ORIGINAL ARTICLE

Incidence of and Risk Factors for Stroke and Cerebral Microembolism after Transcatheter Aortic Valve Replacement: Insights from Diffusion-Weighted Magnetic Resonance Imaging of the Brain

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Background: Transcatheter aortic valve replacement (TAVR) is an established treatment for severe symptomatic aortic stenosis, but it carries a risk of cerebrovascular events, including clinical ischemic stroke, transient ischemic attack (TIA), and silent cerebral ischemic lesions (SCILs). The detection of these lesions using advanced imaging modalities, such as diffusion-weighted magnetic resonance imaging (DW-MRI) of the brain, provides valuable insights into procedural and patient-related factors contributing to their occurrence.

Objective: To evaluate the incidence of and risk factors for stroke, TIA, and SCILs in patients undergoing TAVR.

Materials and Methods: A prospective cohort study was conducted on patients with severe symptomatic aortic stenosis undergoing TAVR at a single center. Cerebral ischemia was assessed using DW-MRI of the brain within seven to fourteen days and three to six months post-procedure. Baseline demographics, procedural details, and outcomes were analyzed to identify predictors of SCILs and stroke.

Results: Of the 48 patients included, SCILs were detected in 91.67% using DW-MRI of the brain, with a mean lesion size of 4.01±2.58 mm. Transient clinical stroke occurred in one patient (2.08%), while a permanent clinical stroke was reported in two patients (4.17%). Lesions predominantly involved the middle cerebral artery territories at 50.81%, consistent with embolic events. Multivariate analysis identified valve dislodgement as a significant predictor of SCILs ($p<0.001$). Procedural factors such as rapid ventricular pacing and post-dilatation were not associated with SCILs.

Conclusion: The present study highlights a high incidence of SCILs following TAVR, driven by procedural and patient-specific factors. Further research is needed to assess the long-term clinical implications of SCILs.

Keywords: Transcatheter aortic valve replacement; TAVR; Silent cerebral ischemic lesions; Stroke; DW-MRI of the brain; Aortic stenosis

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Transcatheter aortic valve replacement (TAVR) has been the standard treatment for patients with severe symptomatic aortic stenosis. TAVR is especially suited for patients with prohibitive surgical risks from the intermediate to high-risk category, with a STS score of 4% or greater or a EuroSCORE II of 10 or greater[1,2]. However, it was revealed that both the 30-day risk and 1-year risk of developing stroke or transient ischemic attack (TIA) in patients who underwent TAVR are statistically higher than those who received medical treatment or underwent surgical aortic valve replacement (SAVR)[3,4]. Manipulation of catheters, guidewires, and balloons and implantation of valve within calcified native aortic valve can possibly dislodge atherosclerotic debris, causing them to embolize and lead to stroke or brain ischemia[5]. According to the study, the 30-day risk and 1-year risk of developing stroke or TIA of SAVR patients

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were 2.4% and 4.3%, respectively, while those of TAVR were 5.5% and 8.3%, respectively[6]. However, in another randomized controlled trial (RCT) that compared the risks of stroke in patients with high surgical risk between patients undergoing TAVR using a self-expandable valve (CoreValve) and SAVR at 30 days and 1 year, the risks were not statistically different between these groups at 4.9% versus 6.2% (p=0.46) and 8.8% versus 12.6% (p=0.1), respectively[7]. It is possible that newer techniques and devices, such as a self-expandable valve, reduce the stroke risk from traditional TAVR procedures. From a meta-analysis, the mortality rate of post-op TAVR patients who developed stroke in 30 days was as high as 6-fold compared to those who did not (OR 6.45, 95% confidence interval 3.90 to 10.66, p<0.0001)[8]. The rate of morbidity and cost of care for the former were also significantly higher[9]. Lately, after better procedures and devices for preventing complications have been developed, stroke remains a significant complication during the procedure and 30 days after the procedure, but the incidence tends to decrease[10]. It also found that stroke occurring 30 days post-procedure was most often associated with the patient's risk factor status[11].

Modern technological advances in radiology have allowed physicians to detect acute strokes swiftly. Despite the absence of clinical symptoms of acute stroke, small cerebral infarction could still be detected with the help of magnetic resonance imaging (MRI). A study showed that the sensitivity of diffusion-weighted magnetic resonance imaging (DW-MRI) of the brain in identifying multiple small cerebral infarctions was as high as 77% among TAVR patients[12]. The sensitivity was 10 times higher compared to patients who already manifested clinical signs of stroke[13,14]. Important factors that increase the risk of cerebral microembolism include increasing age and severity of aortic arch atheroma[15]. While these silent cerebral ischemic lesions (SCILs) might not change management in the acute settings, they are associated with long-term cognitive decline and increased stroke risk[16-18].

