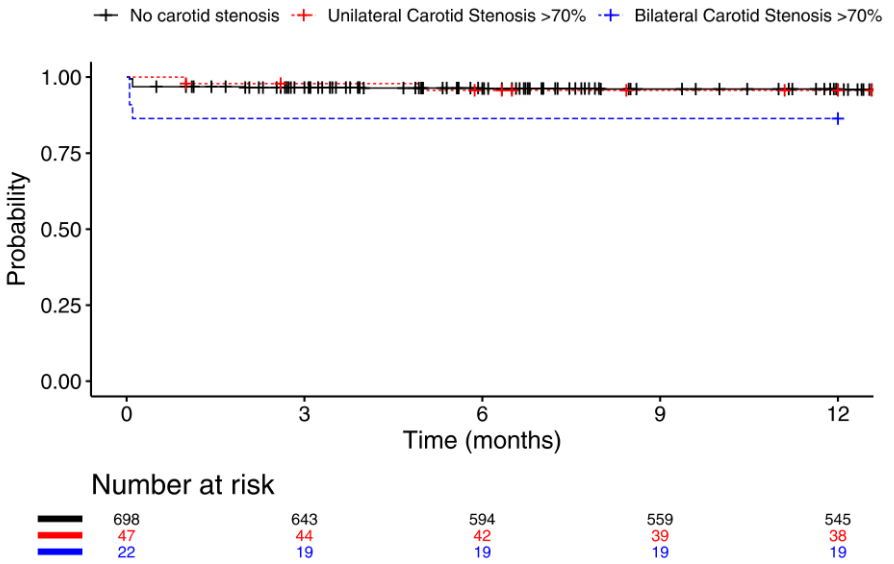

Fig. 1. Kaplan–Meier curves of freedom from stroke/TIA at one year after index TAVI, stratified by the presence of unilateral or bilateral carotid stenosis > 70%.

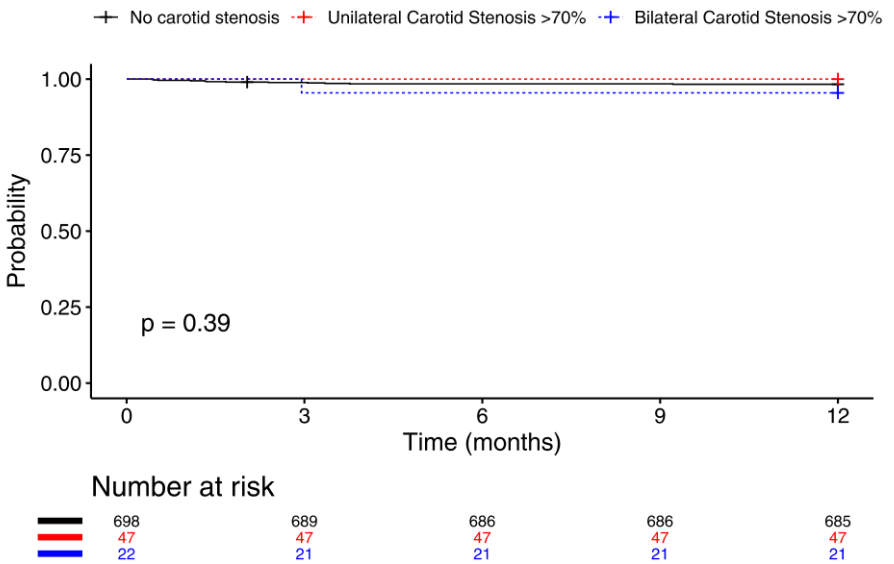

Fig. 2. Kaplan–Meier curves of overall survival at one year after index TAVI, stratified by the presence of unilateral or bilateral carotid stenosis > 70%.

et al.[19] ($n = 63$). Nonetheless, elective treatment of carotid disease could minimize a long-term stroke risk in this vulnerable patient population. In the authors' opinion, staged or synchronous carotid intervention cannot be recommended for the prevention of stroke in patients undergoing TAVI at least in those with unilateral asymptomatic carotid disease, but CEA or CAS may be reasonable in those with bilateral carotid stenosis > 70% (or occlusion) to provide a risk control for both early and late stroke/TIA. Future larger studies may be more powered to assess this clinical question and provide

additional evidence. Until then, it will remain clinically reasonable to offer CEA or CAS to selected patients with significant bilateral ACAD to reduce the long-term risk of stroke.

