

Incidence and Predictors of Cerebrovascular Accidents in Patients Who Underwent Transcatheter Mitral Valve Repair With MitraClip



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Transcatheter mitral edge-to-edge repair (TEER) with transcatheter devices has become a mainstay in the minimally invasive treatment of patients with severe mitral regurgitation at increased surgical risk. Despite its apparently favorable risk profile, there is uncertainty on the risk and features of cerebrovascular accidents (CVAs) early and long after transcatheter mitral valve repair. We aimed to appraise the incidence and predictors of CVA in patients who underwent TEER. We explicitly queried the data set of an ongoing multicenter prospective observational study dedicated to TEER with MitraClip (Abbott Vascular, Santa Clara, California). The incidence of CVAs after TEER was formally appraised, and we explored potential predictors of such events. Descriptive, bivariate, and diagnostic accuracy analyses were performed. Of 2,238 patients who underwent TEER, CVAs occurred in 33 patients (1.47% [95% confidence interval 1.02% to 2.06%]), including 6 (0.27% [0.10% to 0.58%]) in-hospital strokes and 27 events after discharge (0.99% [0.66% to 1.44%]), over a median follow-up of 14 months. Most CVAs were major ischemic strokes during and after the in-hospital phase. Overall, CVAs were more common in patients with atrial fibrillation ($p = 0.018$), renal dysfunction ($p = 0.032$), higher EuroSCORE II ($p = 0.033$), and, as expected, higher CHA2DS2-VASc score ($p = 0.033$), despite the limited prognostic accuracy of the score. Notably, the occurrence of CVA did not confer a significantly increased risk of long-term ($p = 0.136$) or cardiac death ($p = 0.397$). The incidence of CVA in patients who underwent TEER is low, with most events occurring after discharge and being associated with preexisting risk features. These findings, although reassuring on the safety of TEER, call for proactive antithrombotic therapy

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See page 31 for Declaration of Competing Interest.

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whenever CVA risk is increased before and after TEER. © 2024 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>) (Am J Cardiol 2024;228:24–33)

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Mitral regurgitation is a common cause of morbidity and mortality.¹ Although surgical repair represents the gold standard for such disease, it is associated with significant complications in frail patients.² Minimally invasive alternatives to surgical repair have been identified, and transcatheter mitral valve repair (TMVR) approaches may offer significant benefits in patients at increased surgical risk.³ Transcatheter edge-to-edge repair (TEER), in particular, appears as a clinically useful technique with a low risk of acute and postacute complications.^{4,5} Despite the rosy profile of TEER, patients with significant mitral regurgitation may face a substantial risk of stroke and transient ischemic attack (TIA), collectively labeled cerebrovascular accidents (CVAs).^{6–9} Furthermore, the creation of a double orifice, with reduction in mitral valve area, increase in mitral valve gradient, and potentially ensuing atrial stasis, may lead to an increased risk of CVAs.^{10,11} Despite these premises, there is paucity of real-world evidence aiming at disentangling the interplay between TEER and CVA risk.^{12,13} The GISE registry Of Transcatheter treatment of mitral valve regurgitaTiOn (GIOTTO) study is a landmark national registry that includes patients with significant mitral regurgitation who underwent TMVR with the MitraClip (Abbott Vascular, Santa Clara, California) TEER device.^{11,14} We aimed at leveraging the extensive body of data collected in this study to appraise attentively the incidence, timing, risk factors, and outlook of CVAs, with the underlying hypothesis that CVAs occurring during or after TEER may differentially impact patient survival.

