Frequency and Causes of Stroke During or After Transcatheter Aortic Valve Implantation

Rutger-Jan Nuis, MSc[a], Nicolas M. Van Mieghem, MD[a], Carl J. Schultz, MD, PhD[a], Adriaan Moelker, MD, PhD[b], Robert M. van der Boon, MSc[a], Robert Jan van Geuns, MD, PhD[a], Aad van der Lugt, MD, PhD[b], Patrick W. Serruys, MD, PhD[a], Josep Rodés-Cabau, MD[c], Ron T. van Domburg, PhD[d], Peter J. Koudstaal, MD, PhD[e], and Peter P. de Jaegere, MD, PhD[a,*]

Transcatheter aortic valve implantation (TAVI) is invariably associated with the risk of clinically manifest transient or irreversible neurologic impairment. We sought to investigate the incidence and causes of clinically manifest stroke during TAVI. A total of 214 consecutive patients underwent TAVI with the Medtronic-CoreValve System from November 2005 to September 2011 at our institution. Stroke was defined according to the Valve Academic Research Consortium recommendations. Its cause was established by analyzing the point of onset of symptoms, correlating the symptoms with the computed tomography-detected defects in the brain, and analyzing the presence of potential coexisting causes of stroke, in addition to a multivariate analysis to determine the independent predictors. Stroke occurred in 19 patients (9%) and was major in 10 (5%), minor in 3 (1%), and transient (transient ischemic attack) in 6 (3%). The onset of symptoms was early (≤24 hours) in 8 patients (42%) and delayed (>24 hours) in 11 (58%). Brain computed tomography showed a cortical infarct in 8 patients (42%), a lacunar infarct in 5 (26%), hemorrhage in 1 (5%), and no abnormalities in 5 (26%). Independent determinants of stroke were new-onset atrial fibrillation after TAVI (odds ratio 4.4, 95% confidence interval 1.2 to 15.6), and baseline aortic regurgitation grade III or greater (odds ratio 3.2, 95% confidence interval 1.1 to 9.3). In conclusion, the incidence of stroke was 9%, of which >1/2 occurred >24 hours after the procedure. New-onset atrial fibrillation was associated with a 4.4-fold increased risk of stroke. In conclusion, these findings indicate that improvements in postoperative care after TAVI are equally, if not more, important for the reduction of periprocedural stroke than preventive measures during the procedure. **(Am J Cardiol 2012;109:1637–1643)**

Transcatheter aortic valve implantation (TAVI) is increasingly used to treat patients with aortic stenosis who are considered too high a risk for surgical valve replacement (aortic valve replacement).[1] Despite its clinical benefits, TAVI is invariably associated with the risk of clinically manifest transient or irreversible neurologic impairment.[2–5] This can be explained by the various catheter and wire manipulations during TAVI that can result in a cerebral embolus but also by cerebral hypoperfusion due to episodes of hypotension during TAVI resulting from—for instance—rapid right ventricular pacing during aortic balloon valvuloplasty. Also gaseous and atherosclerotic microemboli can provoke ischemia and/or occlusion of deep penetrating arteries of the brain, as recently demonstrated.[5–10] A neurologic deficit can also occur at some point after TAVI for reasons not directly related to the procedure itself, such as is seen in cardiac surgery.[11–13] The understanding of the pathophysiology or cause of stroke during TAVI could help to determine which preventive strategies during and/or after TAVI will most effectively reduce the stroke rates. We, therefore, sought to elucidate the incidence and causes of stroke in a series of 214 consecutive patients by analyzing the time of symptom onset in relation to the procedure and by correlating the symptoms with the computed tomographic (CT)-detected defects in the brain, in addition to the assessment of independent predictors of stroke.