Study Limitations

Several limitations of this study exist mainly inherent to its single-center retrospective nature. As the number of patients with severe carotid stenosis was small, a type 2 error cannot be excluded. Moreover, data on the plaque characteristics and an indication to carotid surgery, discussed in multidisciplinary meetings, were not available in the prospectively maintained database. However, the dedicated interventional cardiologists and vascular surgeons involved were the same during the entire study period, thus eliminating potential confounders related to the learning curve of the techniques.

CONCLUSION

In patients with severe symptomatic AVS undergoing TAVI, carotid stenosis was frequently observed. Unilateral carotid stenosis $>$ 70% did not show a significant association with early stroke/TIA following TAVI. However, in the cohort of patients with bilateral carotid stenosis $>$ 70%, a significant association with postoperative stroke/TIA was observed. Prophylactic carotid intervention (CEA or CAS) before TAVI provided no evidence for the risk control of postoperative cerebrovascular events in patients undergoing TAVI.

SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.avsg.2022.03.018.

REFERENCES

1. Nishimura RA, Otto CM, Bonow RO, et al. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. Circulation 2017;135:1159–95.
2. Vahl TP, Kodali SK, Leon MB. Transcatheter aortic valve replacement 2016: a modern-day ''through the looking-glass'' adventure. J Am Coll Cardiol 2016;67:1472–87.
3. Muralidharan A, Thiagarajan K, Van Ham R, et al. Meta-analysis of perioperative stroke and mortality in transcatheter aortic valve implantation. Am J Cardiol 2016;118:1031–45.
4. Matsuda Y, Nai fovino L, Giacoppo D, et al. Association between surgical risk and 30-day stroke after transcatheter versus surgical aortic valve replacement: a systematic review and meta-analysis. Catheter Cardiovasc Interv 2021;97:E536–43.
5. Naylor AR, Bown MJ. Stroke after cardiac surgery and its association with asymptomatic carotid disease: an updated systematic review and meta-analysis. Eur J Vasc Endovasc Surg 2011;41:607–24.
6. Otto CM, Kumbhani DJ, Alexander KP, et al. 2017 AA expert consensus Cecision Pathway for transcatheter aortic valve replacement in the management of Adults with aortic stenosis: a report of the American College of Cardiology task force on clinical expert consensus documents. J Am Coll Cardiol 2017;69:1313–46.
7. Nishimura RA, O'Gara PT, Bavaria JE, et al. 2019 AATS/ACC/ASE/SCAI/STS expert consensus Systems of Care document: a Proposal to optimize Care for patients with valvular heart disease: a joint report of the American association for thoracic surgery, American College of Cardiology, American Society of Echocardiography, Society for cardiovascular angiography and interventions, and Society of thoracic surgeon. J Am Coll Cardiol 2019;73:2609–35.
8. Baumgartner H, Falk V, Bax JJ, et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J 2017;38:2739–91.
9. Ferguson GG, Eliasziw M, Barr HWK, et al. The North American Symptomatic Carotid Endarterectomy Trial: surgical results in 1415 patients. Stroke 1999;30:1751–8.
10. Ricotta JJ, Aburahma A, Ascher E, et al. Updated Society for Vascular Surgery guidelines for management of extracranial carotid disease. J Vasc Surg 2011;54:1–31.
11. Naylor AR, Ricco JB, de Borst GJ, et al. Management of atherosclerotic carotid and vertebral artery Disease: 2017 clinical practice guidelines of the European Society for Vascular Surgery (ESVS). Eur J Vasc Endovasc Surg 2018;55:3–81.
12. Squizzato F, Antonello M, Taglialavoro J, et al. Clinical impact of routine cardiology consultation prior to elective carotid endarterectomy in neurologically asymptomatic patients. Eur J Vasc Endovasc Surg 2020;59:536–44.
13. Piazza M, Zavatta M, Lamaina M, et al. Early outcomes of routine delayed shunting in carotid endarterectomy for asymptomatic patients. Eur J Vasc Endovasc Surg 2018;56:334–41.
14. Piazza M, Squizzato F, Chincarini C, et al. Quantitative analysis and predictors of embolic filter debris load during carotid artery stenting in asymptomatic patients. J Vasc Surg 2018;68:109–17.
15. Kappetein AP, Head SJ, Généreux P, et al. Valve Academic Research Consortium-2. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. J Thorac Cardiovasc Surg 2013;145:6–23.
16. Viastra W, Jimenez-Quevedo P, Tchetche D, et al. Predictors, incidence and outcomes of patients undergoing transfemoral transcatheter aortic valve implantation complicated by stroke. From the CENTER-Collaboration. Circ Cardiovasc Interv 2019;12:e007546.
17. Huded CP, Tuzcu M, Krishnaswamy A, et al. Association between transcatheter aortic valve replacement and early postprocedural stroke. JAMA 2019;321:2306–15.
18. Thourani VH, O'Brien SM, Kelly JJ, et al. Development and application of a risk prediction model for in-hospital stroke after transcatheter aortic valve replacement: a report from the Society of Thoraci Surgeon/American College of