Methods

Details on the GIOTTO study have already been reported elsewhere. This registry is also registered online in *ClinicalTrials.gov* (NCT03521921).^{15–17} Briefly, the protocol was approved by each participating ethical committee, and all patients provided written informed consent for inclusion in case TEER was attempted considering real-world clinical indications. All procedures were performed under transesophageal echocardiographic guidance, relying on deep sedation or general anesthesia, at the operator's discretion. Clinical follow-up, echocardiographic follow-up, and ancillary medical management were performed according to standard care and ongoing guidelines, with in-person visits every 1 to 3 months up to 12 months and then every 12 months. Similarly, transthoracic echocardiography was routinely repeated to evaluate cardiac dimensions, function, and valve features. Contemporary Mitral Valve Academic Research Consortium recommendations were used for event adjudication.^{18,19} Specifically, for this analysis, we focused on stroke and TIA individually and combined as CVAs. Briefly, stroke was defined as a focal or global neurologic deficit lasting ≥ 24 , < 24 hours if available

neuroimaging documented a new intracranial or subarachnoid hemorrhage or central nervous system infarction, or neurologic deficit resulting in death. A TIA was defined as a focal or global neurologic deficit lasting < 24 hours, with neuroimaging not demonstrating a new hemorrhage or infarct. In terms of classification, a stroke was defined as hemorrhagic if an acute episode of focal or global cerebral or spinal dysfunction caused by intraparenchymal, intraventricular, or subarachnoid hemorrhage, and ischemic if an acute episode of focal cerebral, spinal, or retinal dysfunction caused by infarction of the central nervous system tissue or otherwise undetermined. Notably, a minor stroke was defined as a stroke with a modified Rankin scale (mRS) score < 2 at 90 days or without an increase ≥ 1 mRS category from the prestroke baseline and a major stroke if associated with an mRS score ≥ 2 at 90 days plus an increase in ≥ 1 mRS category from the prestroke baseline. All CVA were diagnosed and adjudicated by a fully certified neurologist, with neuroimaging being performed in all patients. Descriptive analysis was based on reporting median (first quartile to third quartile) and count (%). Inferential analysis was based on computing Wilcoxon rank-sum test and Fisher's exact test and exact 95% confidence intervals for incidence rates. In addition, we generated survival curves using the Kaplan–Meier method and compared them with the Tarone–Ware test. No multiplicity adjustment was carried out. Computations were performed with Stata 13 (StataCorp, College Station, Texas).

Results

A total of 2,238 patients were included: 2,205 (98.5%) without any CVA during hospital stay or follow-up and 33 (1.47% [95% confidence interval 1.02% to 2.06%]) with CVA (Tables 1, 2, 3, and 4). Specifically, there were 6 (0.27% [0.10% to 0.58%]) strokes occurred during the hospital stay and 27 (1.24% [0.78% to 1.71%]) after discharge, with most events being major ischemic strokes (< 0.001). Overall, the median stay after TEER was 4 (first quartile: 3 to third quartile: 6), and follow-up after discharge and up to 1 month thereafter was available in 1,927 (86.1%), with corresponding figures for 6 and 12 months being 1,798 (80.3%) and 1,662 (74.3%), respectively.

Baseline features were largely similar in patients without or with CVAs, with the notable exclusion of risk scores for thrombotic risk in atrial fibrillation and serum creatinine (Table 1) and ensuing antithrombotic therapy. Specifically, CHA2DS2-VASc was 4^{3,5} in subjects without CVA versus 5^{4,5} in those with CVA ($p = 0.026$), with corresponding figures for EuroSCORE II of 4.6 (2.8 to 7.8) vs 6.0 (4.6 to 9.1, $p = 0.033$) and serum creatinine of 1.3 (1.0 to 1.7) versus 1.4 (1.2 to 1.9, $p = 0.032$). Additional clinical or imaging features were also similar in the groups, except for the

