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Risk factors and prognosis of silent cerebral infarction after transcatheter aortic valve replacement

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The Valve Academic Research Consortium (VARC)-3 definition of silent cerebral infarction among neurologic events after transcatheter aortic valve replacement (TAVR) lacks clinical validation, yet its impact on postoperative in-hospital outcomes and long-term prognosis remains uncertain. This study aims to explore the perioperative related factors influencing the risk of SCI post-TAVR as defined by VARC-3 criteria, so as to identify high-risk individuals early and assess the effect of SCI on patient outcomes and one-year mortality following TAVR. This was a single-center study including 613 patients with severe aortic stenosis undergoing TAVR, with all data collected prospectively in a dedicated database.We compared clinical baseline data, preoperative imaging results, perioperative factors, and intraoperative variables between patients with and without SCI according to VARC-3. Multivariate logistic regression was used to identify risk factors associated with SCI. Propensity score matching (PSM) at a 1:2 ratio was employed based on fundamental characteristics such as age, gender, BMI, and medical history to minimize potential confounding. Post-matching, we analyzed differences in postoperative in-hospital outcomes and other results between the two groups. Survival times were compared using the Kaplan–Meier method, and survival curves were plotted. The log-rank test assessed statistical differences between the survival curves. Furthermore, univariate and multivariate Cox regression analyses were conducted to determine risk factors for one-year postoperative mortality. Out of 827 TAVR patients screened, 613 were included in the final analysis—471 in the SCI group and 142 in the non-SCI group—resulting in an incidence rate of 76.8% for SCI. The occurrence of post-induction hypotension was significantly higher in the SCI group compared to the non-SCI group (70.28% vs. 61.27%, P = 0.043). Multivariate logistic regression revealed that post-induction hypotension lasting less than 10 min (odds ratio [OR]: 1.73; 95% confidence interval [CI]: 1.13–3.26; P = 0.009), hypotension lasting more than 10 min (OR: 1.98; 95% CI: 1.18–3.33; P = 0.01), and postoperative tachyarrhythmia (OR: 1.98; 95% CI: 1.27–3.07; P = 0.002) were significant risk factors for developing SCI after TAVR. Following 1:2 PSM, 416 patients remained—274 in the SCI group and 142 in the non-SCI group. After matching, the SCI group had a notably higher incidence of postoperative delirium compared to the non-SCI group (9.12% vs. 2.82%; P = 0.017), and their one-year mortality rate was also elevated (5.47% vs. 0.70%; P = 0.016). Additionally, multivariate Cox regression analysis indicated that elevated preoperative creatinine levels (hazard ratio [HR]: 1.01; 95% CI: 1.01–1.02; P = 0.011), presence of SCI (HR: 10.81; 95% CI: 1.31–89.18; P = 0.027), Society of Thoracic Surgeons (STS) score greater than 7% (HR: 3.32; 95% CI: 1.07–10.33; P < 0.038), age 75 years or older (HR: 7.86; 95% CI: 1.01–14.47; P = 0.049), and a history of stroke (HR: 7.20; 95% CI: 2.32–22.35; P < 0.001) were independent risk factors for one-year mortality post-TAVR. Our findings suggest that post-induction hypotension and postoperative tachyarrhythmia are significant risk factors for SCI following TAVR as defined by VARC-3 criteria. Patients who developed SCI after TAVR exhibited higher rates of postoperative delirium and increased one-year mortality compared to those without this complication. Furthermore, factors such as elevated preoperative creatinine levels, an STS score above 7%, age of 75 years or older, and a prior history of stroke were associated with higher one-year mortality rates after TAVR. Given the negative impact of occult SCI on clinical outcomes, every effort should be made to reduce the risk of neurological complications after TAVR.

Keywords Transcatheter aortic valve replacement, VARC-3, Silent cerebral infarction, Risk factors, Clinical outcomes, Postoperative delirium, Mortality

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Aortic stenosis (AS) is a prevalent valvular heart disease, with multicenter studies demonstrating that its incidence increases with age—from 1–2% in individuals aged 75–76 years to as high as 6% in those aged 85–86 years[1]. The aortic valve may suffer from restricted opening or closure due to congenital anomalies or degenerative processes, resulting in a decreased effective valve area and reduced cardiac output, ultimately leading to clinical manifestations such as heart failure[2–4]. Traditional treatment options comprise conservative medical therapy and surgical aortic valve replacement (SAVR). However, for many elderly patients, those with a history of thoracic surgery, and individuals with significantly impaired cardiac function, surgical intervention carries extremely high risks.

In recent years, transcatheter aortic valve replacement (TAVR) has markedly advanced the interventional treatment landscape for valvular heart diseases[4,5]. TAVR has progressively become a widely accepted therapeutic option, serving as the primary treatment for patients unsuitable for surgery and as a viable alternative for those at high surgical risk. The safety and efficacy of TAVR in AS patients who have contraindications to surgery or are at elevated risk have been confirmed by multiple large-scale global randomized controlled trials, including the Placement of Aortic Transcatheter Valves (PARTNER) trial. Furthermore, extensive clinical studies have demonstrated that, for patients with moderate surgical risk, the therapeutic outcomes of TAVR are comparable to those of SAVR[2–4].

Despite European and American guidelines expanding TAVR indications to encompass moderate-risk patients, perioperative complications remain critical factors affecting patient prognosis. Neurological events after TAVR are associated with worse short-term and long-term survival. This association is related to the NeuroARC (Neurology Academic Research Consortium) event types defined by the VARC-3 criteria[6]. According to the NeuroARC classification, neurologic events are divided into NeuroARC type 1 (stroke), NeuroARC type 2 (Silent Cerebral Infarction), and NeuroARC type 3 (transient ischemic attack and delirium)[7]. Clinically, 3–10% of high-risk patients undergoing TAVR experience postoperative stroke. Brain magnetic resonance imaging (MRI) conducted after TAVR often reveals new cerebral infarctions without accompanying clinical symptoms; these infarcts, which show imaging evidence but lack obvious neurological deficits, are termed silent cerebral infarction (SCI). While overt stroke after TAVR is relatively rare, the incidence of SCI post-TAVR can reach up to 70%[8]. In recent years, there has been increasing attention on the occurrence of SCI in TAVR patients. Post-TAVR, patients might experience various neurological injuries—including vertebral artery obstruction, air embolism, and foreign body embolism—that may contribute to the development of SCI[9,10]. Although SCI do not present noticeable clinical symptoms, their presence may be associated with the progression of postoperative cognitive dysfunction. Studies have reported a high incidence of cognitive dysfunction after TAVR, leading to progressive functional decline, reduced independence, depression, and increased mortality[8,11]. However, the impact of SCI on postoperative cognitive dysfunction and long-term clinical outcomes remains a subject of debate. Previous research has suggested a correlation between the average number of SCI lesions and postoperative cognitive dysfunction[7].

Recent international studies have indicated that SCI following TAVR may be associated with patient-related factors such as age, hyperlipidemia, preoperative atrial fibrillation, and chronic kidney disease, as well as surgical factors like the design of the prosthetic valve and the number of pre-dilation and post-dilation procedures[12–14]. Prior research has identified intraoperative hypotension and postoperative tachyarrhythmias after TAVR as factors linked to an increased risk of postoperative stroke[15–18]. Moreover, both the duration and proportion of time spent in hypotension have been associated with adverse clinical outcomes[19,20].

The Valve Academic Research Consortium (VARC) criteria have historically been the cornerstone for defining and standardizing clinical outcomes following aortic valve interventions. The latest VARC-3 consensus document refines the neurological event endpoints to include stroke and other overt central nervous system (CNS) injury (NeuroARC1), covert CNS injury (NeuroARC2), and neurological deficits without CNS injury (transient ischemic attack and delirium) (NeuroARC3), in line with the Neurological Academic Research Consortium (NeuroARC). However, the VARC-3 definition of neurologic events lacks clinical validation. The study by Marisa Avvedimento et al. provided clinical validation for VARC-3; however, only the following results were obtained: perioperative neurological events were independently associated with a significant increase in mortality 1 year after intervention, NeuroARC type 1 was associated with an increased risk of death, and the occurrence of NeuroARC type 3 events had no effect on mortality[21]. Therefore, this study aimed to evaluate Silent Cerebral Infarction (NeuroARC2) according to the VARC-3 endpoint definition, we explored the incidence of SCI following TAVR at our center from January 2020 to April 2023. We compared clinical baseline data, anesthesia-related factors, and surgical variables between patients with and without SCI. Multivariate logistic regression analysis was employed to identify risk factors for new-onset SCI. The primary aim of this study was to explore the perioperative factors influencing the risk of SCI post-TAVR as defined by VARC-3 criteria, so as to identify high-risk individuals early and assess the effect of SCI on patient outcomes and one-year mortality following TAVR.

Results

Patient baseline characteristics

Between January 2020 to April 2023, a total of 827 patients underwent TAVR at SAHZU. After excluding 214 patients (62 with transapical access, 5 requiring intraoperative conversions to open-heart surgery, 6 undergoing a second surgery, 2 emergency admissions due to sudden heart failure, 6 experiencing postoperative overt strokes,

and 133 lacking postoperative cranial MRI), 613 patients were included in this study(Fig. 1). These patients were categorized into two groups based on the occurrence of SCI post-TAVR: the SCI group and the non-SCI group.

Among the included 613 patients, 471 patients were assigned to the SCI group and 142 patients to the non-SCI group(Fig. 1), resulting in an overall incidence of SCI of 76.8%. Among the variables assessed, two categorical variables had missing data that did not exceed the 10% threshold: NYHA classification was missing in 18 patients (3%), and peripheral vascular disease data were missing in 43 patients (7%). For continuous variables, preoperative C-reactive protein data were missing in 128 patients (21%). Variables with missing rates below 10% were imputed using multiple imputation, while C-reactive protein was excluded from the analysis due to excessive missing data.