The authors aimed to study the incidence of clinical stroke and evidence of microembolism and the risk factors of cerebral ischemia, including both procedural such as valve types, and patient-specific factors. DW-MRI of the brain would guide the surveillance and treatment of stroke for the benefit of selecting patients suitable for the procedure and beneficial treatment and prevention of stroke to reduce disability and increase the quality of life of the patients.

Materials and Methods

The present study utilized a prospective cohort design, including patients with severe symptomatic aortic stenosis who underwent TAVR at the Cardiovascular Center, Chulabhorn Hospital, Chulabhorn Royal Academy, Bangkok, Thailand, between April 4, 2020, and March 31, 2021. The inclusion criteria comprised severe symptomatic aortic stenosis confirmed by echocardiographic parameters such as aortic valve area smaller than 1.0 cm^2, peak aortic valve velocity greater than 4 m/second, or mean aortic valve pressure gradient greater than 40 mmHg) and a Society of Thoracic Surgeons (STS) score greater than 4%. Patients were excluded if they had MRI-incompatible conditions such as pacemakers or claustrophobia, a history of brain surgery or the presence of intracerebral instruments such as ventriculoperitoneal shunt or deep brain stimulation, a history of clinical stroke or TIA, traumatic head injury within the past three months, or a history of brain tumors.

All participants underwent a comprehensive cardiac evaluation, including data collection on demographic characteristics, comorbidities, past surgical history, medication use, vital signs, and laboratory and imaging studies. Imaging evaluations included chest X-ray, electrocardiogram (ECG), transthoracic echocardiography with a GE model with left lateral decubitus positioning, and computed tomography angiography (CTA) for TAVR planning. Neurological assessments were conducted by certified neurologists using the modified Rankin Scale (mRS) and National Institutes of Health Stroke Scale (NIHSS), performed seven days before, 14 days, and three to six months after the procedure. The mRS and NIHSS were utilized to assess functional outcomes and neurological status in the present study.

All DW-MRI of the brain examinations were conducted using 3-T systems following a standardized protocol. This protocol included axial fluid-attenuated inversion recovery fat saturation (FLAIR FS), diffusion-weighted imaging (DWI), and susceptibility-weighted imaging (SWI) sequences to assess SCILs. SCILs are defined as asymptomatic ischemic lesions detected on imaging without corresponding clinical manifestations[16]. All participants also underwent DW-MRI of the brain within the same time intervals to detect cerebral events seven days before and fourteen days after the procedure, except at six weeks for permanent

pacemakers, and subsequently at three to six months. These thorough evaluations ensured a detailed assessment of neurological outcomes associated with the TAVR procedure.

The primary outcome of the present study was the occurrence of SCILs or clinical stroke detected after TAVR that happened immediately and within two weeks. Secondary outcomes included procedural and non-procedural risk factors associated with clinical stroke and SCILs. These outcomes were designed to provide a comprehensive understanding of the neurological risks associated with TAVR and to identify key factors that influence both the incidence and clinical impact of stroke in this patient population.

Statistical analysis

Descriptive statistics were used to summarize the data. Quantitative data were reported as mean ± standard deviation or median (interquartile range), depending on the data distribution. Normality was assessed using the Shapiro-Wilk normality test. Differences between the no SCILs and SCILs groups were analyzed using the independent t-test or Mann-Whitney U test for quantitative data, and the chi-square test or Fisher's exact test for categorical data. Factors associated with the number of SCILs were examined using regression analysis, including both simple regression and multiple regression models. Variables found to be significantly associated with the number of SCILs in the simple linear regression analysis, with a p-value of less than 0.05, were selected for inclusion in the multiple linear regression model to identify independent factors associated with the number of SCILs. All statistical analyses were performed using Stata/SE, version 16.1 (StataCorp LLC, College Station, TX, USA).

Ethical approval

The present study was conducted following the Declaration of Helsinki and was approved by the Ethics Committee of Chulabhorn Hospital research ethics committees (Project code 062/2562, issued 3 April 2020). Written informed consent was obtained from all subjects involved in the study.