Table 1

Baseline features

Feature	No CVA (N=2205)	Any CVA (N=33)	P*
Age (years)	78 (71; 82)	79 (73; 81)	0.453
Female	807 (36.6%)	14 (42.4%)	0.474
Body mass index	24.8 (22.3; 27.6)	24.2 (23.3; 27.1)	0.806
Hypertension	1596 (72.4%)	26 (78.8%)	0.556
Diabetes mellitus	516 (23.4%)	9 (27.3%)	0.678
Dyslipidemia	733 (33.2%)	13 (39.4%)	0.461
Smoking history	318 (14.4%)	7 (21.2%)	0.314
Carotid artery disease	47 (2.1%)	1 (3.0%)	0.514
Prior CVA			0.115
None	2037 (92.4%)	28 (84.9%)	
Transient ischemic attack	55 (2.5%)	2 (6.1%)	
Minor stroke	49 (2.2%)	2 (6.1%)	
Major stroke	64 (2.9%)	1 (3.0%)	
Diagnosis			0.418
Degenerative mitral regurgitation	699 (31.7%)	11 (33.3%)	
Functional ischemic mitral regurgitation	616 (27.9%)	11 (33.3%)	
Functional non-ischemic mitral regurgitation	655 (29.7%)	6 (18.2%)	
Mixed etiology	235 (10.7%)	5 (15.2%)	
New York Heart Association			0.271
I	34 (1.6%)	0	
II	519 (23.6%)	4 (12.5%)	
III	1456 (66.2%)	27 (84.4%)	
IV	190 (8.6%)	1 (3.1%)	
Risk scores			
CHADS ₂	2 (2; 3)	3 (2; 3)	0.080
CHA ₂ DS ₂ -VASc	4 (3; 5)	5 (4; 5)	0.026
EuroSCORE II	4.6 (2.8; 7.8)	6.0 (4.6; 9.1)	0.033
Logistic EuroSCORE	10.8 (6.4; 18.7)	16.0 (9.7; 25.0)	0.166
STS score	3.5 (1.9; 6.1)	4.5 (2.5; 6.4)	0.481
Left ventricular ejection fraction (%)	40 (30; 55)	41 (30; 52)	0.744
Atrial fibrillation	469 (21.3%)	13 (39.4%)	0.018
Coronary artery disease	893 (40.5%)	17 (51.5%)	0.215
Prior procedures			
Coronary artery bypass grafting	309 (14.0%)	7 (21.2%)	0.215
Patent foramen ovale closure	4 (0.2%)	0	1
Atrial ablation	17 (0.8%)	0	1
Left atrial appendage closure	13 (0.6%)	0	1
Frailty	645 (29.3%)	14 (42.4%)	0.122
Chronic obstructive pulmonary disease	338 (15.3%)	2 (6.1%)	0.217
Serum creatinine (mg/dL)	1.3 (1.0; 1.7)	1.4 (1.2; 1.9)	0.032
Therapy at admission			
Aspirin	946 (42.9%)	12 (36.4%)	0.484
Thienopyridine	481 (21.8%)	9 (27.3%)	0.523
Anti-vitamin K oral anticoagulants	522 (23.7%)	12 (36.4%)	0.100
For atrial fibrillation	183 (8.3%)	7 (21.2%)	0.018
For other indications	339 (15.4%)	5 (15.2%)	1
Novel oral anticoagulants	493 (22.4%)	5 (15.2%)	0.403
For atrial fibrillation	181 (8.2%)	2 (6.1%)	1
For other indications	312 (14.2%)	3 (9.1%)	0.613

* At Wilcoxon rank-sum test or Fisher's exact test, as appropriate; CHADS₂=Congestive heart failure, Hypertension, Age ≥75, Diabetes, Stroke (doubled); CHA₂DS₂-VASc=Congestive heart failure or left ventricular dysfunction Hypertension, Age ≥75 (doubled), Diabetes, Stroke (doubled)-Vascular disease, Age 65–74, Sex category.

presence at electrocardiogram of any abnormality (601 [27.3%] vs 15 [45.5%], $p = 0.029$) or atrial fibrillation (469 [21.3%] vs 13 [39.4%], $p = 0.018$) (Table 2).

Focusing on procedural features and in-hospital outcomes, no differences for success rates or other outcomes were evident (all $p > 0.05$) (Table 3) (Figure 1). At long-term follow-up, patients with CVA apparently exhibited a numerically increased risk of death (528 [24.0%] vs 16

[48.5%], $p = 0.003$) and a worse functional class (New York Heart Association class III or IV 352 [22.4%] vs 12 [46.2%], $p = 0.018$) (Tables 4, 5). However, the survival analysis disproved a significant impact of CVA on all-cause or cardiac death ($p = 0.136$ and $p = 0.397$, respectively, at Tarone–Ware test) (Figure 2).