Table 1 shows that there were no significant differences between the two groups regarding baseline data, preoperative laboratory indicators, medical history, or surgical-related factors ($P > 0.05$). Preoperative echocardiography revealed no significant differences in ejection fraction, maximum transvalvular gradient, mean transvalvular gradient, or peak flow velocity between the groups ($P > 0.05$). Moderate to severe aortic regurgitation was present in 338 patients (55.14%) overall, with a lower incidence in the SCI group compared to the non-SCI group (55.8% vs. 66.2%, $P = 0.03$). Post-induction hypotension occurred in 418 patients (68.19%) overall, with a higher incidence in the SCI group compared to the non-SCI group (70.28% vs. 61.27%, $P = 0.043$). The incidence of postoperative tachyarrhythmia was also higher in the SCI group compared to the non-SCI group (32.09% vs. 22.54%, $P = 0.003$), indicating a statistically significant difference.

Table 1 Continuous variables are presented as mean (standard deviation) or median (interquartile range), Categorical variables are expressed as frequencies (percentages). BMI, Body Mass Index; AF, Atrial Fibrillation; HF, Heart Failure; MI, Myocardial Infarction; COPD, Chronic Obstructive Pulmonary Disease; PVD, Peripheral Vascular Disease; HB, Hemoglobin;Cr, Serum Creatinine; EF, Ejection Fraction; STS, American Society of Thoracic Surgeons scoring system; NYHA, New York Heart Association classification; ACEI, Angiotensin-Converting Enzyme Inhibitor; ARB, Angiotensin II Receptor Blocker. $P < 0.05$ was considered statistically significant.

Risk factors for silent cerebral infarction after TAVR

Univariate logistic regression analysis revealed that post-induction hypotension lasting less than 10 min (OR: 1.73, 95% CI: 1.13–2.64, $P = 0.011$), post-induction hypotension lasting more than 10 min (OR: 1.94, 95% CI: 1.16–3.26, $P = 0.012$), and postoperative tachyarrhythmia (OR: 1.94, 95% CI: 1.27–3.07, $P = 0.003$) were identified as risk factors for postoperative SCI (Fig. 2). After adjusting for these factors in multivariate logistic regression analysis, post-induction hypotension lasting less than 10 min (OR: 1.76, 95% CI: 1.15–2.70, $P = 0.009$), post-induction hypotension lasting more than 10 min (OR: 1.98, 95% CI: 1.18–3.33, $P = 0.01$), and postoperative tachyarrhythmia (OR: 1.98, 95% CI: 1.26–3.00, $P = 0.002$) remained significant risk factors for postoperative SCI (Fig. 2).

Propensity score matching

Prior to assessing the impact of SCI on clinical outcomes after TAVR, PSM was performed to mitigate bias. Following matching, a total of 416 patients were included—142 in the non-SCI group and 274 in the SCI group (Table 3、4 and Fig. 3). Post-matching analysis confirmed that all variables had SMDs below 0.1, indicating good balance between the groups.

Table 2 & Table 3: Continuous variables are presented as mean (standard deviation) or median (interquartile range), Categorical variables are expressed as frequencies (percentages). BMI, Body Mass Index; AF, Atrial Fibrillation; HF, Heart Failure; COPD, Chronic Obstructive Pulmonary Disease; PVD, Peripheral Vascular

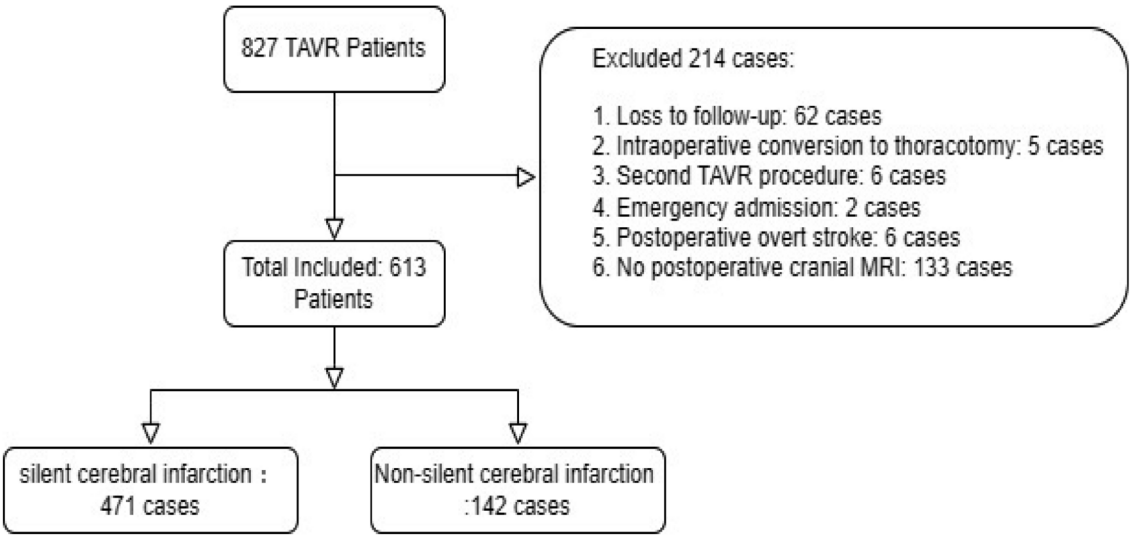

Fig. 1. Patient Screening Flowchart. *TAVR* transcatheter aortic valve replacement.

Variable	Total (n = 613)	Non silent cerebral infarction (n = 142)	Silent cerebral infarction (n = 471)	*P*
Baseline characteristics				
Age (years)	74.64 ± 7.01	74.15 ± 6.93	74.78 ± 7.03	0.349
Male, n (%)	352 (57.42)	76 (53.52)	276 (58.60)	0.283
BMI (kg/m^2)	22.72 ± 3.42	22.71 ± 3.24	22.72 ± 3.47	0.982
Smoking, n (%)	148 (24.14)	33 (23.24)	115 (24.42)	0.774
Drinking, n (%)	115 (18.76)	23 (16.20)	92 (19.53)	0.372
Comorbidities and Medical History				
Hypertension, n (%)	346 (56.44)	79 (55.63)	267 (56.69)	0.824
Corony Heart Disease, n (%)	204 (33.28)	48 (33.80)	156 (33.12)	0.88
Pre AF, n (%)	114 (18.6)	25 (17.61)	89 (18.90)	0.729
Pre HF, n (%)	125 (20.39)	31 (21.83)	94 (19.96)	0.627
Cardiac Surgery History, n (%)	60 (9.79)	15 (10.56)	45 (9.55)	0.723
Pre COPD, n (%)	58 (9.46)	11 (7.75)	47 (9.98)	0.426
Pre Pulmonary Infection, n (%)	24 (3.92)	9 (6.34)	15 (3.18)	0.089
Pre Hydrothorax, n (%)	22 (3.59)	2 (1.41)	20 (4.25)	0.111
Pre Respinary Failure, n (%)	5 (0.82)	1 (0.70)	4 (0.85)	1
Previous Stroke, n (%)	37 (6.04)	9 (6.34)	28 (5.94)	0.863
Diabetes, n (%)	122 (19.9)	28 (19.72)	94 (19.96)	0.95
Pre Myocardial Infarction, n (%)	2 (0.33)	1 (0.70)	1 (0.21)	0.41
PVD, n (%)	40 (6.53)	6 (4.23)	34 (7.22)	0.206
Pre Renal Failure, n (%)	11 (1.79)	2 (1.41)	9 (1.91)	0.972
Laboratory Findings				
Pre HB (g/L)	124.02 ± 20.21	122.54 ± 18.80	124.47 ± 20.61	0.319
Pre Cr (μmol/L)	76.10 (62.00, 93.90)	75.00 (59.78, 88.95)	77.00 (63.55, 96.10)	0.071
Pre Albumin (g/L)	36.50 (34.20, 38.60)	35.80 (33.62, 38.27)	36.60 (34.35, 38.70)	0.058
Pre EF (%)	57.57 ± 12.39	58.22 ± 10.93	57.38 ± 12.81	0.441
Pre Max Gradient (mmHg)	80.00 (64.00, 104.00)	80.50 (65.00, 104.75)	80.00 (62.50, 102.50)	0.652
Pre Maximum Velocity (m/s)	4.46 (4.00, 5.10)	4.48 (4.04, 5.17)	4.46 (3.95, 5.09)	0.647
Pre Mean Gradient (mmHg)	45.00 (34.00, 63.00)	46.00 (34.00, 61.25)	45.00 (34.00, 63.00)	0.943
Pre Aortic Valve Area (cm^2)	0.70 (0.52, 0.88)	0.73 (0.52, 0.93)	0.70 (0.52, 0.88)	0.289
Pre Aortic Regurgitation, n (%)	338 (55.14)	94 (66.20)	244 (51.80)	0.003
Pre Mitral Regurgitation, n (%)	185 (30.18)	39 (27.46)	146 (31.00)	0.421
Perioperative Data				
Anesthesia Type, n (%)	468 (76.35)	114 (80.28)	354 (75.16)	0.208
Postinduction Hypotension, n (%)	418 (68.19)	87 (61.27)	331 (70.28)	0.043
Duration of Procedure (min)	100.00 (80.00, 125.00)	95.00 (80.00, 123.75)	100.00 (80.00, 125.00)	0.23
Total Fluid (ml)	1500.00 (1000.00, 1500.00)	1500.00 (1000.00, 1500.00)	1500.00 (1000.00, 1500.00)	0.771
Blood Loss (ml)	50.00 (50.00, 50.00)	50.00 (50.00, 50.00)	50.00 (50.00, 50.00)	0.727
Valve Brand, n (%)	104 (16.97)	28 (19.72)	76 (16.14)	0.319
Predilate, n (%)	434 (70.8)	100 (70.42)	334 (70.91)	0.91
Postdilate, n (%)	328 (53.51)	70 (49.30)	258 (54.78)	0.251
Rapid Arrythmia, n (%)	202(32.95)	32(22.54)	170(36.09)	0.003
STS, n (%)	3.14 (1.94, 5.58)	3.31 (2.04, 5.51)	3.10 (1.92, 5.59)	0.719
NYHA class III or IV, n (%)	459 (74.88)	101 (71.13)	358 (76.01)	0.24
Medications				
β Receptor Blocker, n (%)	113 (18.43)	29 (20.42)	84 (17.83)	0.486
Aspirin, n (%)	147 (23.98)	36 (25.35)	111 (23.57)	0.662
Diuretics, n (%)	176 (28.71)	44 (30.99)	132 (28.03)	0.494
ACEI/ARB, n (%)	172 (28.06)	40 (28.17)	132 (28.03)	0.973
Hypolipidemic Drug, n (%)	228 (37.19)	47 (33.10)	181 (38.43)	0.249
Calcium Channel Blocker, n (%)	148 (24.14)	43 (30.28)	105 (22.29)	0.051
Cardiotonic Drug, n (%)	13 (2.12)	5 (3.52)	8 (1.70)	0.323

Table 1. Baseline characteristics.

