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Occurrence and Classification of Cerebrovascular Events after Isolated Bioprosthetic Surgical Aortic Valve Replacement: A Competing Risk Analysis of the CAREAVR Study

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ABSTRACT

Background: The long-term incidence of stroke and the proportion of cardioembolic events after bioprosthetic surgical aortic valve replacement (SAVR) remain largely unknown.

Methods: The CAREAVR study sought to assess the rate of stroke and transient ischemic attack (TIA) in patients who underwent isolated surgical aortic valve replacement with a bioprosthesis at four Finnish university hospitals between 2002 and 2014. Data was collected retrospectively and included 721 patients. Median follow-up time was 4.8 [3.0–7.0] years.

Results: At 5 years, freedom from stroke was 89.0%, from TIA 94.1%, and from stroke and TIA 83.7%. The median time between index procedure and stroke or TIA was 1.7 years [29 days–3.9 years]. Stroke was of cardioembolic origin in 44.4% of patients. In multivariable competing risk analysis, increased age (HR 1.03, 95%CI 1.00–1.06, $p = 0.022$), previous stroke or TIA (HR 1.75, 95%CI 1.14–2.70, $p = 0.010$), New York Heart Association (NYHA) class III or more (HR 1.51, 95%CI 1.01–2.24, $p = 0.044$) and insulin treatment at discharge (HR 1.20, 95%CI 1.09–3.64, $p = 0.024$) were independent predictors of stroke or TIA. Cerebrovascular events occurred in 47.2% of patients with ongoing anticoagulation therapy.

Conclusion: In this study, the incidence of stroke in the early postoperative period after bioprosthetic SAVR was higher than previously documented. Almost half of strokes were of cardioembolic etiology. These findings highlight the need for the better prevention strategies for cardioembolic events after bioprosthetic SAVR.

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KEYWORDS Aortic valve replacement; bioprosthesis; cerebral infarction; stroke; transient ischemic attack

Introduction

Stroke and transient ischemic attack (TIA) are frequent complications after surgical aortic valve replacement (SAVR) with a bioprosthesis.[1] The adverse events increase mortality and disability, prolong hospitalization with incremental costs. In previous registry-based studies, the incidence of stroke varied between 1.4% and 2.4% of patients during the in-hospital stay and between 6.1% and 13.8% during long-term follow-up.[1–7] Recent randomized studies, however, have suggested that in intermediate-risk patients the occurrence of stroke and TIA can already be as high as 6.5% within 30 days after surgery and 9.7% at 12 months.[8] This discrepancy may derive from register-based analyses, which are prone to an underestimation of the complication rates. Moreover, no data exists on the classification of subtypes and etiology of acute ischemic strokes in patients undergoing bioprosthetic SAVR. Thus, there is an unmet clinical need for more accurate long-term assessment of cerebrovascular events as well as a need to classify these events according to their etiology. This data might be useful when designing and testing approaches aimed at reducing the risk of cerebrovascular events, for assessing risks and benefits of treatment options as well as for patient counseling in patients undergoing surgical or transcatheter aortic valve replacement.

In this observational, multicenter study we sought to evaluate the short- and long-term occurrence, nature and predictors of stroke and TIA after isolated bioprosthetic SAVR.

Material and methods

Data collection

The CAREAVR (Consortium of Studies in the Field of Atrial Fibrillation, Stroke, and Bleeding in Patients Undergoing Aortic Valve Replacement) is a Finnish multicenter

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retrospective study (ClinicalTrials.gov Identifier: NCT02626871) assessing the rate of atrial fibrillation, thromboembolic complications, and bleeding events in patients undergoing isolated bioprosthetic SAVR. The data is collected as part of a broader ongoing protocol in Finland to evaluate the thromboembolic and bleeding complications of atrial fibrillation management in patients undergoing cardiac procedures.[9–11]

Patient data was retrieved from cardiac surgery units of four Finnish university hospitals (Helsinki, Turku, Oulu, and Kuopio) over the period of 2002–2014 (in Helsinki 2006–2014). Hospital records were reviewed for patients who underwent isolated bioprosthetic SAVR. Patients who underwent any other major concomitant cardiac surgery procedure were excluded from this study. In order to obtain accurate follow-up data, only patients from the hospitals' catchment areas were included. All the major adverse events including cerebrovascular events, bleeding and myocardial infarctions were treated in the same index hospitals, and therefore, the patient follow-up for adverse events can be considered reliable. Patient records were individually reviewed with a standardized structured data collection protocol for pre- and perioperative data, discharge data, and long-term follow-up events, including postoperative atrial fibrillation, stroke, TIA, bleeding events, and mortality. The endpoints of this pre-specified substudy included the occurrence of TIA and stroke. The causes of death were derived from Statistics Finland. This governmental office monitors the time and causes of death in the whole of Finland. Therefore, each case was carefully monitored even if the person moved.

During the period under study, the routine anticoagulation practice was enoxaparin 40 mg given subcutaneously once a day starting in the evening of the day of the surgery and continuing until vitamin K antagonist treatment (started on the first postoperative day) reached the therapeutic level (international normalized ratio [INR] ≥ 2.0).