Results

Study flow chart and baseline characteristics

Fifty-six patients with severe aortic stenosis who underwent TAVR were initially enrolled. After applying the exclusion criteria, eight patients were excluded, leaving 48 patients in the study. These

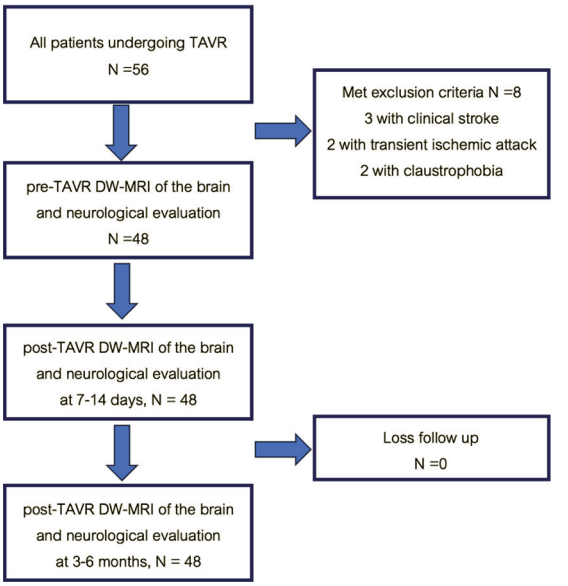

Figure 1. The study flow diagram.

DW-MRI, diffusion-weighted magnetic resonance imaging; TAVR, trans-catheter aortic valve replacement

participants underwent DW-MRI of the brain and neurological evaluations at baseline, which is before TAVR, and at seven to fourteen days and three to six months post-TAVR (Figure 1).

The mean age of patients in the present study was 79.23±5.87 years, with approximately 56% being male. Common comorbidities included diabetes mellitus with 35.42%, hypertension with 77.08%, and dyslipidemia with 72.92%, with 20% being current smokers. The mean body mass index (BMI) was 22.59±4.70 kg/m², and the STS score was 3.75. The mean age was lower in patients with SCILs or clinical stroke, demonstrating statistical significance. No other significant differences in baseline characteristics were observed between patients with and without SCILs (Table 1).

The median aortic valve calcium score was 3,017 AU (IQR 2,338 to 4,314), with no statistical difference between groups (p=0.386). The left ventricular ejection fraction (LVEF) was comparable between groups, averaging 59.48±14.56%. Aortic valve pressure gradients also showed no significant differences.

Incidence of stroke and SCILs

The incidence of clinical stroke and SCILs was assessed among the study population following TAVR. Clinically evident stroke occurred in 6.25% of patients, whereas 91.67% demonstrated SCILs

Table 1. Baseline clinical profile

Demographic	Total (n=48)	No SCILs (n=4)	SCILs/clinical stroke (n=44)	p-value
Age (years); mean±SD	79.23±5.87	86.00±4.16	78.61±5.64	0.014[3]
Male, n (%)	27 (56.25)	3 (75.00)	24 (54.55)	0.621[2]
Diabetes mellitus, n (%)	17 (35.42)	1 (25.00)	16 (36.36)	1.000[2]
Hypertension, n (%)	37 (77.08)	3 (75.00)	34 (77.27)	1.000[2]
Hypercholesterolemia; n (%)	35 (72.92)	4 (100.00)	31 (70.45)	0.563[2]
CKD; n (%)				0.407[2]
eGFR <60 ml/min/1.73 m^2	9 (18.75)	1 (25.00)	8 (18.18)	
Hemodialysis	7 (14.58)	1 (25.00)	6 (13.64)	
Current cigarette smoking; n (%)	10 (20.83)	0 (0.00)	10 (22.73)	0.566[2]
Family history of CAD; n (%)	8 (16.67)	0 (0.00)	8 (18.18)	1.000[2]
Previous PCI; n (%)	19 (39.58)	1 (25.00)	18 (40.91)	1.000[2]
Previous CABG; n (%)	2 (4.17)	0 (0.00)	2 (4.55)	1.000[2]
Peripheral artery disease; n (%)	2 (4.17)	0 (0.00)	2 (4.55)	1.000[2]
History of heart failure; n (%)	26 (54.17)	1 (25.00)	25 (56.82)	0.320[2]
Atrial fibrillation; n (%)	8 (16.67)	0 (0.00)	8 (18.18)	1.000[2]
Cardiogenic shock; n (%)	1 (2.08)	0 (0.00)	1 (2.27)	1.000[2]
BMI (kg/m^2); mean±SD	22.59±4.70	21.32±2.92	22.71±4.83	0.576[3]
STS score; median (IQR)	3.75 (5.11 to 3.07)	4.81 (3.28 to 7.94)	3.75 (3.07 to 4.95)	0.456[4]

BMI=body mass index; CABG=coronary artery bypass grafting; CAD=coronary artery disease; eGFR=estimated glomerular filtration rate; PCI=percutaneous coronary intervention; STS=Society of Thoracic Surgeons; SCILs=silent cerebral ischemic lesions; SD=standard deviation

[1] Chi-square test; [2] Fisher's exact; [3] Independent t-test; [4] Mann-Whitney U test

on post-procedural imaging. The results emphasize the value of advanced neuroimaging in detecting asymptomatic brain lesions that may otherwise go unrecognized (Figure 2).