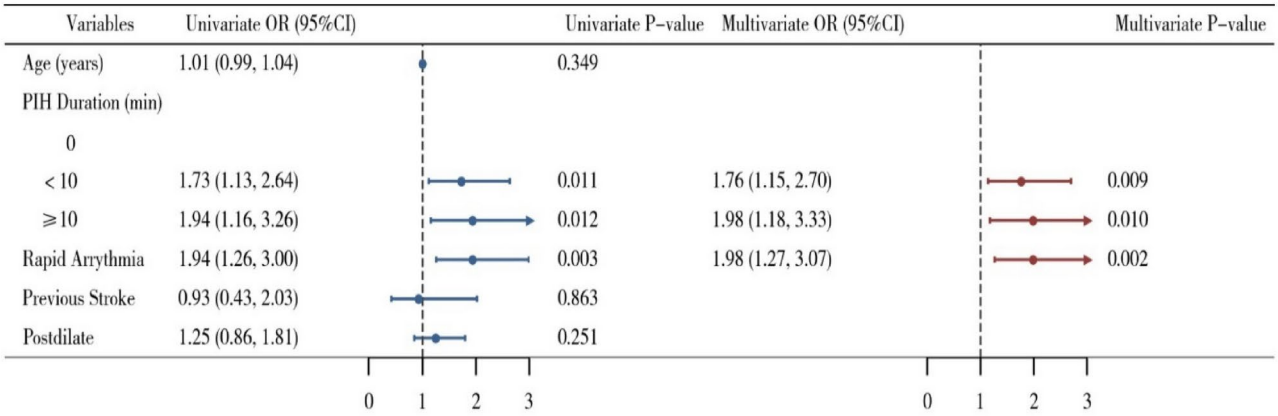

Fig. 2. Analysis of risk factors for silent cerebral infarction after TAVR.

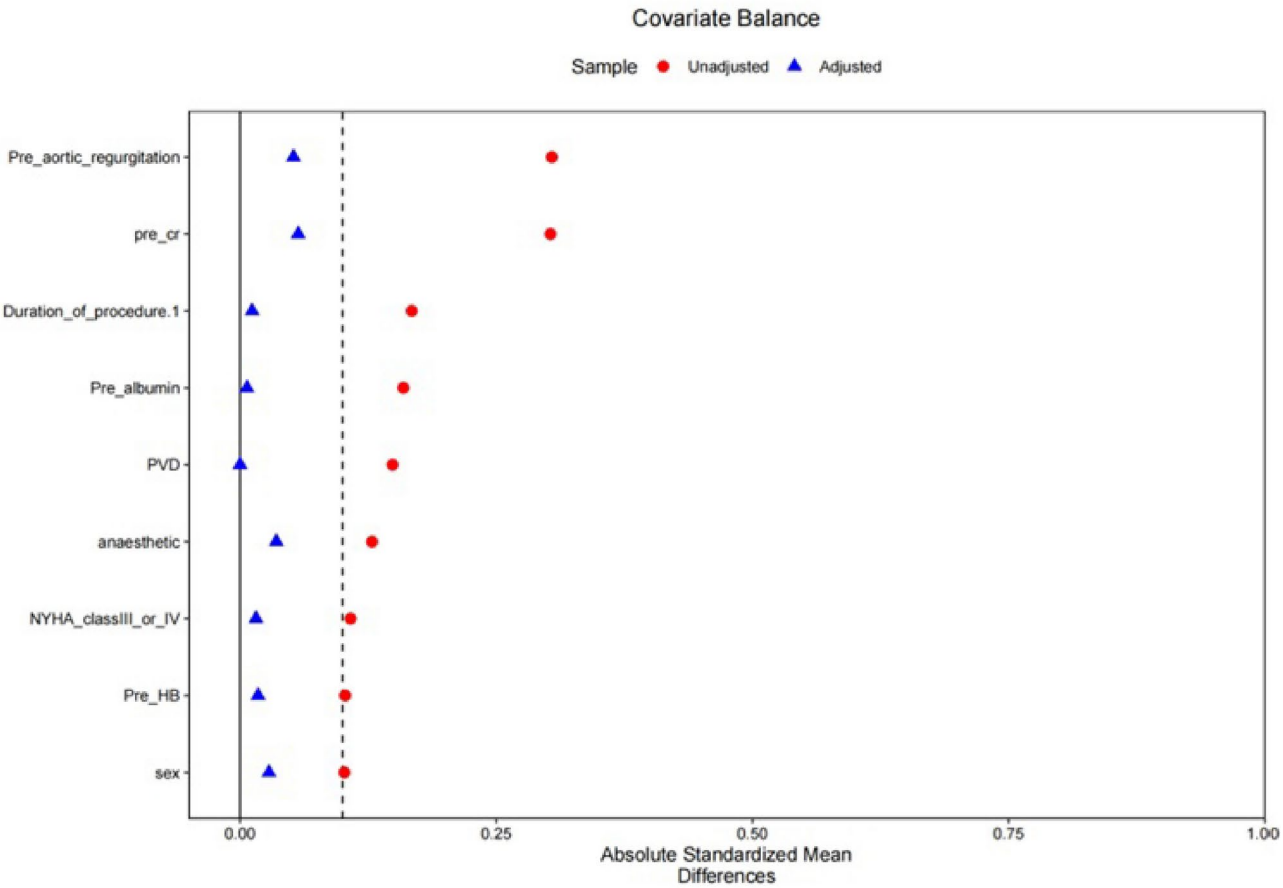

Fig. 3. SMD diagram before and after matching.

Disease; HB, Hemoglobin;Cr, Serum Creatinine; EF, Ejection Fraction; STS, American Society of Thoracic Surgeons scoring system; NYHA, New York Heart Association classification; ACEI, Angiotensin-Converting Enzyme Inhibitor; ARB, Angiotensin II Receptor Blocker; SMD, Standard Mean Difference.$P < 0.05$ was considered statistically significant.

Clinical outcomes before and after propensity score matching

Before Matching: A total of 46 patients experienced postoperative delirium, resulting in an incidence rate of 7.5%. The SCI group had a higher incidence of postoperative delirium compared to the non-SCI group (8.92% vs. 2.82%, P = 0.016), which was statistically significant. Additionally, the one-year mortality rate was higher

Variable	Total (n = 613)	Silent cerebral infarction (n = 471)	Non silent cerebral infarction (n = 142)	*P*-value	SMD
Pre HB (g/L)	124.02 ± 20.21	124.47 ± 20.61	122.54 ± 18.80	0.319	−0.103
BMI (kg/m^2)	22.72 ± 3.42	22.72 ± 3.47	22.71 ± 3.24	0.982	−0.002
STS	3.14 (1.94, 5.58)	3.10 (1.92, 5.59)	3.31 (2.04, 5.51)	0.719	−0.09
Pre Cr (μmol/L)	76.10 (62.00, 93.90)	77.00 (63.55, 96.10)	75.00 (59.78, 88.95)	0.071	−0.303
Pre Albumin (g/L)	36.50 (34.20, 38.60)	36.60 (34.35, 38.70)	35.80 (33.62, 38.27)	0.058	−0.159
Duration of Procedure (min)	100.00 (80.00, 125.00)	100.00 (80.00, 125.00)	95.00 (80.00, 123.75)	0.23	−0.167
Total Fluid (ml)	1500.00 (1000.00, 1500.00)	1500.00 (1000.00, 1500.00)	1500.00 (1000.00, 1500.00)	0.771	−0.06
Blood Loss (ml)	50.00 (50.00, 50.00)	50.00 (50.00, 50.00)	50.00 (50.00, 50.00)	0.727	−0.028
Pre EF (%)	60.50 (51.00, 65.80)	60.40 (50.70, 66.20)	60.90 (52.92, 65.10)	0.835	0.077
Age ≥ 75, n (%)	303 (49.43)	231 (49.04)	72 (50.70)	0.729	0.033
PVD, n (%)	40 (6.53)	34 (7.22)	6 (4.23)	0.206	−0.149
Male, n (%)	352 (57.42)	276 (58.60)	76 (53.52)	0.283	−0.102
Anesthesia Type, n (%)	468 (76.35)	354 (75.16)	114 (80.28)	0.208	0.129
Smoking, n (%)	148 (24.14)	115 (24.42)	33 (23.24)	0.774	−0.028
Drinking, n (%)	115 (18.76)	92 (19.53)	23 (16.20)	0.372	−0.091
NYHA Class III or IV, n (%)	459 (74.88)	358 (76.01)	101 (71.13)	0.24	−0.108
Hypertension, n (%)	346 (56.44)	267 (56.69)	79 (55.63)	0.824	−0.021
Corony Heart Disease, n (%)	204 (33.28)	156 (33.12)	48 (33.80)	0.88	0.014
Cardiac History, n (%)	60 (9.79)	45 (9.55)	15 (10.56)	0.723	0.033
Previous Stroke, n (%)	37 (6.04)	28 (5.94)	9 (6.34)	0.863	0.016
Diabetes, n (%)	122 (19.9)	94 (19.96)	28 (19.72)	0.95	−0.006
Pre Aortic Regurgitation, n (%)	338 (55.14)	244 (51.80)	94 (66.20)	0.003	0.304
Aspirin, n (%)	147 (23.98)	111 (23.57)	36 (25.35)	0.662	−0.041
Pre Renal Failure, n (%)	11 (1.79)	9 (1.91)	2 (1.41)	0.972	0.043
ACEI/ARB, n (%)	172 (28.06)	132 (28.03)	40 (28.17)	0.973	0.003

Table 2. Patient baseline indicators before matching.

in the SCI group compared to the non-SCI group (5.01% vs. 4.08%, P = 0.02), also indicating a statistically significant difference (Table 5).