Despite the use of antivitamin K oral anticoagulants in patients with atrial fibrillation being more prevalent in the

Table 2
Imaging, electrocardiographic and coronary angiography features

Feature	No CVA (N=2205)	Any CVA (N=33)	P*
LV end-diastolic diameter (mm)	59 (52; 66)	63 (52; 69)	0.252
LV end-systolic diameter (mm)	44 (35; 53)	46 (38; 60)	0.239
LV end-diastolic volume (mL)	146 (109; 193)	170 (110; 198)	0.776
LV end-systolic volume (mL)	82 (50; 129)	89 (50; 126)	0.780
LV ejection fraction (%)	40 (30; 55)	41 (30; 52)	0.744
Left atrial antero-posterior diameter (mm)	50 (45; 55)	51 (43; 59)	0.508
Mean mitral valve gradient (mm Hg)	2 (1; 3)	3 (2; 4)	0.098
Severe mitral regurgitation	1721 (78.1%)	25 (75.8%)	0.678
Mitral valve area (cm ²)			
Tethering			0.147
No	1448 (65.7%)	19 (57.6%)	
Symmetric	481 (21.8%)	6 (18.2%)	
Asymmetric	276 (12.5%)	8 (24.2%)	
Leaflet prolapse	626 (28.4%)	11 (33.3%)	0.561
Flail leaflet	451 (20.5%)	6 (18.2%)	1
Severe calcification	106 (4.8%)	1 (3.0%)	1
Tricuspid regurgitation			0.501
None	110 (5.0%)	2 (6.1%)	
Mild	830 (37.6%)	14 (42.4%)	
Moderate	971 (44.0%)	11 (33.3%)	
Severe	294 (13.3%)	6 (18.2%)	
Systolic pulmonary artery pressure (mm Hg)	45 (37; 55)	44 (39; 55)	0.613
Any electrocardiographic abnormality	601 (27.3%)	15 (45.5%)	0.029
Second degree atrioventricular block	4 (0.2%)	0	1
Third degree atrioventricular block	7 (0.3%)	0	1
Right bundle branch block	55 (2.5%)	1 (3.0%)	0.569
Left bundle branch block	82 (3.7%)	0	0.632
Atrial fibrillation	469 (21.3%)	13 (39.4%)	0.018
Coronary angiography performed	971 (44.0%)	18 (54.6%)	0.289
Coronary artery disease extent			0.144
None	614 (63.2%)	9 (50.0%)	
Single-vessel disease	159 (16.4%)	3 (16.7%)	
Two-vessel disease	97 (10.0%)	1 (5.6%)	
Three-vessel disease	56 (5.8%)	3 (16.7%)	
Left main disease	45 (4.6%)	2 (11.1%)	

LV = left ventricular.

* At Wilcoxon rank-sum test or Fisher's exact test, as appropriate.

CVA group, exploratory analyses to discern the impact of different antithrombotic regimens did not show any significant association between anticoagulant therapy and outcomes (Table 6). In addition, even if the group with CVA had significantly higher CHADsVASC scores than the non-CVA group, such scores showed a poor overall ability to predict CVA events in patients who underwent TEER (Figure 3).

Discussion

We hereby present an extensive and detailed study focusing on the incidence and predictors of CVAs in patients who underwent TMVR with the MitraClip device. This study, which is part of the GIOTTO research project, originally presents a comprehensive examination of how often strokes and TIA occur in this patient population, what factors might predict their occurrence, and the overall safety of this recent yet already established minimally invasive procedure.

Previous studies on stroke risk in patients who underwent TEER have highlighted a nuanced understanding of CVA outcomes.^{6,8,12,20} In particular, scholarly studies consistently indicate that although TEER offers a promising, minimally invasive alternative for patients with significant mitral regurgitation, particularly, those at a high surgical risk, it does not contribute substantially to stroke risk, which is often already non-negligible given baseline patient characteristics such as atrial fibrillation.^{8,13,21,22} Overall, the evidence base and expert opinion call for a balanced approach to patient selection and postprocedural care, emphasizing the need for individualized risk assessment and the potential benefits of antithrombotic therapy to mitigate stroke risk.^{12,23,24}