Methods

The study population consisted of all 214 patients (3 intraprocedural deaths excluded) who underwent transfemoral or transsubclavian TAVI with the Medtronic CoreValve System between November 2005 and September 2011 in the Erasmus Thoraxcenter (Rotterdam, The Netherlands). The patient selection criteria and the methods used for Doppler echocardiography have been previously described in detail.[14,15] The treatment strategy (TAVI, aortic valve replacement, or medical therapy) was discussed at a joint cardiothoracic surgical and medical conference.[16]

TAVI was performed with the patient under general

[a]Department of Cardiology, Erasmus Medical Center, Rotterdam, The Netherlands; [b]Department of Radiology, Erasmus Medical Center, Rotterdam, The Netherlands; [c]Department of Cardiology, Quebec Heart and Lung Institute, Quebec City, Quebec, Canada; [d]Department of Biostatistics, Erasmus Medical Center, Rotterdam, The Netherlands; [e]Department of Neurology, Erasmus Medical Center, Rotterdam, The Netherlands. Manuscript received December 19, 2011; revised manuscript received and accepted January 17, 2012.

*Corresponding author: Tel: (00) 311-0703-1763; fax: (00) 311-0703-4320.

E-mail address: p.dejaegere@erasmusmc.nl (P.P. de Jaegere).

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Table 1
Baseline characteristics of patients with and without stroke after transcatheter aortic valve implantation (TAVI)

Variable	Entire Cohort (n = 214)	No Stroke (n = 195)	Stroke (n = 19)	p Value
Age (years)	80 ± 8	80 ± 8	82 ± 6	0.48
Men	107 (50%)	101 (52%)	6 (32%)	0.093
Height (cm)	167 ± 11	167 ± 12	166 ± 8	0.75
Weight (kg)	74 ± 13	74 ± 13	76 ± 12	0.50
Body mass index (kg/m^2)	26.2 ± 4.1	26.1 ± 4.1	27.3 ± 4.3	0.25
Body surface area (m^2)	1.85 ± 0.19	1.85 ± 0.19	1.86 ± 0.17	0.78
New York Heart Association class III or greater	175 (82%)	158 (81%)	17 (90%)	0.54
Previous cerebrovascular event	49 (23%)	47 (24%)	2 (11%)	0.26
Previous myocardial infarction	51 (24%)	49 (25%)	2 (11%)	0.26
Previous coronary artery bypass graft surgery	58 (27%)	55 (28%)	3 (16%)	0.25
Previous percutaneous coronary intervention	56 (26%)	51 (26%)	5 (26%)	1.0
Diabetes mellitus	50 (24%)	46 (24%)	4 (21%)	1.0
Hypertension	126 (59%)	116 (60%)	10 (53%)	0.56
Peripheral vascular disease	26 (21%)	24 (12%)	2 (11%)	1.0
Chronic obstructive pulmonary disease	60 (28%)	53 (27%)	7 (37%)	0.37
Creatinine	95 (76–123)	96 (77–123)	84 (66–112)	0.27
Glomerular filtration rate	57 ± 20	57 ± 20	58 ± 18	0.86
Hemoglobin (g/dl)	12.3 ± 1.7	12.3 ± 1.7	12.1 ± 1.2	0.62
Thrombocyte count	225 ± 67	223 ± 67	244 ± 63	0.21
Prothrombin time (s)	14 ± 8	14 ± 8	14 ± 3	0.89
International normalized ratio	1.21 ± 1.01	1.22 ± 1.05	1.16 ± 0.28	0.83
Atrial fibrillation				
All	64 (30%)	57 (29%)	7 (37%)	0.49
Chronic	44 (21%)	38 (20%)	6 (32%)	0.24
Paroxysmal	20 (9%)	19 (10%)	1 (5%)	1.0
Preprocedural rhythm				
Atrial fibrillation	48 (23%)	44 (23%)	4 (21%)	1.0
Paced	10 (5%)	8 (4%)	2 (11%)	0.22
Porcelain aorta	45 (21%)	38 (20%)	7 (37%)	0.084
Aortic valve area (cm^2)	0.66 ± 0.21	0.66 ± 0.22	0.61 ± 0.16	0.33
Peak velocity	4.3 ± 0.8	4.3 ± 0.8	4.2 ± 0.8	0.76
Mean aortic gradient	45 ± 17	46 ± 17	44 ± 18	0.68
Left ventricular ejection fraction ≤35%	24 (14%)	23 (14%)	1 (6%)	0.70
Aortic regurgitation grade III or greater	42 (20%)	34 (17%)	8 (42%)	0.016
Mitral regurgitation grade III or greater	26 (12%)	23 (12%)	3 (16%)	0.71
Logistic European system for cardiac operative risk evaluation	13.8 (10.0–22.0)	13.8 (10.0–22.8)	12.0 (8.4–16.5)	0.14
Society of Thoracic Surgeon score	5.0 (3.4–7.5)	5.0 (3.4–7.3)	4.3 (3.5–7.5)	0.96
Antiplatelets	105 (49%)	96 (50%)	9 (47%)	1.0
Anticoagulants	67 (32%)	63 (33%)	4 (21%)	0.30