After Matching: In the matched cohort, the SCI group had 25 cases of postoperative delirium (9.12%), while the non-SCI group had 4 cases (2.82%). This difference was statistically significant (P = 0.017). Among the 16 patients who died within one year postoperatively, 6 died of cardiac causes, 4 of severe pneumonia, 3 of multiple organ failure, 1 of traumatic cerebral hemorrhage, 1 of septic shock, and 1 of unknown causes. The one-year mortality rate remained higher in the SCI group compared to the non-SCI group (5.47% vs. 3.85%, P = 0.02), showing a statistically significant difference (Table 4).

Table4&Table5: Continuous variables are presented as mean (standard deviation) or median (interquartile range), Categorical variables are expressed as frequencies (percentages). AKI, Acute Kidney Injury; MI, Myocardial Infarction; AF, Atrial Fibrillation; LBBB, Left Bundle Branch Block; AVB, Atrioventricular Block. $P < 0.05$ was considered statistically significant.

Risk factors for postoperative delirium before and after propensity score matching

Before Matching: Multivariate logistic regression analysis indicated that postoperative SCI (OR: 3.38, 95% CI: 1.19–9.59, P = 0.021), preoperative atrial fibrillation (OR: 3.15, 95% CI: 1.68–5.93, P = 0.001), and diabetes (OR: 2.02, 95% CI: 1.14–4.39, P = 0.02) were identified as risk factors for postoperative delirium (Fig. 4).

After Matching: Multivariate logistic regression analysis revealed that postoperative SCI (OR: 3.39, 95% CI: 1.14–10.04, P = 0.028) and preoperative atrial fibrillation (OR: 3.8, 95% CI: 1.72–8.38, P < 0.001) remained significant risk factors for postoperative delirium (Fig. 5).

Survival curves and analysis of one-year mortality risk factors

Before Matching: The Kaplan–Meier survival analysis demonstrated that the one-year survival curve was lower in the SCI group compared to the non-SCI group, with a statistically significant difference (HR: 7.727, 95% CI: 1.045–57.121, P = 0.018) (Fig. 6).

After Matching: Similarly, after PSM, the SCI group exhibited a lower one-year survival curve compared to the non-SCI group, which was statistically significant (HR: 8.172, 95% CI: 1.079–61.870, P = 0.015) (Fig. 7).

To investigate risk factors for one-year mortality after TAVR, variables from preoperative clinical baseline data, preoperative examinations, and surgical data were included in a univariate Cox regression analysis. Factors with p-values below 0.05 in the univariate regression were subsequently included in a multivariate Cox regression analysis. The results of both Cox univariate and multivariate analyses are presented in Fig. 8 and Fig. 9.

Variable	Total (n = 416)	Silent cerebral infarction (n = 274)	Non silent cerebral infarction (n = 142)	*P*-value	SMD
Pre HB (g/L)	122.58 ± 19.72	122.60 ± 20.21	122.54 ± 18.80	0.978	−0.003
BMI (kg/m^2)	22.64 ± 3.41	22.60 ± 3.51	22.71 ± 3.24	0.758	0.034
STS	3.19 (1.99, 5.60)	3.17 (1.98, 5.62)	3.31 (2.04, 5.51)	0.984	−0.092
Pre Cr (μmol/L)	75.00 (61.00, 90.15)	74.35 (62.00, 91.88)	75.00 (59.78, 88.95)	0.369	−0.055
Pre Albumin (g/L)	36.00 (33.70, 38.23)	36.25 (33.80, 38.20)	35.80 (33.62, 38.27)	0.803	−0.013
Duration of Procedure (min)	100.00 (75.75, 120.00)	100.00 (75.25, 120.00)	95.00 (80.00, 123.75)	0.703	−0.027
Total Fluid (ml)	1500.00 (1000.00, 1500.00)	1500.00 (1000.00, 1500.00)	1500.00 (1000.00, 1500.00)	0.761	−0.006
Blood Loss (ml)	50.00 (50.00, 50.00)	50.00 (20.00, 50.00)	50.00 (50.00, 50.00)	0.148	0.073
Pre EF (%)	60.70 (52.30, 65.82)	60.45 (52.12, 66.47)	60.90 (52.92, 65.10)	0.995	0.053
Age ≥ 75, n (%)	207 (49.76)	135 (49.27)	72 (50.70)	0.781	0.029
PVD, n (%)	18 (4.33)	12 (4.38)	6 (4.23)	0.942	−0.008
Male, n (%)	221 (53.12)	145 (52.92)	76 (53.52)	0.907	0.012
Anesthesia Type, n (%)	328 (78.85)	214 (78.10)	114 (80.28)	0.606	0.055
Smoking, n (%)	96 (23.08)	63 (22.99)	33 (23.24)	0.955	0.006
Drinking, n (%)	68 (16.35)	45 (16.42)	23 (16.20)	0.953	−0.006
NYHA Class III or IV, n (%)	299 (71.88)	198 (72.26)	101 (71.13)	0.807	−0.025
Hypertension, n (%)	232 (55.77)	153 (55.84)	79 (55.63)	0.968	−0.004
Corony Heart Disease, n (%)	129 (31.01)	81 (29.56)	48 (33.80)	0.375	0.09
Cardiac History, n (%)	42 (10.1)	27 (9.85)	15 (10.56)	0.82	0.023
Previous Stroke, n (%)	22 (5.29)	13 (4.74)	9 (6.34)	0.491	0.065
Diabetes, n (%)	79 (18.99)	51 (18.61)	28 (19.72)	0.785	0.028
Pre Aortic regurgitation, n (%)	280 (67.31)	186 (67.88)	94 (66.20)	0.728	−0.036
Aspirin, n (%)	95 (22.84)	59 (21.53)	36 (25.35)	0.379	0.088
Pre Renal Failure, n (%)	5 (1.2)	3 (1.09)	2 (1.41)	1	0.027
ACEI/ARB, n (%)	117 (28.12)	77 (28.10)	40 (28.17)	0.989	0.001

Table 3. Baseline indicators of matched patients.

Variables	Total (n = 613)	Non silent cerebral infarction (n = 142)	Silent cerebral infarction (n = 471)	*P*-value
Total Hospital Stay (days)	7.00 (5.00, 9.00)	6.00 (5.00, 9.00)	7.00 (5.00, 9.00)	0.103
Postopetarive Stsy (days)	3.00 (1.00, 5.00)	2.00 (1.00, 5.00)	3.00 (1.00, 5.00)	0.367
Month Mortality, n (%)	10 (1.63)	0 (0.00)	10 (2.12)	0.17
Year Mortality, n (%)	25 (4.08)	1 (0.70)	24 (5.10)	0.02
Post Delirium, n (%)	46 (7.5)	4 (2.82)	42 (8.92)	0.016
Post AKI, n (%)	35 (5.71)	6 (4.23)	29 (6.16)	0.384
Post MI, n (%)	4 (0.65)	1 (0.70)	3 (0.64)	1
Death, n (%)	1 (0.16)	0 (0.00)	1 (0.21)	1
Post Transfusion, n (%)	9 (1.47)	1 (0.70)	8 (1.70)	0.642
Post Acute Heart Failure, n (%)	4 (0.65)	0 (0.00)	4 (0.85)	0.578
Post Cardiac Arrest, n (%)	4 (0.65)	0 (0.00)	4 (0.85)	0.578
Post Respiratory Failure, n (%)	6 (0.98)	0 (0.00)	6 (1.27)	0.387
Post Hydrothorax, n (%)	12 (1.96)	0 (0.00)	12 (2.55)	0.115
Post Pulmonary Infection, n (%)	22 (3.59)	5 (3.52)	17 (3.61)	0.96
Post AF, n (%)	25 (4.08)	5 (3.52)	20 (4.25)	0.702
Post Conduction Block, n (%)				0.022
LBBB	126 (20.55)	20 (14.08)	106 (22.51)	
AVB	25 (4.08)	7 (4.93)	18 (3.82)	
Perivalvular Leakage, n (%)	63 (10.28)	13 (9.15)	50 (10.62)	0.615
Post Severe Vascular Complication, n (%)	2 (0.33)	0 (0.00)	2 (0.42)	1
Minor Vascular Complications, n (%)	5 (0.82)	1 (0.70)	4 (0.85)	1

Table 4. Clinical outcomes before matching.