Building upon such premises, the present GIOTTO analysis focusing on CVAs and distinguishing them according to type, etiology, severity, and timing revealed an overall low incidence of CVA in patients who underwent TEER with the MitraClip, with most CVAs occurring after discharge and being predominantly major ischemic strokes. Our study notably identified atrial fibrillation, renal

Table 3
Procedural features and in-hospital outcomes

Feature	No CVA (N=2205)	Any CVA (N=33)	P*
Device success	2153 (97.6%)	33 (100%)	1
Procedural success	2111 (95.7%)	32 (97.0%)	1
Post-procedural mitral regurgitation			0.968
1+	1394 (63.2%)	22 (66.7%)	
2+	702 (31.8%)	10 (30.3%)	
3+	72 (3.3%)	1 (3.0%)	
4+	37 (1.7%)	0	
Post-procedural smoke-like effect	143 (6.5%)	1 (3.0%)	0.720
Mean mitral valve gradient (mm Hg)	3 (2; 4)	3 (2; 5)	0.659
Systolic pulmonary artery pressure (mm Hg)	40 (33; 48)	40 (33; 50)	0.706
Total number of implanted MitraClip			0.252
Failed implant	10 (0.5%)	0	
1	888 (40.3%)	16 (48.5%)	
2	1110 (50.3%)	13 (39.4%)	
3	183 (8.3%)	3 (9.1%)	
4	13 (0.6%)	1 (3.0%)	
5	1 (0.1%)	0	
In-hospital death	61 (2.8%)	1 (3.0%)	0.607
Bleeding			1
No	2185 (99.1%)	33 (100)	
Minor	12 (0.5%)	0	
Major	5 (0.2%)	0	
Disabling	3 (0.1%)	0	
Major vascular complication	16 (0.7%)	0	1
Transient ischemic attack	0	0	1
Stroke	0	6 (18.2%)	<0.001
Myocardial infarction	0	0	1
Total hospital stay (days)	5 (4; 8)	6 (4; 13)	0.128
Atrial fibrillation at discharge	193 (8.8%)	5 (15.2%)	0.207
Mitral regurgitation at discharge			0.519
1+	1228 (57.3%)	23 (71.9%)	
2+	750 (35.0%)	8 (25.0%)	
3+	128 (6.0%)	1 (3.1%)	
4+	38 (1.8%)	0	
Any of the following: atrial fibrillation, anti-vitamin K oral anticoagulant therapy or mean mitral valve gradient >2.5 mm Hg at baseline; or smoke effect or mean mitral valve gradient >5.0 mm Hg at discharge	1032 (46.8%)	20 (60.6%)	0.159
Combination of the following: atrial fibrillation, anti-vitamin K oral anticoagulant therapy and mean mitral valve gradient >5.0 mm Hg at discharge	935 (42.4%)	19 (57.6%)	0.109

* At Wilcoxon rank-sum test or Fisher's exact test, as appropriate.

dysfunction, and higher thrombotic risk scores as significant bivariate predictors of CVA risk, as expected, suggesting that these established features could possibly guide risk stratification and management strategies.²⁵ Indeed, atrial fibrillation obviously increases stroke risk acutely and chronically and should be proactively managed with

anticoagulant therapy or with left atrial appendage occlusion, when anticoagulants are contraindicated.²⁶ The pathophysiologic link between renal failure and surgical risk scores on one hand and stroke risk on the other is more complex and may recognize several alternative or complementary mechanisms.^{27,28} Irrespectively, in the GIOTTO

Table 4
Timing and type of cerebrovascular events (p<0.001)

Feature	In-hospital (N=2238)	Follow-up (N=2176)	Total (N=2238)
Transient ischemic attack	0	6 (0.28%)	6 (0.26%)
Minor ischemic stroke	0	2 (0.09%)	2 (0.09%)
Major ischemic stroke	4 (0.17%)*	17 (0.78%)	21 (0.90%)
Minor hemorrhagic stroke	1 (0.04%)	1 (0.05%)	2 (0.09%)
Major hemorrhagic stroke	1 (0.04%)	1 (0.05%)	2 (0.09%)

* One fatal in a 64-year-old man.