Procedure and complications

The transfemoral approach was the predominant access site, utilized in 97.92% of patients (47 out of 48 patients), while direct aortic access was rare, accounting for only one case (2.08%), with no significant differences between patients with or without SCILs (p=1.000). Balloon-expandable valves, specifically the SAPIEN 3 (Edwards Lifesciences, Irvine, California), were employed in 35.42% of procedures, whereas self-expandable valves were more frequently used, comprising 64.58% of the cases. Among self-expandable devices, CoreValve Evolut R and CoreValve Evolut Pro (Medtronic, Minneapolis, MN) were the most commonly utilized, representing 52.1% and 12.5% of the cases, respectively. Post-dilation of valves was performed in 31.25% of the patients to optimize placement. The median sheath size was 14 French, with no significant difference between groups (p=0.606). Rapid ventricular pacing was conducted in 89.58% of the patients (43 out of 48 patients), showing no significant variation across groups. Pre-dilatation balloon valvuloplasty was performed

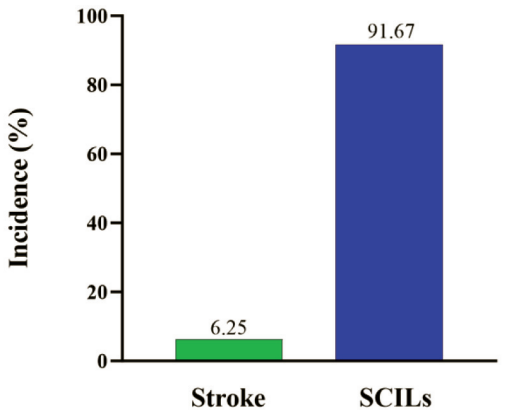

Figure 2. Incidence of stroke and silent cerebral ischemic lesions (SCILs).

in 70.83% of the patients, including 100% in those without SCILs compared to 68.18% in those with SCILs, though this difference was not statistically significant (p=0.307). The median contrast volume administered was 185 mL, with slightly higher usage in patients with SCILs, yet the difference did not reach statistical significance (p=0.255).

Complications and adjustments during the procedure included valve mispositioning requiring snaring, which occurred in two cases (4.17%), and valve dislodgement, a rare complication observed

Table 2. Details of preexisting white matter abnormalities (Fazekas scale)

MRI brain	Total (n=48); n (%)	No SCILs (n=4); n (%)	SCILs/clinical stroke (n=44); n (%)	p-value
Preexisting white matter abnormalities (Fazekas scale)				0.157[2]
0	3 (6.25)	1 (25.00)	2 (4.55)	
1	27 (56.25)	1 (25.00)	26 (59.09)	
2	18 (37.50)	2 (50.00)	16 (36.36)	
3	0 (0.00)	0 (0.00)	0 (0.00)	

MRI=magnetic resonance imaging; SCILs=silent cerebral ischemic lesions
[2] Fisher's exact

in two cases (4.17%). Blood loss was generally minimal, with a median estimated loss of 55 mL (IQR 50 to 100), however, 4.17% of patients required intraoperative blood transfusion. Malignant arrhythmias and cardiac arrest were extremely rare complications, with only one case of cardiac arrest reported (2.08%), and no occurrences of malignant arrhythmias. Additionally, no instances of TAVR embolization were observed during the procedures.

The immediate postoperative course revealed a low incidence of complications among the study cohort. Atrial fibrillation occurred postoperatively in three patients (6.25%), with no significant difference between patients with or without SCILs (p=1.000). Similarly, post-procedural clinical strokes were observed in three patients (6.25%), of which one patient experienced transient clinical symptoms, and two patients experienced a permanent stroke. Regarding discharge medication, the majority of patients (83.33%) were prescribed dual antiplatelet therapy, while single antiplatelet therapy was used in 4.17% of the cases. Anticoagulation was initiated in seven patients (14.58%), primarily for preexisting indications such as atrial fibrillation. No statistically significant differences in antithrombotic strategies were found between patients with and without SCILs (p=1.000). Early postoperative atrial fibrillation, thus within 72 hours, was recorded in five patients (10.42%), with no significant variation between the groups. These findings suggested that while postoperative complications such as atrial fibrillation and stroke occurred in a minority of patients, the risk was not disproportionately higher in patients with SCILs.