Variables	Total (n = 416)	Non silent cerebral infarction (n = 142)	Silent cerebral infarction (n = 274)	*P*-value
Total Hospital Stay (days)	7.00 (5.00, 9.00)	6.00 (5.00, 9.00)	7.00 (5.00, 10.00)	0.052
Postoperative stay (days)	3.00 (1.00, 5.00)	2.00 (1.00, 5.00)	3.00 (1.00, 5.00)	0.187
Month Mortality, n (%)	5 (1.2)	0 (0.00)	5 (1.82)	0.252
Year Mortality, n (%)	16 (3.85)	1 (0.70)	15 (5.47)	0.016
Post delirium, n (%)	29 (6.97)	4 (2.82)	25 (9.12)	0.017
Post AKI, n (%)	24 (5.77)	6 (4.23)	18 (6.57)	0.331
Post MI, n (%)	2 (0.48)	1 (0.70)	1 (0.36)	1
Death, n (%)	1 (0.24)	0 (0.00)	1 (0.36)	1
Post Transfusion, n (%)	8 (1.92)	1 (0.70)	7 (2.55)	0.354
Post Acute Heart Failure, n (%)	2 (0.48)	0 (0.00)	2 (0.73)	0.549
Post Cardiac Arrest, n (%)	1 (0.24)	0 (0.00)	1 (0.36)	1
Post Respiratory Failure, n (%)	4 (0.96)	0 (0.00)	4 (1.46)	0.359
Post Hydrothorax, n (%)	6 (1.44)	0 (0.00)	6 (2.19)	0.179
Post Lung Infection, n (%)	15 (3.61)	5 (3.52)	10 (3.65)	0.947
Post AF, n (%)	18 (4.33)	5 (3.52)	13 (4.74)	0.561
Post Conduction Block, n (%)				0.022
LBBB	91 (21.88)	20 (14.08)	71 (25.91)	
AVB	18 (4.33)	7 (4.93)	11 (4.01)	
Perivalvular Leakage, n (%)	44 (10.58)	13 (9.15)	31 (11.31)	0.497
Post Severe Vascular Complication, n (%)	1 (0.24)	0 (0.00)	1 (0.36)	1
Minor Vascular Complications, n (%)	2 (0.48)	1 (0.70)	1 (0.36)	1

Table 5. Clinical outcomes after matching.

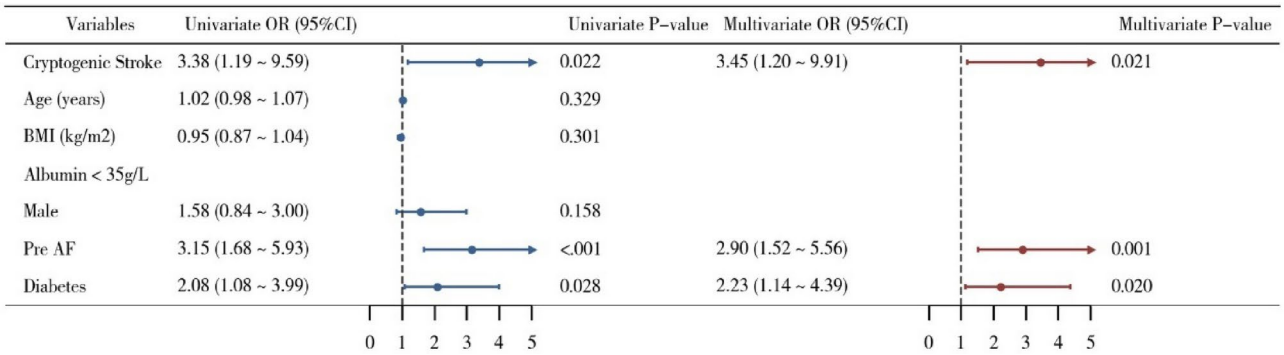

Fig. 4. Analysis of risk factors for postoperative delirium before matching.

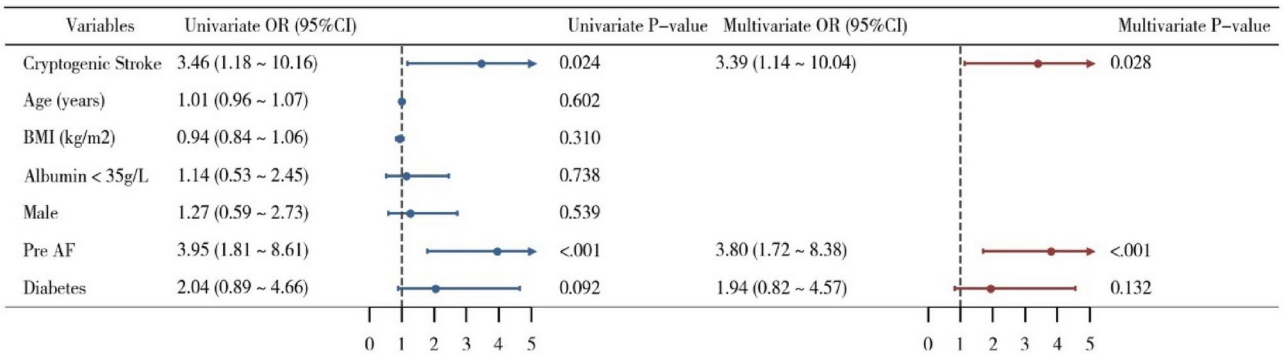

Fig. 5. Analysis of risk factors for postoperative delirium after matching.

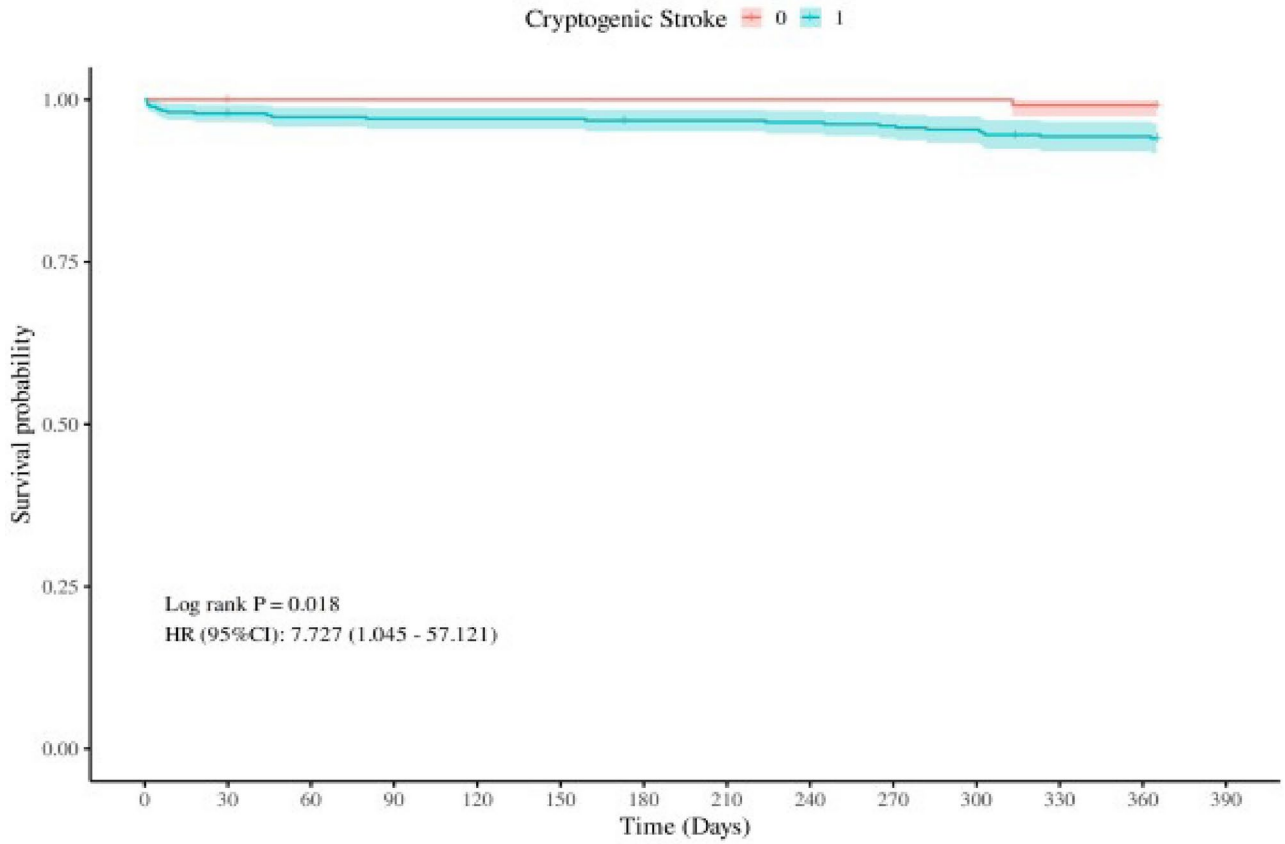

Fig. 6. One-year survival curve after TAVR before matching.