Data are expressed as mean ± SD, median (IQR), or number of patients (%).

anesthesia. The first 5 patients underwent TAVI with a 21F delivery catheter that was inserted into the common femoral (n = 4) or subclavian (n = 1) artery after a surgical cut down. All other patients underwent TAVI with an 18F compatible delivery catheter that was inserted into the common femoral artery using an ultrasound-guided Seldinger technique, except for 5 patients who underwent TAVI by way of the left subclavian artery (surgical exposure and closure).[14] Extracorporal support (extracorporeal membrane oxygenation/TandemHeart, CardiacAssist, Pittsburgh, PA) was used in patients with impaired left ventricular function and a suspected increased risk of periprocedural hemodynamic instability. The subsequent phases of the transfemoral TAVI procedure have been described previously.[17]

Patients who were not taking aspirin and/or clopidogrel received a dose of 80 and 600 mg, respectively, the day before TAVI. Patients who were receiving oral anticoagulant therapy were instructed to stop this treatment 3 days before the procedure. Anticoagulant therapy was replaced by enoxaprin until the day before TAVI in patients with a strict indication for anticoagulant therapy. At admission, a full blood examination was performed, including the prothombin time and international normalized ratio (INR).

After insertion of the arterial sheath, a bolus of 70 U/kg IU unfractionated heparin was administered, followed by additional doses to maintain the activated clotting time at 250 to 350 seconds. The activated clotting time was checked every 30 minutes. The activated partial thromboplastin time was checked within 6 hours after the procedure.

After completion of the procedure (percutaneous or surgical closure of the access site), sedation was stopped, followed by extubation. All patients were transferred to the intensive care unit/cardiac care unit for 12 to 24 hours, or longer if clinically indicated. They were then transferred to the medium care unit until hospital discharge. According to the TAVI protocol, rhythm monitoring by telemetry was

Table 2
Procedural and postprocedural results of patients with and without stroke after transcatheter aortic valve implantation (TAVI)

Variable	No Stroke (n = 195)	Stroke (n = 19)	p Value
Procedural results			
Vascular access			
Surgical—femoral artery	4 (2%)	0	1.0
Surgical—subclavian artery	6 (3%)	0	1.0
Percutaneous—femoral artery	185 (95%)	19 (100%)	0.25
Circulatory support	15 (8%)	3 (16%)	0.21
Additional interventions during TAVI			
Percutaneous transluminal angioplasty iliac artery	6 (3%)	0	1.0
Percutaneous coronary intervention	15 (8%)	2 (11%)	0.65
Prosthesis size* (mm)			
26	59 (30%)	9 (47%)	0.13
29 or 31	135 (69%)	10 (53%)	0.14
Valve/annulus ratio	1.15 ± 0.08	1.16 ± 0.08	0.73
Life-threatening arrhythmia	9 (5%)	0	1.0
Any complication leading to severe hypotension	4 (2%)	0	1.0
Highest activated clotting time (s)	284 ± 87	283 ± 64	0.97
Lowest activated clotting time (s)	221 ± 72	231 ± 73	0.65
Red blood cell transfusions	1.2 ± 2.2	1.3 ± 1.3	0.86
Hemoglobin decrease—uncorrected for red blood cell transfusion (g/dl)	2.0 ± 1.3	2.1 ± 1.0	0.82
Hemoglobin decrease—corrected for red blood cell transfusion (g/dl)	3.2 ± 2.6	3.4 ± 1.7	0.77
Thrombocyte decrease	60 ± 45	60 ± 36	0.98
Therapy-specific results			
Postimplantion balloon dilation	34 (17%)	1 (5%)	0.33
Valve dislodgement†	19 (10%)	1 (5%)	1.0
Valve-in-valve implantation	10 (5%)	1 (5%)	1.0
Duration of procedure (min)	215 ± 75	197 ± 83	0.32
Postprocedural results			
Activated partial thromboplastin time (s)‡	128 ± 92	133 ± 92	0.85
Prosthetic-valve associated results			
Permanent atrial fibrillation§	40 (21%)	6 (33%)	0.23
New atrial fibrillation‖	17 (9%)	5 (26%)	0.032
New left bundle branch block	85 (46%)	6 (32%)	0.31
New permanent pacemaker	41 (21%)	2 (11%)	0.38
Echocardiography			
Peak velocity	2.0 ± 0.5	2.1 ± 0.7	0.59
Mean aortic gradient	9 ± 4	11 ± 6	0.19
Aortic regurgitation grade III or greater	24 (12%)	3 (16%)	0.72
Mitral regurgitation grade III or greater	20 (10%)	3 (16%)	0.44