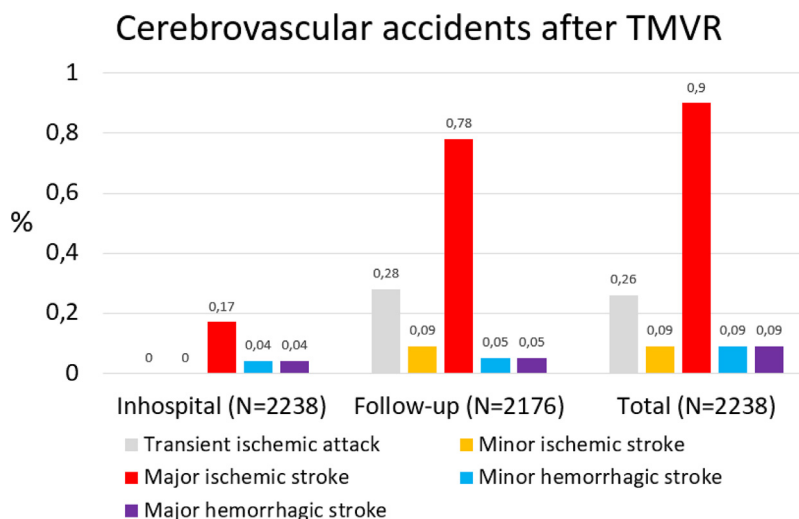


Figure 1. Breakdown of type of cerebrovascular accident according to timing.

study, although at short-term CVA was not associated with other in-hospital adverse outcomes, at midterm follow-up, the occurrence of CVA was significantly associated with fatality and worse functional class, thus confirming the important role of stroke in shaping the clinical trajectory of patients who underwent TEER.

Future research on the topic of stroke risk in patients who underwent TEER with MitraClip should explore the development of refined risk prediction models that

incorporate a wider range of clinical and procedural variables to better identify patients at high risk for CVA, including follow-up monitoring.²⁹ Investigating the optimal antithrombotic therapy regimens and their timing relative to the procedure could offer insights into minimizing post-procedural CVA risk while balancing bleeding risks.³⁰ In addition, longitudinal studies focusing on the long-term neurocognitive outcomes of patients experiencing CVA after TEER would provide valuable information on patient

Table 5

Long-term outcomes

Feature	No CVA (N=2205)	Any CVA (N=33)	P
Death	528 (24.0%)	16 (48.5%)	0.003
Cardiac death	289 (13.1%)	2 (6.1%)	0.304
Rehospitalization for heart failure	228 (10.3%)	5 (15.2%)	0.382
Cardiac death or rehospitalization for heart failure	457 (20.7%)	6 (18.2%)	0.831
Endocarditis	5 (0.2%)	0	1
Mitral valve surgery	25 (1.1%)	0	1
Heart transplant	9 (0.4%)	0	1
Implantation of pacemaker	58 (2.6%)	2 (6.1%)	0.210
Implantation of implantable cardioverter defibrillator	26 (1.2%)	1 (3.0%)	0.314
New York Heart Association			0.018
I	276 (17.6%)	1 (3.9%)	
II	945 (60.1%)	13 (50.0%)	
III	327 (20.8%)	11 (42.3%)	
IV	25 (1.6%)	1 (3.9%)	
Atrial fibrillation	509 (23.1%)	14 (42.4%)	0.020
Left ventricular ejection fraction (%)	30 (23; 40)	40 (29; 58)	0.944
Mitral gradient (mm Hg)	4 (3; 5)	4 (3; 6)	0.460
Mitral regurgitation			0.840
1+	1010 (47.1%)	14 (43.8%)	
2+	825 (38.4%)	15 (46.9%)	
3+	224 (10.4%)	2 (6.3%)	
4+	87 (4.1%)	1 (3.1%)	
Therapy at follow-up			
Aspirin	684 (44.7%)	10 (34.5%)	0.347
Thienopyridine	314 (14.2%)	3 (9.1%)	0.612
Anti-vitamin K oral anticoagulants	529 (24.9%)	11 (40.7%)	0.072
Novel oral anticoagulants	533 (25.0%)	4 (14.8%)	0.269