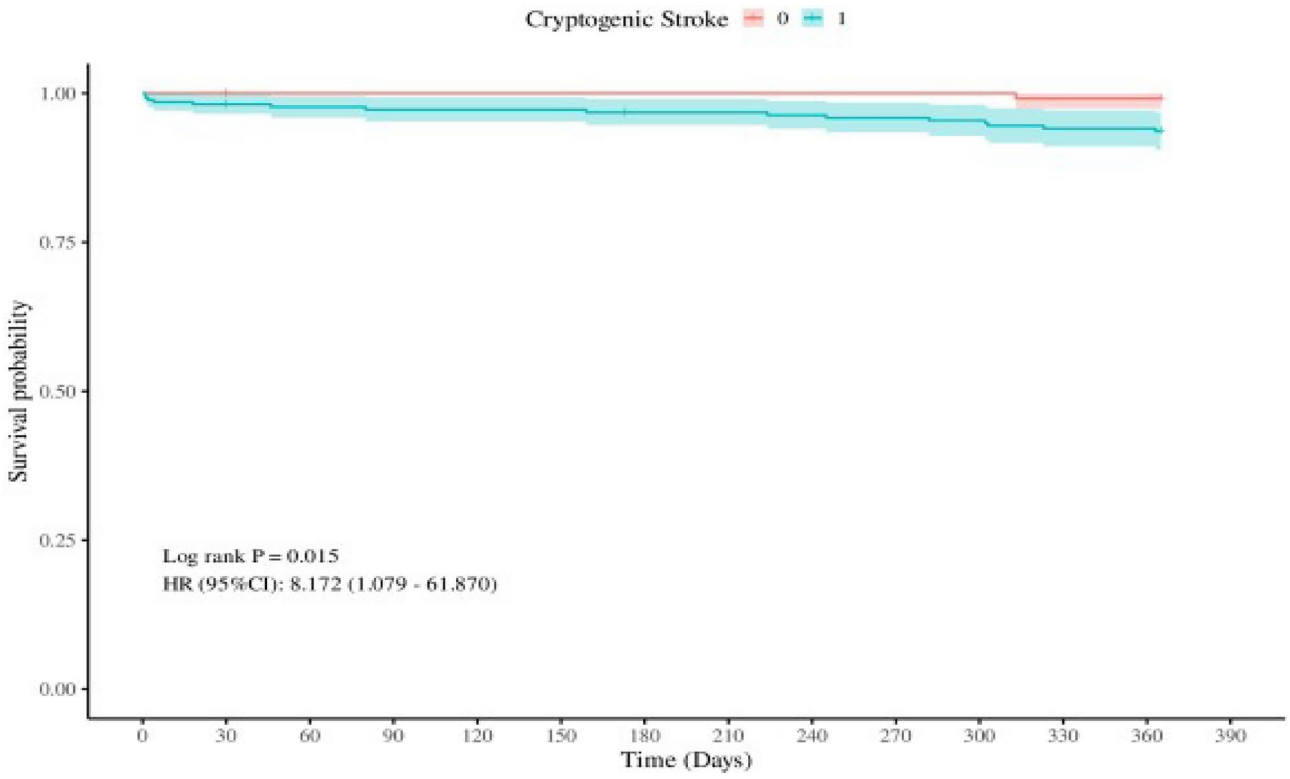

Fig. 7. One-year survival curve after TAVR after matching.

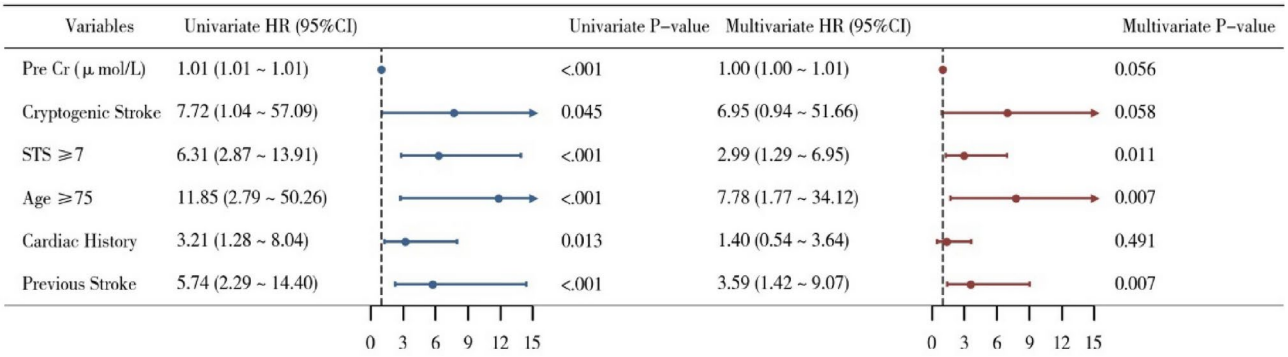

Fig. 8. Risk factors for mortality 1 year before matching.

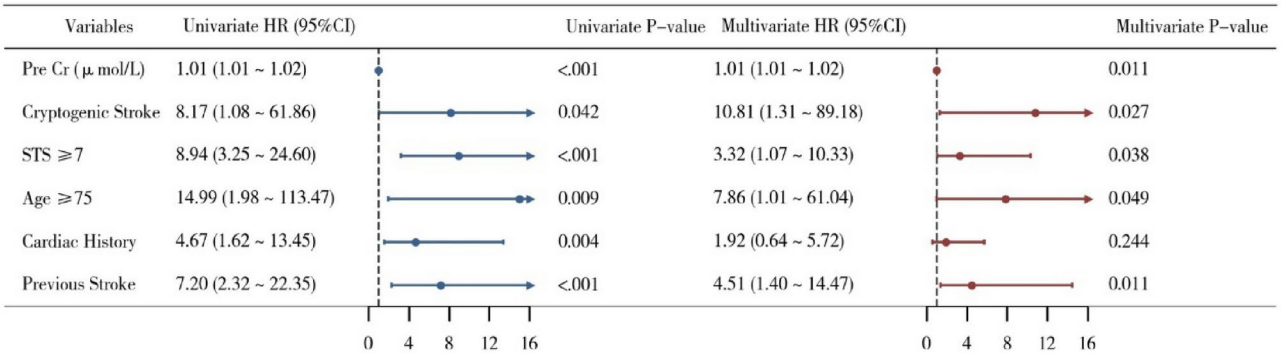

Fig. 9. Risk factors for mortality 1 year after matching.

Before Matching: Multivariate Cox regression analysis indicated that SCI (HR: 6.95, 95% CI: 0.94–51.66, P = 0.058) was not significantly associated with one-year mortality. However, an STS score greater than 7% (HR: 2.99, 95% CI: 1.29–6.95, P = 0.011), age of 75 years or older (HR: 7.78, 95% CI: 1.77–34.12, P = 0.007), and history of stroke (HR: 3.59, 95% CI: 1.42–9.07, P = 0.007) were identified as significant risk factors for one-year mortality following TAVR.

After Matching: Post-match multivariate Cox regression analysis revealed that SCI (HR: 10.81, 95% CI: 1.31–89.18, P = 0.027) was a significant risk factor for one-year mortality. Additionally, preoperative creatinine levels (HR: 1.01, 95% CI: 1.01–1.02, P = 0.011), an STS score greater than 7% (HR: 3.32, 95% CI: 1.07–10.33, P = 0.038), age of 75 years or older (HR: 7.86, 95% CI: 1.01–14.47, P = 0.049), and history of stroke (HR: 7.20, 95% CI: 2.32–22.35, P < 0.001) were also identified as significant risk factors for one-year mortality following TAVR.

Discussion

To our knowledge, this is the first study to evaluate the incidence, risk factors, and clinical impact of Silent Cerebral Infarction according to VARC-3 criteria (neuroARC 2) from an anesthetic perspective. The main findings are as follows: 1) Post-induction hypotension and postoperative tachyarrhythmia are risk factors for Silent Cerebral Infarction according to VARC-3 criteria. 2) Postoperative delirium and 1-year mortality in patients with SCI were significantly higher than those in patients with non-SCI. At the same time, clinical data supported the correctness of VARC-3 incorporating postoperative delirium into the new definition; 3)SCI, preoperative creatinine, STS >7%, age ≥75 years, and history of stroke are risk factors for death 1 year after TAVR.

It is known that stroke risk peaks immediately after TAVR, with up to 50% of cerebrovascular events occurring in the perioperative period, primarily mediated by mechanical interactions between the transcatheter valve system and calcified native valves, leading to central nervous system embolism. In addition, Even though the overall incidence of neurological events appears to be high, it must be emphasized that the new VARC-3 definition is quite broad and encompasses clinical events that differ significantly due to pathophysiological mechanisms[21].Previous research indicates that the incidence of SCI after TAVR ranges between 62 and 93%[22]. Our findings align with this range, showing a 76.8% incidence rate. The risk factors contributing to SCI after TAVR have remained unclear. Samim et al. identified age, hyperlipidemia, and balloon post-dilation as independent predictors of SCI post-TAVR[23]. Similarly, Ciccarelli et al. reported that diabetes, chronic kidney disease, valve dilation, and postoperative new-onset atrial fibrillation are significant risk factors[12]. Conversely, Suhai et al. found that the number of pre-dilations independently influences the risk of SCI, whereas factors like

age, cardiovascular comorbidities, aortic calcification, access route, valve type and size, and the number of post-dilations did not show a significant association[24].

Bijker et al. discovered that intraoperative hypotension and the duration of hypotension significantly increase the incidence of postoperative stroke[25], which is consistent with our findings. Specifically, their study highlighted that each additional minute of hypotension raises the risk of postoperative stroke by 1.3%. Therefore, a cumulative hypotension period of 10 min could elevate the stroke risk by approximately 14%[26]. Elderly patients often have underlying cardiovascular conditions, impaired vasodilatory reserve, focal cerebrovascular stenosis, and endothelial dysfunction. These issues can disrupt the microcirculatory mechanisms essential for maintaining cerebral blood flow autoregulation. Consequently, hypotension and vascular factors diminishing cerebral blood flow may lead to watershed infarcts and hinder the clearance of microemboli, resulting in insufficient cerebral perfusion and causing postoperative silent or overt cerebral infarctions[16,19,20]. Prior studies have shown that post-induction hypotension, caused by decreased preload and afterload secondary to the vasodilatory and cardiac depressant effects of anesthetics, is a risk factor for SCI. SCI increases the risk of postoperative delirium and 1-year mortality, so active treatment of post-induction hypotension with appropriate fluid replacement and vasoactive drugs is critical[27–29]. Intraoperative hypotension can be related to various factors, including bleeding, surgical manipulation, and systemic inflammatory response. More specifically, addressing hypotension during a rapid pacing sequence for TAVR requires coordination between the anesthesiologist and the surgeon.