Baseline white matter abnormalities and post-TAVR cerebral ischemia on MRI

Preexisting white matter abnormalities were assessed using the Fazekas scale, revealing the following distribution in the overall cohort of 48 patients, with grade 0 in three patients (6.25%), grade 1 in 27 patients (56.25%), grade 2 in 18 patients (37.50%), and no grade 3 abnormalities (0.00%). Among the four patients without SCILs, the distribution was grade 0 in one patient (25.00%, grade 1 in one patient (25.00%), and grade 2 in two patients (50.00%). The 44 patients with SCILs exhibited a slightly different pattern, with grade 0 in two patients (4.55%), grade 1 in 25 patients (59.09%), and grade 2 in 15 patients (36.36%). No significant difference in Fazekas grades was observed between the groups (p=0.157), suggesting that preexisting white matter abnormalities were not strongly associated with the presence of SCILs (Table 2).

Lesion characteristics observed post-TAVR revealed that the majority of ischemic lesions were located in the cerebral cortex with 243 lesions (65.68%), followed by the deep white matter with 81 lesions (21.89%), deep grey nuclei with 16 lesions (4.32%), and infratentorial regions with 30 lesions (8.11%). The mean lesion size was 4.01±2.58 mm. Lesion distribution by vascular territory showed a predominance of ischemic events in the middle cerebral artery (MCA) territories, with the right MCA at 30.00% and left MCA at 20.81% accounting for the majority of detected lesions. Posterior circulation territories, including the right posterior cerebral artery (RPCA) 11.48% and left posterior cerebral artery (LPCA) 12.43%, also demonstrated significant lesion burdens. Lesions in smaller vessels, such as the right posterior inferior cerebellar arteries (RPICA) 4.59%, the left posterior inferior cerebellar arteries (LPICA) 4.32%, and the right superior cerebellar artery (RSCA) 0.54%, were less frequent, reflecting the complexity and distribution of embolic events during TAVR (Table 3, Figure 3).

Three hundred seventy new lesions were identified on DWI (b1000) (Figure 4), and apparent diffusion coefficient (ADC) images were performed seven to fourteen days following the TAVR procedure (Table 3).

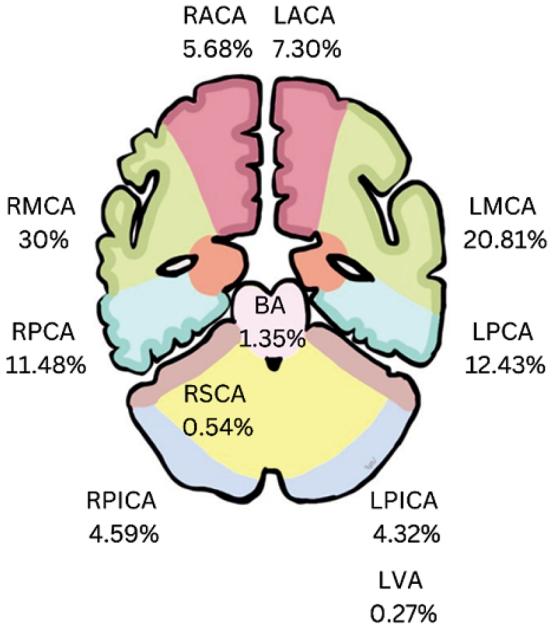

Figure 3. The lesion distribution by the vascular territory of acute infarct foci.

BA, basilar artery; LACA, left anterior cerebral artery; LMCA, left middle cerebral artery; LPCA, left posterior cerebral artery; LPICA, left posterior inferior cerebellar artery; LVA, left vertebral artery; RMCA, right middle cerebral artery; RACA, right anterior cerebral artery; RPCA, right posterior cerebral artery; RPICA, right posterior inferior cerebellar artery; RSCA, right superior cerebellar artery

Baseline and post-TAVR cerebral ischemia neurological function

Baseline evaluations showed that most patients had no significant disability using mRS with a score of 0 for 83.33%, and normal neurological status using NIHSS with a score of 0 for 95.83%. At 14 days and three months post-TAVR, the mRS and NIHSS scores demonstrated slight variability, with minimal increases in scores indicative of mild disability or neurological deficits. These findings suggested that while some patients experienced mild post-procedural changes, the overall functional and neurological outcomes remained favorable.

Clinical stroke manifestations and outcomes in patients following TAVR

Three patients experienced clinical strokes following TAVR, each presenting with distinct manifestations and outcomes. The first patient developed right MCA syndrome four days post-procedure, exhibiting left-sided weakness, left neglect, left homonymous hemianopia, and dysarthria. DW-MRI confirmed an acute infarction in the right MCA territory, with magnetic resonance angiography (MRA) revealing severe focal stenosis in the right MCA proximal M1 segment and moderate stenosis in the left MCA M1 segment. Pre-procedure MRI noted a Fazekas scale score of 2. Despite residual mild left-sided weakness and dysarthria at a three-month follow-up, the mRS score was 2, with imaging showing chronic changes from the prior infarction. The second patient presented with transient dysarthria on the first day post-TAVR. MRI identified acute infarctions in the left middle frontal cortex, occipital cortex, and medial thalamus, consistent with embolic phenomena. The patient recovered completely, with