* One patient did not receive a valve because of aborted TAVI after failed introduction of 18F sheath.
† In all cases, the valve was recaptured and successfully implanted in a second attempt.
‡ Checked within 6 hours after the procedure.
§ Atrial fibrillation before, during, and after TAVI.
‖ Neither preprocedural nor a history of AF.

performed during the hospital stay. All patients received aspirin 80 mg and clopidogrel 75 mg for 6 months. Patients with an indication for oral anticoagulant therapy only received clopidogrel. In these patients, unfractionated heparin was continued after TAVI until adequate INR levels were obtained by acenocoumarol. In-hospital anticoagulant treatment was guided by the prothombin time, INR and activated partial thromboplastin time.

Stroke was defined according to the Valve Academic Research Consortium end point definitions.[18] This implies the following: (1) exclusion of metabolic or toxic encephalopathy or pharmacologic influences explaining the symptoms, in addition to a solely nonfocal neurologic syndrome, (2) execution of a CT study to confirm the clinical diagnosis, (3) the distinction between stroke and transient ischemic attack, and (4) classification of stroke as major or minor according to the degree of disability (modified Rankin score after the procedure and at 30 and 90 days). For patients in whom a modified Rankin score was not documented during the 3 intervals, a detailed chart review was performed to estimate this and accurately classify strokes as major or minor events.

The brain CT scan findings were analyzed using a standard protocol.[19] The cause of stroke was established by (1) analyzing the time of symptom onset, (2) correlating the symptoms with CT-detected defects in the brain, and (3) analyzing the presence of potential coexisting causes of stroke, in addition to multivariate analysis to determine the independent predictors of stroke. Infarcts were categorized as old or new, with the latter

Table 3
Clinical symptoms, computed tomographic (CT) analysis, stroke classification, and atrial fibrillation in patients with stroke after transcatheter aortic valve implantation (TAVI)