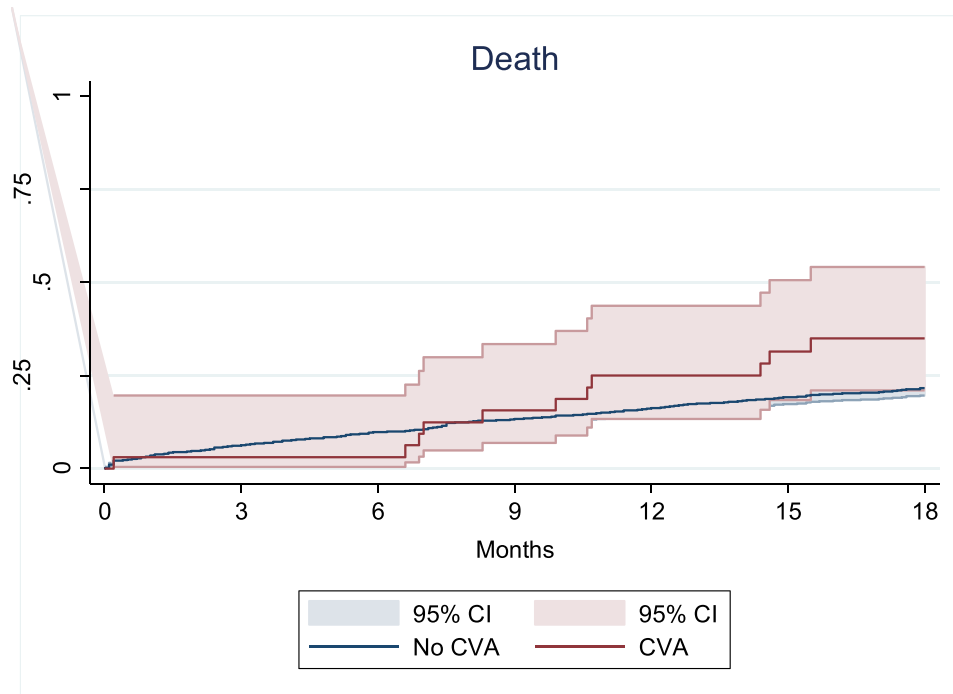


Figure 2. Overall risk of death in patients with or without cerebrovascular accident (CVA) ($p = 0.136$ at Tarone-Ware test).

quality of life and help tailor postprocedural care and surveillance strategies. Another intriguing avenue for research and practice is transcatheter left atrial appendage occlusion in patients with atrial fibrillation and increased surgical risk before, during, or after TEER.³¹ It is worth highlighting that minor strokes were less common than more severe types of CVA. Indeed, we can speculate that minor events were less common than major strokes potentially because of the higher incidence of significant preexisting conditions, such as atrial fibrillation and renal dysfunction, which are more likely to result in severe ischemic events, as also highlighted before.

Our study, although providing significant insights, is limited by its observational design, which, despite rigorous analysis, cannot establish causality between the identified predictors and CVAs. The reliance on data from a multicenter registry may introduce variability in patient management and reporting standards across sites potentially affecting the generalizability of the findings, especially considering the subtleties inherent in adjudicating CVAs.⁹ Notably, although we are positive that no stroke occurred during or shortly after the procedure, no precise dates for in-hospital events were collected. However, given that median hospital stay after discharge was 4 days, we can

Table 6
Exploratory subgroup analyses for post-discharge cerebrovascular accident (CVA) according to anticoagulant regimen.