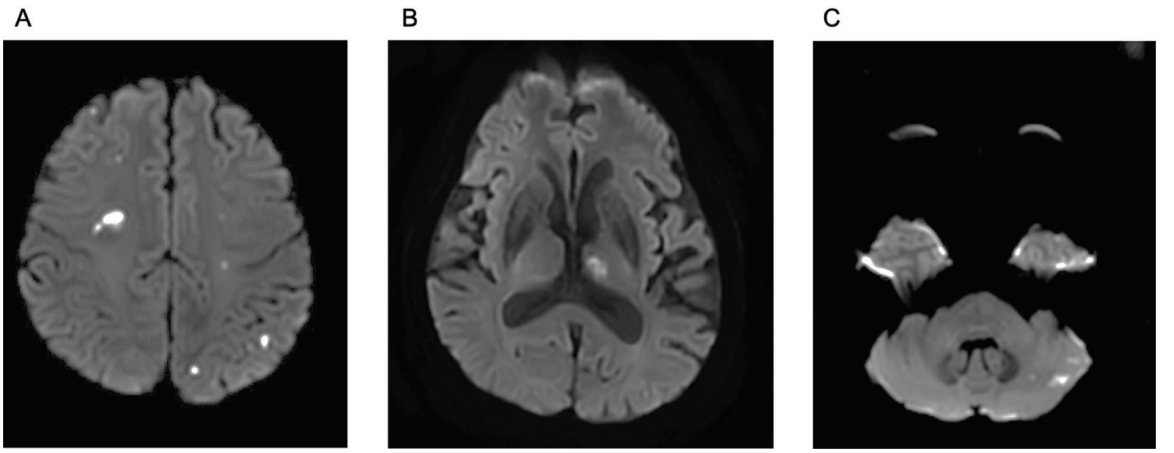

Figure 4. Brain MRI, DWI (b1000) sequence of three patients on the 5th day following TAVR showed multiple variably sized of restricted diffusion foci scattered across the bilateral cerebral cortices, subcortical regions, and deep white matter (A), the left thalamus (B), and the left cerebellar cortices (C) representing acute infarction with embolic nature. The following MRI at 3 to 6 months revealed the disappearance of the lesions as mentioned above (not shown).

DWI, diffusion weighted imaging; MRI, magnetic resonance imaging; TAVR, transcatheter aortic valve replacement

Table 3. Post-procedural MRI of patients who developed SCILs

MRI brain (DW-MRI)	Post TAVR MRI 7 to 14 days	Post TAVR MRI 3 to 6 months
The number of patients with detected lesions; n	44	5
Number of lesions; n	370 lesions	13 lesions
Location; n (%)		
Cerebral cortex	243 (65.68)	7 (53.85)
Deep white matter	81(21.89)	2 (15.38)
Deep grey nuclei	16(4.32)	3 (23.08)
Infratentorial	30(8.11)	1 (7.69)
Size (mm); mean±SD	4.01±2.58	3.98±2.53
Number stroke lesion; mean±SD	8.36±11.55	2.16±2.29
Territory (lesions); n (%)		
RMCA	111 (30.00)	5 (38.46)
LMCA	77 (20.81)	5 (38.46)
RACA	21 (5.68)	0 (0.00)
LACA	27 (7.30)	0 (0.00)
RPCA	44 (11.48)	0 (0.00)
LPCA	46 (12.43)	2 (15.38)
BA	5 (1.35)	0 (0.00)
RSCA	2 (0.54)	0 (0.00)
RPICA	17 (4.59)	0 (0.00)
LPICA	16 (4.32)	1 (7.70)
LVA	1 (0.27)	0 (0.00)
ADC value ($\times 10^{-2}$ mm^2/second); mean±SD	0.61±0.16	-

ADC=apparent diffusion coefficient; BA=basilar artery; SCILs=silent cerebral ischemic lesions; LACA=left anterior cerebral artery; LMCA=left middle cerebral artery; LPCA=left posterior cerebral artery; LPICA=left posterior inferior cerebellar artery; LVA=left vertebral artery; MRI=magnetic resonance imaging; RMCA=right middle cerebral artery; RACA=right anterior cerebral artery; RPCA=right posterior cerebral artery; RPICA=right posterior inferior cerebellar artery; RSCA=right superior cerebellar artery; SD=standard deviation; TAVR=transcatheter aortic valve replacement

an mRS score and NIHSS score of 0 at discharge. Follow-up imaging at five months showed resolution of acute lesions, except for chronic changes in the left thalamus. The third patient experienced a stroke on day five, presenting with dysarthria and mild right cerebellar signs. DW-MRI revealed multi-territorial acute infarctions in both cerebral and cerebellar hemispheres and the left upper pons, alongside moderate stenosis in the bilateral MCA and basilar arteries. Pre-procedural imaging indicated small vessel disease and an old hemorrhagic infarction in the left lentiform nucleus. At the presentation, the NIHSS score was 4, and the mRS score was 2. Follow-up evaluations showed symptom improvement, with imaging confirming chronic changes in previously affected regions. These cases highlighted the diverse presentations, mechanisms, and recovery trajectories of stroke following TAVR.