Event No.	Pt. No.	Clinical Symptoms				CT Analysis			Classification		AF
		Timing (d)	Symptoms	Duration >24 h	Rankin Score 3 Intervals*	Timing (d)	Infarct Type†	Localization (Hemisphere)	Stroke Type	Ischemic Subtype§	New Onset or Permanent‖
1	7	0	Left-sided hemiparesis, dysarthria-clumsy hand syndrome	No	2; 0; 0	1	Old lacunar	Left	TIA	Lacunar	No
2	16	3	Left-sided hemiparesis, left-sided neglect	Yes	4; 2; 2	3	New cortical (territorial)	Right	Major stroke	Cortical territorial	Permanent
3	17	1¶	Right-sided hemianopia, minimal motor aphasia	Yes	4; 3; 3	2	New cortical (watershed)	Left	Major stroke	Cortical watershed	No
4	18	4	Right leg paresis	No	4; 0; 0	7	Old lacunar	Right + stem	TIA	Uncertain	No
5	19	1¶	Pure motor right hemiparesis	No	4; 0; 0	1	Old lacunar	Left	TIA	Lacunar	Permanent
6	22	5	Left-sided hemiparesis	No	4; 0; 0	6	Negative imaging	Na	TIA	Uncertain	New-onset Day 4
7	26	1	Right-sided hemiparesis	Yes	4; 3; 2	2	Old lacunar (multiple)	Bilateral	Major stroke	Lacunar	No
8	44	0	Buccofacial apraxia	Yes	3; 3; 2	0	Old lacunar	Left	Major stroke	Cortical	Permanent
9	53	0	Right-sided hemiparesis, aphasia	Yes	6; 6; 6	0	Old lacunar; new cortical (watershed)	Left; left	Major stroke	Cortical watershed	Permanent
10	54	2	Right-sided hemiparesis	Yes	2; 0; 0	2	Negative imaging	Na	Minor stroke	Uncertain	Permanent
11	64	6	Right-sided hemiparesis, aphasia	Yes	6; 6; 6	6	Old lacunar; new cortical	Left; left	Major stroke	Cortical territorial	New-onset Day 4
12	86	3	Dysarthria	No	1; 0; 0	3	Old lacunar	Right	TIA	Lacunar	No
13	105	6	Left arm paresis	Yes	3; 2; 2	7	Old lacunar; old cortical (watershed)	Left; right	Major stroke‡	Uncertain	Permanent
14	120	2	Left-sided hemiparesis, dysarthria	Yes	3; 2; 2	2	Old lacunar (multiple)	Left	Major stroke	Lacunar	No
15	137	5	Blurry vision, loss of balance	Yes	4; 4; 3	6	New cortical	Right	Major stroke	Cortical	No
16	146	0	Right-sided hemiparesis	Yes	6; 6; 6	1	New cortical (territorial)	Left	Major stroke	Cortical territorial	New-onset Day 0
17	184	1¶	Right arm paresis	No	2; 0; 0	1	Old cortical	Left	TIA	Uncertain	New-onset Day 0
18	194	0	Right arm paresis, aphasia	Yes	2; 0; 0	6	Subdural hemorrhage	Left	Minor stroke	Na	New-onset Day 12
19	205	2	Hemianopia	Yes	2; 2; 1	2	New cortical (territorial)	Right	Minor stroke	Cortical territorial	No

CT = computed tomography; TIA = transient ischemic attack.
* Modified Rankin score immediately and 30 and 90 days after stroke.
† Not applicable for event number 18 in which a subdural hemorrhage occurred.
‡ Followed by a second stroke 2 days later (CT was performed 1 day after symptom onset and showed no change).
§ Classified by correlating the symptoms with CT-detected defects in the brain.
‖ Atrial fibrillation before, during, and after TAVI.
¶ Symptom onset at day 1 but within 24 hours after TAVI initiation.

further defined as cortical (territorial), cortical watershed, or lacunar infarct.

With respect to the timing of stroke, a distinction was made between stroke that occurred during versus after TAVI. The first was considered directly related to the procedure itself (e.g., due to catheter manipulations or hemodynamic changes) and the second was considered indirectly related to the procedure but not to the procedure itself. Stroke during TAVI was defined if the first symptoms and/or signs were detected ≤24 hours after termination of TAVI. Stroke after TAVI was defined when the first symptoms and/or signs were detected >24 hours after termination of TAVI. The termination of TAVI was defined by the time of vascular closure and hemostasis by either a percutaneous closure device or surgically.

All pre-, intra-, and postprocedural and follow-up data were prospectively collected and entered in a dedicated database as previously described.[17] Porcelain aorta was defined as an extensive circumferential calcification of the thoracic aorta, as assessed by computed tomography and/or fluoroscopy.[20] The blood coagulant status was assessed by collecting the prothombin time, INR, and thrombocyte levels before the procedure. The maximum and minimum activated clotting time levels were documented during the procedure, and the activated partial thromboplastin time was checked within 6 hours after the procedure. Data on red blood cell transfusions were recorded by the institution's blood bank laboratory and used to determine the corrected hemoglobin decrease within 24 hours after TAVI according to the modified Landefeld equation.[21,22] In this equation, 1 U of packed red blood cells is considered to represent 1 g/dl of hemoglobin; therefore, the net hemoglobin decrease corresponds to the addition of the number of packed red blood cells to the baseline minus the measured nadir hemoglobin level.