Multiple studies have recognized postoperative tachyarrhythmia as an independent predictor of stroke[30]. Tachyarrhythmias encompass both atrial arrhythmias—such as atrial tachycardia, flutter, and fibrillation—and ventricular arrhythmias, including ventricular tachycardia, flutter, and fibrillation[31]. Despite advancements in procedural techniques and device improvements reducing overall risks for TAVR patients, about 10% still develop new-onset atrial fibrillation after the procedure[32]. Observational studies suggest that early adverse events following TAVR are predominantly cerebrovascular, while subacute events (occurring 1 to 30 days post-procedure) are mainly linked to new-onset atrial fibrillation[12].Atrial fibrillation and other tachyarrhythmias can create irregular atrial blood flow patterns, increasing thrombosis risk. These thrombi may travel through the bloodstream to cerebral vessels, leading to SCI and other cerebrovascular complications[14]. Given that TAVR is an invasive intervention, it may elevate the risk of intravascular thrombosis[33]. Patients with concurrent tachyarrhythmia might face an even higher thrombosis risk. Moreover, supraventricular tachycardia independently heightens the risk of ischemic stroke, irrespective of atrial fibrillation[34,35]. The presence of ectopic electrical activity increases the likelihood of cardiac embolism and subsequent stroke. Atrial tachycardia often signals more severe hypertension, diabetes, physical inactivity, or lipid metabolism disorders—all factors that amplify vascular risk and stroke incidence. Additionally, it can result in left atrial enlargement, stasis within the left atrial appendage, fibrosis, and endothelial dysfunction, ultimately creating a hypercoagulable state[34,35]. Tachyarrhythmias, most commonly atrial fibrillation or atrial flutter, may occur during TAVR procedures, which greatly increases the risk of persistent tachyarrhythmias after surgery. Treatment with antiarrhythmic drugs should be judicious and discussed with the procedural team.

This study observed that patients with SCI post-TAVR exhibited higher incidences of postoperative delirium and one-year mortality. Delirium in the form of neuroARC type 3 was the most common event, and its inclusion in the new VARC-3 definition identified a significantly higher incidence of neurologic complications compared with the VARC-2 definition[21].Postoperative delirium typically presents with acute symptoms and is associated not only with sudden cognitive and attentional fluctuations in patients but also with increased mortality and prolonged hospital stays. Tse et al. reported an incidence of postoperative delirium after transfemoral TAVR ranging from 8 to 12%[36], while Eggebrecht et al. noted an incidence of delirium requiring treatment after TAVR of 3.5% to 3.8%. This study found an incidence of 7.5%, which aligns with previous findings. Variations in the incidence of postoperative delirium across different studies may be attributed to differences in study populations and assessment methodologies. This study employed the Confusion Assessment Method (CAM) and CAM-ICU for delirium assessment, which are effective and widely used methods for identifying delirium.

Auffret et al. identified that 7.8% of patients experienced cognitive dysfunction within 30 days post-TAVR[37]. Similarly, Sarah et al. reported that the presence of SCI is associated with a significant decline in overall cognitive function, where asymptomatic thalamic infarcts correlate with memory decline and non-thalamic infarcts with decreased psychomotor speed[38]. Samir et al. demonstrated a significant relationship between changes in neurocognitive scores and the volume of silent cerebral infarct lesions[39]. Additionally, Marco et al. observed that patients with SCI exhibited marked declines in neurocognitive function at discharge, with incomplete recovery during follow-up. They also identified a correlation between decreased neurocognitive scores and the volume of SCI lesions. While this mild and transient decline may have limited clinical impact on elderly patients, it becomes increasingly important when considering TAVR for younger, low-risk individuals[40].

Bagienski et al. determined that the occurrence of postoperative delirium is associated with prolonged hospital stays and serves as an independent predictor of mortality in patients undergoing transfemoral TAVR. Factors such as frailty, advanced age, carotid artery disease, atrial fibrillation, and smoking may contribute to postoperative delirium after cardiac surgery. These factors may be involved in the pathogenic chain of ischemic brain injury through atherosclerosis or thromboembolism[41,42]. This study found that preoperative atrial fibrillation is associated with postoperative delirium after TAVR. The underlying mechanism may involve preoperative atrial fibrillation leading to hypotension and inadequate cerebral perfusion, as well as causing blood turbulence that facilitates the formation of microthrombi, resulting in embolic brain injury and an increased incidence of postoperative delirium. Studies have indicated that microembolus formation and underlying pathological factors (including coronary artery disease and arrhythmias) may mediate the occurrence of postoperative delirium after TAVR[32]. Procedures during TAVR, such as vascular delivery of the aortic valve, balloon expansion during valve implantation, retrograde positioning of the valve, or stent expansion, may generate microemboli.

In a prospective observational study, Avinee et al. found that improvements in surgical techniques and equipment led to a yearly decrease in the one-month postoperative mortality rate from 2010 to 2014[43]. This suggests that perioperative complications significantly influence early mortality rates after TAVR. With the adoption of the Edwards SAPIEN 3 valve in 2014, the one-month mortality rate sharply declined to 1.5%, and the one-year mortality rate reduced to between 3 and 4% by 2014[43,44]. This study reported a one-month mortality rate of 1.2% and a one-year rate of 3.85%, consistent with these trends.

Liebetrau et al. discovered that both overt stroke and SCI increase the incidence of dementia and three-year mortality. Bokura et al. found that the occurrence of clinical stroke was significantly higher in patients with SCI compared to those without. The presence of SCI indicates an elevated risk of clinical stroke and death in elderly patients[45]. SCI and significant periventricular high signal intensities markedly increase the risk of death, independent of age and gender. Overt stroke remains the most common cause of death in patients with SCI. Two large longitudinal community studies indicated that mortality in patients with SCI increased by three to four times compared to those without[46–48].

Further studies have linked higher STS scores to increased postoperative mortality. Hermiller et al. identified that an STS score exceeding 7% predicts one-year mortality post-TAVR[49], while Yoon et al. also found a significant association between STS scores and two-year mortality[50]. Ricardo et al. noted that in TAVR patients under 90 years old, factors such as STS score, stroke occurrence, and renal impairment are connected to one-year mortality. Additionally, David et al. determined that advancing age, male gender, severe pulmonary disease, renal failure (both dialysis-dependent and non-dialysis-dependent), non-transfemoral access routes, and higher baseline STS scores correlate with increased one-year mortality following TAVR, with mortality rates rising progressively with age[51].

Further study on the risk factors and prognosis of silent cerebral infarction after transcatheter aortic valve replacement may lead to the identification and understanding of currently unrecognized neuroprotective factors, thereby improving anesthetic and surgical strategies for this procedure.

Limitations

This study has several limitations:

1. Single-Center and Retrospective Design: Being a single-center retrospective study with a relatively small sample size, and excluding patients without postoperative cranial MRI, may introduce bias in analyzing risk factors for SCI after TAVR.

2. Potential for Unidentified Variables: Given the retrospective nature, although numerous variables influencing the occurrence of SCI were collected, other potential unknown variables may have been overlooked.

3. Intergroup Differences: There were differences in patient baseline data and surgical-related variables between groups. PSM was utilized to minimize these differences, albeit at the cost of some sample size reduction.

4. Variability in Assessments Across Centers: Differences in patient characteristics and methods for assessing postoperative delirium across different centers may result in variations in delirium incidence, potentially affecting the analysis of its risk factors.

5. Association only: The study's conclusions indicate association between post-induction hypotension and tachyarrhythmia with SCI after TAVR, and between SCI with postoperative delirium and one-year mortality after TAVR. However, causality cannot be firmly established and requires further research.

6. Sixth, the incidence, predictors, and prognostic impact of stroke and other overt CNS injury (NeuroARC1) and transient ischemic attack without CNS injury (NeuroARC3) among neurologic events after TAVR according to VARC-3 criteria were not analyzed in this study.

Conclusion

Silent cerebral infarction after TAVR has a significant impact on clinical outcomes and is associated with increased mortality at 1-year follow-up. This study provides clinical data to support the Valve Academic Research Consortium (VARC)−3 definition of SCI in neurological events after TAVR.This study found that post-induction hypotension and postoperative tachyarrhythmia are risk factors for SCI after TAVR. Patients who developed SCI after TAVR exhibited higher rates of postoperative delirium and increased one-year mortality compared to those without this complication. Furthermore, factors such as elevated preoperative creatinine levels, an STS score above 7%, age of 75 years or older, and a prior history of stroke were associated with higher one-year mortality rates after TAVR.

Materials and methods

Study population

This retrospective study included patients who underwent TAVR at the Second Affiliated Hospital of Zhejiang University School of Medicine (SAHZU) between January 2020 and April 2023.The study was approved by the Human Research Ethics Committee of the SAHZU(no. 2022–0521). And we followed the opt-out model with approval of the Human Research Ethics Committee of the SAHZU. The study was conducted in compliance with the Declaration of Helsinki. The requirement for patient approval or informed consent was waived by the Human Ethics Committee of the SAHZU, owing to the retrospective nature of the study.

Inclusion criteria

This retrospective study included patients who underwent TAVR at the Second Affiliated Hospital of Zhejiang University School of Medicine (SAHZU) between January 2020 and April 2023. Inclusion criteria were patients aged 50 years or older who received transfemoral TAVR at SAHZU during this period. Exclusion criteria included patients who underwent TAVR via transapical, carotid, or other access routes; those without

postoperative cranial MRI examinations; patients admitted urgently due to sudden heart failure requiring emergency intervention; those who underwent intraoperative conversion to open-heart surgery; patients who experienced overt postoperative stroke; and those undergoing a second TAVR procedure.

Data collection

This retrospective study utilized patient data from the TAVR database. Hospitalization and follow-up information were obtained from our center's electronic medical records, the anesthesia *Docare* system, and the Cardiovascular Medicine Clinical Research Center database. Post-induction hypotension data were collected through intensive vital sign monitoring in the anesthesia *Docare* system, while tachyarrhythmia data were gathered from patients' postoperative electrocardiograms, medical records, and nursing notes.

Data collection

7. Demographic information

Gender, age, BMI, smoking history, and alcohol consumption history.