Risk factors associated with the development of SCILs following TAVR

Linear regression analysis identified several factors associated with the development of SCILs following TAVR. Age was negatively associated with the number of SCILs in univariate analysis (B= –0.60, p=0.042), though this association lost significance in multivariate analysis (p=0.155). Similarly, a higher BMI showed a positive correlation with the number of SCILs in univariate analysis (B=0.72, p=0.041), but this was not sustained in multivariate analysis (p=0.609). Procedural factors, particularly valve dislodgement, emerged as a strong predictor of SCILs, showing significant associations in both univariate (B=46.20, p<0.001) and multivariate analysis (B=38.04, p<0.001). Additionally, postoperative clinical stroke independently predicted a higher number of SCILs in multivariate analysis (B=12.52, p=0.035).

Discussion

In the present study, clinical stroke events were observed in three patients (6.25%), consisting of two cases of permanent clinical stroke and one case of transient clinical deficit. This rate is higher compared to a meta-analysis that reported an average 30-day stroke or TIA rate of 3.3±1.8% associated with TAVR[19]. The study also revealed a significant incidence of SCILs, with SCILs detected in 91.67%

of patients using DW-MRI of the brain. While most lesions were asymptomatic, their high prevalence highlights the substantial cerebral embolic risk inherent to TAVR. These findings are higher than the previous studies reporting SCILs in 68% to 77% of TAVR patients, underscoring the importance of advanced neuroimaging techniques like DWI in detecting subclinical embolic events and informing strategies to mitigate neurological risks[12,16,20]. The clinical significance of SCILs remains a topic of debate. While these lesions are often asymptomatic in the short term, they have been associated with long-term cognitive decline and increased stroke risk[16-18].

The evaluation of white matter abnormalities using the Fazekas scale revealed no significant difference in preexisting conditions between patients with and without SCILs. While grade 2 abnormalities were more prevalent in patients with SCILs, at 35.71% compared to those without, at 5%, this difference was not statistically significant (p=0.157). Interestingly, the lack of significant differences in preoperative white matter abnormalities between SCIL and non-SCIL groups suggests that preexisting cerebral pathology may not strongly predispose patients to periprocedural embolic events. This finding is consistent with prior research suggesting that SCIL risk is more closely tied to procedural factors than chronic cerebrovascular disease[21].

The detection of 370 acute ischemic lesions post-TAVR highlights the cerebrovascular risks associated with the procedure. The predominance of lesions in the cerebral cortex for 65.68% and the deep white matter for 21.89%, is consistent with embolic patterns often observed in TAVR[22]. The small lesion size, with a mean size of 4.01±2.58 mm, and low ADC values, with a mean of $0.61\pm0.16 \times 10^{-2}$ mm²/second confirm the acute ischemic nature of these findings[23].

The acute infarct lesion distribution analysis revealed a predominant involvement of the MCA territories, particularly the right and left MCA. This distribution aligns with the pattern of embolic events associated with TAVR, likely originating from calcific or thrombotic debris dislodged during valve deployment. The MCA territories are commonly affected due to their direct perfusion via the internal carotid arteries, as well as their extensive supply to cortical and subcortical regions, making them particularly susceptible to embolic burden. These findings underscore the cerebral vulnerability inherent to TAVR and highlight the importance of strategies aimed at reducing embolic load[24]. Posterior circulation territories, including the right and left posterior cerebral arteries, were also notably affected, albeit less frequently than anterior territories. Lesions in the posterior inferior cerebellar arteries and the superior cerebellar artery highlight the involvement of smaller vessels, potentially reflecting microemboli or procedural factors influencing the vertebrobasilar system. This lesion pattern is consistent with embolic events often observed in the postoperative period following aortic interventions, underscoring the multifaceted nature of cerebral embolization during and after TAVR[25].