The occurrence and timing of new atrial fibrillation (AF) after TAVI—defined as any episode of AF lasting >30 seconds in patients with no history of chronic/paroxysmal AF—was determined by collecting the baseline and all postoperative 12-lead ECGs and 24-hour telemetry rhythm strips.[23,24] Follow-up information was prospectively collected during the structured outpatient clinic visits after hospital discharge. In addition, the survival and cause of death was obtained every 6 months by contacting the Dutch Civil Register.

The categorical variables are presented as frequencies and percentages and were compared using the chi-square test or Fisher's exact test. The normality of distributions was assessed with the Shapiro-Wilk test. Normal and skewed continuous variables are presented as the mean ± SD and median (interquartile range [IQR]), respectively. A comparison of continuous variables was done using Student *t* tests or Wilcoxon's rank sum test, when appropriate. Univariate analysis was performed to characterize the patients with and without stroke. Multivariate logistic regression analysis was performed to determine the predictive factors for stroke or transient ischemic attack, taking into account the restricted number of events. Preprocedural AF rhythm was included in the model. A 2-sided p value <0.05 was considered to indicate significance, and all statistical analyses were performed with SPSS software, version 17 (SPSS, Chicago, IL).

Results

The baseline characteristics and procedural details are listed in Tables 1 and 2. The incidence of stroke was 9% (19 patients) and—in accordance with the Valve Academic Research Consortium criteria—consisted of major stroke in 10 patients (5%), minor in 3 (1%), and transient ischemic attack in 6 (3%).

In all patients, except 1, who experienced a subdural hemorrhage (event number 18), the stroke was ischemic (Table 3) and occurred early (≤24 hours after TAVI) in 8 patients (42%) and was delayed (>24 hours, mean 3.5 days after TAVI) in 11 (58%). CT scan analysis of the brain revealed that stroke consisted of a cortical infarct in 8 patients (of which 4 were territorial and 2 were watershed) and a lacunar infarct in 5. In descending order of odds, new AF (odds ratio 4.4, 95% confidence interval 1.2 to 15.6) and baseline aortic regurgitation grade III or greater (odds ratio 3.2, 95% confidence interval 1.1 to 9.3) were identified as independent predictors. New AF occurred in 22 (14%) at a median of 2 days (IQR 1 to 4.5) after TAVI and resolved spontaneously within 12 hours in 8 patients (36%). Seven patients (32%) received pharmacologic treatment (n = 6) or electric (n = 1) conversion. Antithrombotic therapy (aspirin and clopidogrel) without anticoagulant therapy was maintained in 7 patients (36%) in whom the risk of bleeding was considered greater than the risk of thromboembolism. None of the 5 patients with new AF who experienced a stroke had received anticoagulant therapy.

The hospital or 30-day mortality rate in patients with a stroke was 16% (n = 3) and was 6% (n = 15) in patients without a stroke (p = 0.14). The cause of death in these 3 patients was the neurologic event itself. Clinical follow-up was complete for all patients (median 13 months, IQR 6 to 30). During follow-up, 3 patients developed a fatal stroke (2 hemorrhagic, 1 uncertain) and 6, a nonfatal stroke (all ischemic).

Discussion

The present study of 214 consecutive patients who underwent TAVI has shown that a clinically manifest neurologic impairment occurred in 19 patients (9%), with most events (n = 11; 58%) occurring >24 hours after TAVI at a mean of 3.5 days. Furthermore, we found that new-onset AF after TAVI was associated with a 4.4-fold greater risk of stroke.