Subgroup	Feature	No CVA	Any CVA	P*
Overall	Patients	2130	27	
	Anti-vitamin K oral anticoagulants	529 (24.9%)	11 (40.7%)	0.072
Risk of CVA in patients with AF	Novel oral anticoagulants	533 (25.0%)	4 (14.8%)	0.269
	Patients	490	11	
Risk of CVA in patients with mean MVG ≥ 5.0 mm Hg at discharge	Anti-vitamin K oral anticoagulants	208 (42.5%)	8 (72.7%)	0.063
	Novel oral anticoagulants	203 (41.4%)	2 (18.2%)	0.213
Risk of long-term CVA in patients with AF or mean MVG ≥ 5 mm Hg at discharge	Patients	1197	20	
	Anti-vitamin K oral anticoagulants	280 (23.4%)	8 (40.0%)	0.108
Risk of long-term CVA in patients with AF and mean MVG ≥ 5 mm Hg at discharge	Novel oral anticoagulants	324 (27.1%)	2 (10.0%)	0.124
	Patients	271	8	
Risk of long-term CVA in patients with AF or mean MVG ≥ 5 mm Hg at discharge	Anti-vitamin K oral anticoagulants	119 (44.1%)	6 (75.0%)	0.146
	Novel oral anticoagulants	103 (38.0%)	1 (12.5%)	0.265
Risk of long-term CVA in patients with AF and mean MVG ≥ 5 mm Hg at discharge	Patients	263	8	
	Anti-vitamin K oral anticoagulants	101 (38.4%)	1 (12.5%)	0.265
	Novel oral anticoagulants	115 (43.9%)	6 (75.0%)	0.145

AF = atrial fibrillation; MVG = mitral valve gradient.

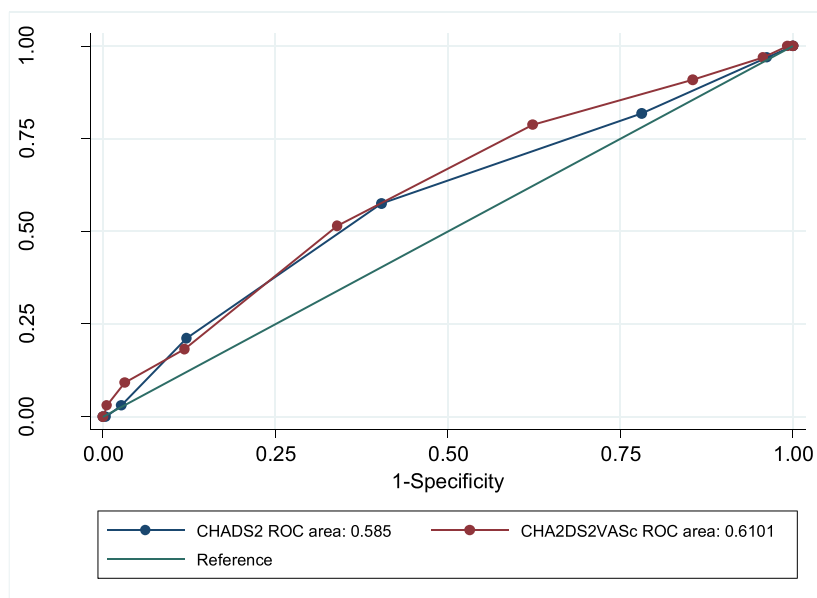


Figure 3. Areas under the curve of the receiver operating characteristic (ROC) curves for prediction of cerebrovascular accident according to the CHADS2 and CHA2DS2-VASc scores (0.59 [0.48 to 0.69] and 0.6101 [0.52 to 0.71], respectively, $p = 0.347$).

expect that all in-hospital strokes occurred in the few days after TEER. Furthermore, the study focuses on a specific patient population who underwent TEER with MitraClip, which may limit the applicability of the results to broader patient groups or those who underwent different mitral valve interventions.

In conclusion, the incidence of CVAs in patients who underwent TEER is low, with most events occurring after discharge and being associated with preexisting risk features. These findings, although reassuring on the safety of TEER, call for proactive antithrombotic therapy whenever CVA stroke risk is increased before and after TEER.

Declaration of competing interest

Dr. Adamo has received speaker fees from speaker fees from Abbott Structural Heart. Giuseppe Biondi-Zoccai has consulted for aleph, Amarin, Balmed, Cardionovum, Cranmedical, Endocore Lab, Eukon, Guidotti, Innovheart, Meditrial, Menarini, MicroPort, Opsens Medical, Terumo, and Translumina outside the present work. The remaining authors have no competing interests to declare.

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