All the small acute embolic infarct foci on follow-up MRI after TAVR were absent. It can be explained by various factors, including the temporal evolution of infarct characteristics, the resolution of cytotoxic edema, the limitations of standard MRI sequences in detecting small resolved lesions, and potential tissue recovery in cases of small emboli with early reperfusion[26]. This highlights the dynamic nature of cerebral embolic events following TAVR and underscores the importance of considering the timing of imaging in patient evaluation and management. It also emphasizes the necessity of correlating initial and follow-up imaging to avoid underestimating the cerebral impact of the TAVR procedure when relying solely on follow-up MRI findings[25,26].

In patients who experienced a clinical stroke, which was two permanent deficits and one transient deficit, imaging revealed embolic phenomena scattered across both the anterior and posterior circulations. Clinically, these patients presented with small NIHSS scores ranging from 1 to 4, and at follow-up, their mRS scores ranged from 0 to 2. Notably, pre-procedural MRI findings indicated a moderate degree of small vessel disease, with a Fazekas scale score of 2, along with mild to moderate intracranial stenosis, in permanent clinical stroke cases.

The high prevalence of acute ischemic lesions following TAVR underscores the urgent need for preventive strategies to mitigate embolic risk during the procedure[21]. The susceptibility of the MCA territories suggests a significant potential role for embolic protection devices (EPDs) targeting carotid circulation in reducing lesion burden and improving patient outcomes. Furthermore, the observed involvement of posterior circulation territories highlights the importance of comprehensive neuroimaging and neurological assessments post-TAVR to identify and manage subtler cerebral deficits effectively. Evidence from a large study suggested that the use of EPDs is associated with

a modest but borderline significant reduction in stroke-related mortality, reinforcing their potential utility as a critical adjunct to enhance procedural safety and long-term neurological outcomes in TAVR patients[27,28]. Currently, there are many EPDs available, such as the Sentinel™ Cerebral Protection Device (Claret Medical Inc.), the Embrella Embolic Deflector™ device (Edwards Lifesciences, Irvine, CA), and others[29,30]. These devices could reduce ischemic stroke after the TAVR procedure. Even though patients who underwent the TAVR procedure with these devices may have benefited from stroke prevention, for SCILs and long-term outcomes, further studies are still needed.

In the present study, procedural factors such as rapid ventricular pacing, pre-dilatation balloon valvuloplasty, TAVR valve type such as balloon-expandable or self-expandable, and post-dilatation did not differ significantly between patients with and without SCILs. However, valve dislodgement, observed in two cases, emerged as a strong predictor of SCILs in the multivariate analysis. This finding aligns with previous studies indicating that the dislodgement of calcific and atheromatous plaques during TAVR is a common cause of cerebral embolism and stroke[31,32]. These results underscore the importance of meticulous procedural techniques to minimize valve dislodgement and reduce the risk of embolic events during TAVR.

The results of the present study have implications. Firstly, the information on the incidence of SCILs and the risk factors of developing SCILs should be brought into the discussion of the risks and benefits of TAVR. Patients should be informed of the risk of SCILs and their long-term cognitive effects before the procedure. Secondly, it is reasonable to advise vascular risk reduction strategies, such as statins, tight blood pressure and glycemic control, and lifestyle modification[33] and continued cognitive assessment in patients with SCILs, because the SCILs mostly originated from dislodged thrombotic debris.

The small sample size in the present study may limit the generalizability of the findings, particularly in understanding the role of preexisting white matter abnormalities in the development of cerebral ischemic lesions. Additionally, the study's low statistical power restricts its ability to identify significant associations between risk factors and the occurrence of SCILs. Future research should focus on larger, multicenter cohorts to validate these results and establish robust correlations between lesion characteristics and clinical outcomes, such as neurocognitive function and long-term stroke risk. Such investigations are essential to thoroughly elucidate the implications of SCILs in TAVR patients and to inform the development of more effective preventive and therapeutic strategies.

Conclusion

The present study highlights a high incidence of SCILs following TAVR, driven by procedural and patient-specific factors. Further research is needed to assess the long-term clinical implications of SCILs.

What is already known about this topic?

TAVR is an established treatment for severe symptomatic aortic stenosis, but it carries a risk of cerebrovascular events, including clinical ischemic stroke, TIA, and SCILs.

What does this study add?

This study shows a high incidence of SCILs following TAVR, detected by DW-MRI of the brain, driven by procedural and patient-specific factors.

Authors' contributions

Conceptualization, WL and NT; data curation, WL, AC, TA, AJ, and CW; format analysis, WL; funding acquisition, WL and NT; investigation, WL, PP, WT, DS, and VM; methodology, WL and KS; project administration, WL; resources, WL; software, WL and KU; supervision, AC and KU; validation, WL and CH; visualization, WL, AC, and NT; writing-original draft preparation, WL; writing-review and editing, WL, AC, NS, and NT; all authors have read and agreed to the published version of the manuscript.

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Conflicts of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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