Our observation that most events occur after and not during TAVI is consistent with the findings of the Canadian multicenter TAVI registry (345 patients) in which procedural stroke was reported in 0.6% of the patients and stroke at 30 days in 2.3%.[20] Supplementary information from the Placement of AoRtic TraNscathetER Valves (PARTNER) Cohort B study revealed that 5 of the 11 strokes occurred at day 0 or 1 after TAVI (45%) and 6 (55%) at day 2 or later.[2] Of note, in cardiac surgery, ≤65% of the neurologic events are seen after the operation.[11–13] In addition, patients undergoing TAVI appear to be at a high risk of stroke, irre-

spective of any intervention (cardiac or otherwise), as indicated by the rather frequent occurrence of stroke during follow-up, such as seen in this and other studies.[2,25]

That most strokes occurred after TAVI indicate that—in a number of patients—there is no direct relation between the intervention and the cerebral complication. These findings suggest that clinical, rather than technical or procedural, factors play a more important role in the occurrence of stroke during TAVI and that, therefore, preventive measures should, above all, be directed at improved postoperative management. It also suggests that endovascular embolic protection devices used during the procedure—if safe and effective—might reduce the stroke rates in only about ½ of the patients.[26] This is further supported by the fact that 26% of the strokes were lacunar, which is widely regarded as caused by cerebral hypoperfusion in the presence of local atherosclerosis. This implies that all efforts should be made during TAVI to maintain adequate brain perfusion. In this respect, TAVI without balloon valvuloplasty, such as proposed by Grube et al,[27] might be beneficial if this technique does not induce the dislodgement of calcified atherosclerotic emboli, while advancing the prosthesis in the aortic annulus.[27]

The role of improved postoperative care is supported by the finding that new AF after TAVI was the main determinant of stroke. Because the present study lacks the power to perform a comprehensive multivariate analysis, other factors might have remained undetected. The reason patients with aortic regurgitation grade ≥3 before TAVI are at increased risk of stroke remains to be elucidated. Although this might be a finding by chance owing to the small sample size and the absence of a pathophysiologic concept, these patients possibly had a more impaired and/or dilated left atrium, which is known to predict new AF after cardiac surgery and also after TAVI.[28,29] Scant information is available on new AF after TAVI. In the PARTNER cohort B study, new AF was seen in 1 of the 151 patients with no previous AF (0.7%), who underwent transfemoral TAVI.[2] The incidence of new AF in the PARTNER Cohort A study was 7.5% after transfemoral and 11.5% after transapical TAVI.[3] Similar to the results of Amat-Santos et al,[29] who found new AF in 16% of the patients undergoing transfemoral TAVI, we found new AF in 22 (14%) of the 154 patients with no previous AF.[29] In accordance with the findings from Amat-Santos et al,[29] the data of our study also indicate that suboptimal anticoagulant therapy in patients with new AF plays a role in the occurrence of stroke because none of the 5 patients with new AF who experienced a stroke received anticoagulant therapy. No clear guidelines are available on anticoagulation therapy after short episodes of AF after cardiac surgery.[24] However, patients undergoing TAVI are at high risk of thromboembolism when atrial fibrillation occurs (median $CHADS_2$ score 3 [IQR 2 to 4] in patients with new AF). Therefore, immediate anticoagulant therapy should probably be implemented in these patients on the diagnosis of AF.

The results of the multivariate analysis must be interpreted in the context of the number of patients included in the present study. In the control group, 17 of the 195 patients had new AF compared to 5 of the 19 in the stroke group. One patient less or more in 1 group can significantly affect the results of the analysis. However, it is quite conceivable that new AF is an important cause of stroke in the present reported patients, because new AF is known to be associated with an increased risk of cardioembolism.[29,30] New AF preceded the first signs of neurologic impairment in all patients with an ischemic stroke (Table 3) and in 3 of the 6 patients with a (territorial) cortical infarct—typically of thrombotic origin—were preceded by new AF and no patient with a lacunar infarct—typically not caused by a large thrombus or embolus—had new AF after TAVI.

The main limitation of the present study was the number of patients, thereby limiting the precision of the observed point estimate of the incidence of stroke and the power and robustness of the multivariate analysis. In particular, the lack of statistical correction in the present study might have influenced the significance of the predictors of stroke; therefore, these findings merit confirmation in larger series. Furthermore, we lacked a standardized, complete diagnostic workup for all patients with stroke. For instance, duplex or angiography of the carotid and vertebral arteries was not performed in the large majority of the present series of patients.

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