8. Preoperative data

New York Heart Association (NYHA) functional classification, Society of Thoracic Surgeons (STS) score, preoperative comorbidities (hypertension, hyperlipidemia, diabetes, coronary heart disease, myocardial infarction, atrial fibrillation, heart failure, peripheral vascular disease, history of stroke, chronic obstructive pulmonary disease, pneumonia, atelectasis, pleural effusion, renal failure), history of previous thoracotomy, preoperative medication history (β-blockers, calcium channel blockers, cardiotonics, diuretics, ACEIs, and ARBs), preoperative laboratory tests (hemoglobin, creatinine, albumin), preoperative echocardiography (left ventricular ejection fraction, maximum transaortic valve gradient, mean transaortic valve gradient, aortic valve area, peak transaortic valve flow velocity, moderate to severe aortic regurgitation). Preoperative auxiliary examination results were the most recent ones within one week before surgery.

9. Intraoperative Data

Type of anesthesia, fluid infusion volume, blood loss, urine output, operation time, contrast agent volume, valve type, number of balloon pre-dilations, number of balloon post-dilations.

10. Postoperative data

All-cause mortality from the postoperative period to discharge, incidence of stroke, myocardial infarction, acute kidney injury, vascular complications (categorized as major and minor), paravalvular leak, tachyarrhythmia, postoperative length of stay, and the rate of intensive care unit (ICU) admissions.

Definitions of clinical outcomes

Definitions of adverse events following TAVR adhered to the VARC-3 guidelines published by the Valve Academic Research Consortium in 2021. Key definitions in this study include:

1. Silent Cerebral Infarction

Neurological lesions with imaging or pathological evidence of focal or multifocal ischemia or hemorrhage in the central nervous system but without acute neurological symptoms corresponding to the lesion or hemorrhage location.

2. *Myocardial infarction*

Within 48 hours postoperatively, creatine kinase-MB (CK-MB) elevated more than 10 times the upper limit of normal or elevated more than 5 times the upper limit of normal accompanied by one or more of the following: 2 or more new pathological Q waves in continuous leads; new persistent left bundle branch block (LBBB).

3. *Acute kidney injury*

Serum creatinine increased by ≥150–200% (≥1.5–2.0 times) compared to baseline within 7 days or increased by ≥0.3 mg/dL (≥26.4 μmol/L) within 48 hours postoperatively.

4. Vascular complications

Major Vascular Complications: Aortic dissection or rupture; vascular (arterial or venous) injury (perforation, rupture, dissection, stenosis, ischemia, arterial or venous thrombosis including pulmonary embolism, arteriovenous fistula, pseudoaneurysm, hematoma, retroperitoneal hematoma, infection) or ventricular septal syndrome leading to death, life-threatening bleeding or major bleeding, visceral ischemia, or cerebrovascular events.

Minor Vascular Complications: Vascular injuries not leading to death, life-threatening bleeding or major bleeding, visceral ischemia, or cerebrovascular events.

5. *Cardiac Death*

Deaths related to heart failure, cardiogenic shock, bioprosthetic valve dysfunction, myocardial infarction, stroke, thromboembolism, bleeding, cardiac tamponade, vascular complications, arrhythmias or conduction system disorders, cardiovascular infections (e.g., mediastinitis, endocarditis), or other clearly cardiovascular causes; intraoperative deaths; sudden deaths; deaths from unknown causes.

6. Post-induction hypotension

Hypotension occurring from induction of anesthesia to the start of surgery, defined as a mean arterial pressure at least 20% below the average mean arterial pressure of the 5 minutes before induction.

7. Postoperative New-Onset Atrial Fibrillation

Any arrhythmia not present preoperatively, with electrocardiographic features of atrial fibrillation (or flutter), persisting for at least 30 seconds on a 12-lead electrocardiogram.

8. Tachyarrhythmia

Includes atrial arrhythmias (atrial tachycardia, atrial flutter, and atrial fibrillation) and ventricular arrhythmias (ventricular tachycardia, ventricular flutter, and ventricular fibrillation)[17].

Anesthesia, surgical methods, neuroimaging and postoperative delirium assessment

Anesthesia induction and maintenance

Two anesthesia methods were employed at our center: general endotracheal anesthesia and non-intubated general anesthesia. The anesthesia method was determined by the anesthesiologist based on the patient's condition and surgical factors, in consultation with the patient, their family, and the surgeon. After surgery, the decision to transfer the patient to the ICU was made collaboratively with the surgeon, based on the patient's preoperative status, surgical details, and anesthesia-related factors.

1. General Endotracheal Anesthesia

Induction was performed using etomidate at a dosage of 0.3 mg/kg or propofol at 1.0 mg/kg, combined with sufentanil ranging from 0.3 to 0.5 μg/kg, and rocuronium administered at 50 mg. Maintenance involved a continuous infusion of propofol and remifentanil, along with intermittent doses of rocuronium or cisatracurium. The anesthesiologist decided on the use of sevoflurane inhalation anesthesia based on intraoperative conditions.

2. Non-intubated General Anesthesia

Induction was performed using propofol 0.5–1.0 mg/kg and fentanyl 0.05–0.1 mg. Anesthesia was maintained with continuous infusion of propofol and dexmedetomidine, with intermittent administration of fentanyl as needed.

Surgical procedure

All patients underwent TAVR via the transfemoral approach. Preoperatively, radial artery and internal jugular vein punctures were performed. Patients were positioned supine, with standard aseptic preparation and draping, and a temporary pacemaker was placed. After anesthesia induction, the surgical procedure began. For patients with AS, transvalvular pressure gradients were measured across the aortic valve. Balloon pre-dilation was performed under rapid pacing after confirming the position via angiography at the aortic annulus. Subsequently, a valve of appropriate size, as determined preoperatively, was positioned and deployed under angiographic guidance. Immediate aortic root angiography and transesophageal or transthoracic echocardiography were used to evaluate the coronary arteries and assess for paravalvular leaks. Once satisfactory surgical outcomes were confirmed, the delivery system was withdrawn, and the procedure was concluded.

Neuroimaging assessment

Each scan was independently assessed by two experienced neuroradiologists, blinded to all clinical/procedural details. Cerebral embolism or microinfarction was defined as a new restricted diffusion lesion on DWI.

Postoperative delirium assessment

Postoperative delirium was assessed using the Confusion Assessment Method (CAM) and the CAM for the ICU (CAM-ICU). Assessments were conducted within 12 h after the patient was admitted to the ICU or ward postoperatively and subsequently every 12 h for up to two days. Delirium was defined by the presence of:

1.Acute onset and fluctuating course.
2.Inattention.
3.Disorganized thinking.
4.Altered level of consciousness.

A diagnosis of postoperative delirium required criteria (1) and (2) to be met, along with either criterion (3) or (4).

Outcome measures

The primary outcome of this study was the incidence of delirium within two days following TAVR. Secondary outcomes encompassed postoperative length of stay, in-hospital mortality, and one-year mortality.

Statistical analysis

Data analysis was conducted using R version 4.2.3 statistical software. Variables were categorized as either continuous or categorical. The Shapiro–Wilk test was employed to assess the normality of continuous variables. Normally distributed continuous variables were reported as means ± standard deviations, while Student's t-test and Welch's t-test were utilized to compare between-group differences for these variables. Non-normally distributed continuous variables were expressed as medians with interquartile ranges and compared using the Wilcoxon rank-sum test. Categorical variables were presented as frequencies and percentages, with Pearson's chi-square test or Fisher's exact test used to determine statistical significance between groups. All analyses were two-tailed, with a p-value of less than 0.05 considered statistically significant.

Baseline differences between patients excluded due to the absence of postoperative MRI and those included in the analysis were compared to assess potential selection bias. Multivariate logistic regression analysis was performed with postoperative SCI as the dependent variable to identify associated risk factors. Factors potentially related to SCI after TAVR, based on previous literature and available data, were selected for analysis. Specifically, age, post-induction hypotension, tachyarrhythmia, history of stroke, and balloon post-dilation were included in univariate logistic regression models. Variables with p-values below 0.2 in univariate analyses were considered as candidate variables in the multivariate logistic regression model.

Post-induction hypotension was categorized into three groups based on its occurrence and duration: no post-induction hypotension, hypotension lasting less than 10 min, and hypotension lasting more than 10 min. Variables with missing data exceeding a 10% threshold were excluded from analysis, whereas those with less than 10% missingness were imputed using multiple imputation techniques.

Propensity score matching (PSM) was implemented to balance the non-SCI group with the SCI group at a 1:2 ratio. Using R version 4.2.3, PSM was conducted with a caliper value set at 0.2. Post-matching, standardized mean differences (SMDs) were compared, with values below 0.1 indicating satisfactory balance between the groups.

For postoperative delirium as the dependent variable, multivariate logistic regression analysis was utilized to identify risk factors. Variables with p-values below 0.2 in univariate analyses were included as candidate variables in the multivariate model.

Survival times were compared using the Kaplan–Meier method, and survival curves were plotted. The log-rank test was applied to assess statistical differences between the survival curves of the SCI group and the non-SCI group. Cox regression models were employed for both univariate and multivariate analyses of one-year postoperative mortality. The regression results are presented in the form of a forest plot. Results from the Cox regression models were expressed as hazard ratios (HRs) with 95% confidence intervals (CIs).

The primary endpoint focused on the incidence of postoperative delirium within the study population. Based on preliminary data, the incidence of postoperative delirium was approximately 9% in the SCI group and 3% in the non-SCI group. With a two-sided α of 0.05, a power $(1-\beta)$ of 0.8, and an allocation ratio of 3:1 between the SCI and non-SCI groups, the required sample size was calculated using R software. The calculated sample sizes were 369 cases for the experimental group and 123 cases for the control group. The study ultimately included 471 patients in the SCI group and 142 patients in the non-SCI group, thereby meeting the sample size requirements.

Data availability

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

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Author contributions

Min Yan and Yuanyuan Yao conceived the design of the study. Shuguang Wu performed the experiments, analyzed the data and wrote the manuscript. Yi Liu, Tingting Ni, and Tao Lv performed the experiments and collected the data. Shuguan Wu, Yi Liu and Tingting Ni confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

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Declarations

Competing interests

The authors declare no competing interests.

Additional information

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