Cardiology Transcatheter Valve Therapy Registry. Ann Thorac Surg 2019;107:1097−103.
19. Kochar A, Li Z, Harrison JK, et al. Stroke and cardiovascular outcomes in patients with carotid disease undergoing transcatheter aortic valve replacement. Circ Cardiovasc Interv 2018;11:e006322.
20. Novo G, Guarneri FP, Ferro G, et al. Association between asymptomatic carotid atherosclerosis and degenerative aortic stenosis. Atherosclerosis 2012;223:519−22.
21. Ben-Shoshan J, Zahler D, Steinvil A, et al. Extracranial carotid artery stenosis and outcomes of patients undergoing transcatheter aortic valve replacement. Int J Cardiol 2017;227:278−83.
22. Huded CP, Youmans QR, Puthumana JJ, et al. Lack of association between extracranial carotid and vertebral artery disease and stroke after transcatheter aortic valve replacement. Can J Cardiol 2016;32:1419−24.
23. Condado JF, Jensen HA, Maini A, et al. Should we perform carotid Doppler screening before surgical or transcatheter aortic valve replacement? Ann Thorac Surg 2017;103:787−94.
24. Thirumala PD, Muluk S, Udesh R, et al. Carotid artery disease and periprocedural stroke risk after transcatheter aortic valve implantation. Ann Card Anaesth 2012;20:145−51.
25. Lin JC, Kabbani LS, Peterson EL, et al. Clinical utility of carotid duplex ultrasound prior to cardiac surgery. J Vasc Surg 2016;63:710−4.
26. Santarpino G, Nicolini F, De Feo M, et al. Prognostic impact of asymptomatic carotid artery stenosis in patients undergoing coronary artery bypass grafting. Eur J Vasc Endovasc Surg 2018;56:741−8.
27. Masabni K, Sabik JF III, Raza S, et al. Nonselective carotid artery ultrasound screening in patients undergoing coronary artery bypass grafting: is it necessary? J Thorac Cardiovasc Surg 2016;151:402−8.
28. D'Oria M, Mani K, DeMartino R, et al. Narrative review on endovascular techniques for left subclavian artery revascularization during thoracic endovascular aortic repair and risk factors for post-operative stroke. Interactive Cardiovasc Thorac Surg 2021;32:764−72.
29. Seeger J, Gonska B, Otto M, et al. Cerebral embolic protection during transcatheter aortic valve replacement significantly reduces death and stroke compared with unprotected procedures. J Am Coll Cardiol Intv 2017;10:2297−303.
30. Giustino G, Mehran R, Veltkamp R, et al. Neurological outcomes with embolic protection devices in patients undergoing transcatheter aortic valve replacement. A systematic review and meta-analysis of randomized controlled trials. J Am Coll Cardiol Intv 2016;9:2124−33.
31. Lam HT, Kwong JM, Lam PN, et al. Evidence for cerebral embolic protection in transcatheter aortic valve implantation and thoracic endovascular aortic repair. Ann Vasc Surg 2019;55:292−306.
32. Kroon HG, van der Werf HW, Hoeks SE, et al. Early clinical impac of cerebral embolic protection in patient undergoing transcatheter aortic valve replacement. Circ Cardiovasc Interv 2019;12:e007605.
33. Seeger J, Kapadia SR, Kodali S, et al. Rate of periprocedural stroke observed with cerebral embolic protection during transcatheter aortic valve replacement: a patient-level propensity-matched analysis. Eur Heart J 2019;40:1334−9.