An ischemic stroke was defined as a permanent focal neurological deficit adjudicated by a neurologist and confirmed via computed tomography or magnetic resonance imaging. TIA was defined as a transient (< 24 hours) focal neurological deficit adjudicated by a neurologist. If a stroke or TIA was clinically diagnosed during index hospitalization by the treating physician and confirmed by computed tomography or magnetic resonance imaging, a separate adjudication by a neurologist was not required. Only ischemic strokes and TIAs considered definite by the treating neurologist or physician were included in the present study. Subtypes of ischemic strokes were categorized by treating physicians using the Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification system.[12] Lacunar stroke was defined as an infarct < 20 mm in diameter. Diabetes, dyslipidemia and hypertension were defined as a disease requiring medical treatment and chronic lung disease as a pulmonary disease requiring long-term use of bronchodilators or steroids. Peripheral arterial disease was defined as one or more of the following: claudication, carotid artery disease of >50% diameter and previous or planned intervention on the abdominal aorta, limb arteries or carotids. Heavy alcohol consumption was defined as >14 doses a week for women and >21 doses a week for men. Poor mobility was defined as severe impairment of mobility secondary to musculoskeletal or neurological dysfunction. Urgent operation was defined as an operation performed during the same in-hospital stay, emergency operation as an operation before the next working day and salvage procedure as an operation where patients require cardiopulmonary resuscitation en route to the operating theatre or prior to the induction of anesthesia.

An independent, certified third-party data monitor controlled the integrity of the data at each study site.

The study protocol was approved by the Medical Ethics Committee of the Hospital District of Southwest Finland and the ethics committee of the National Institute for Health and Welfare (Finland). Because of the retrospective, observational nature of the study, informed consent was not required. The study conforms to the Declaration of Helsinki.

Statistical analysis

Statistical analyses were conducted with Stata version 14.0 statistical software (StataCorp LLC, College Station, TX, USA) and SPSS version 23.0 statistical software (SPSS, IBM SPSS Inc., Chicago, IL, USA). Continuous variables were reported as mean ± standard deviation if normally distributed, and as median [25th–75th percentiles] if they were skewed. The data were tested for normal distribution using Kolmogorov-Smirnov and Shapiro-Wilk tests. Categorical variables were described as counts and percentages. Pearson χ^2, Fisher's exact test, unpaired t-test, Mann-Whitney test and Cox regression were used for univariable analysis. Multivariable competing risk analysis was performed by including variables of relevance with a $p < 0.10$ in the univariable analysis. This method was chosen because postoperative death is a competing risk, i.e. an adverse event that modifies the chance that stroke and/or TIA occur during follow-up. A p value < 0.05 was considered statistically significant. Multiple testing correction was not applied due to the explorative nature of the study.

Results

Incidence of stroke and TIA

A total of 721 patients underwent isolated bioprosthetic SAVR at the four participating hospitals during the study period. The median follow-up time was 4.8 [3.0–7.0] years. Kaplan-Meier estimates of freedom from stroke at 30 days and at 1, 5 and 10 years were 96.9%, 95.5%, 89.0%, and 77.3%, and from TIA 99.3%, 98.1%, 94.1%, and 92.8%, respectively. The median time between the operation and stroke or TIA was 1.7 years [29 days–3.9 years]. Freedom from stroke and TIA is presented in Figure 1. At 30 days and at 1, 5 and 10 years, freedom from stroke and TIA were 95.9%, 93.2%, 83.7%, and 72.7%, respectively. When lacunar strokes were excluded, freedom from stroke at 30 days and at 1, 5 and 10 years were 97.1%, 96.2%, 90.9%, and 82.4%, respectively. TOAST classification of subtypes of stroke after surgery is detailed in Table 1 and the cumulative stroke incidence according to the

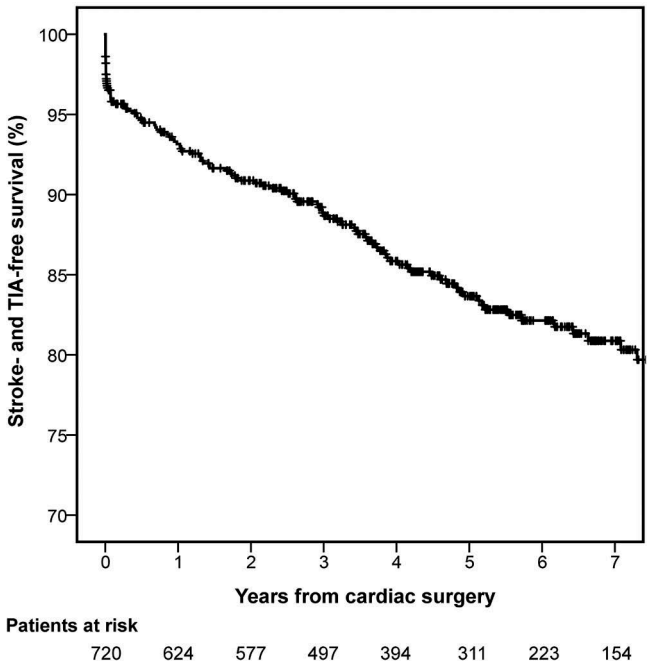

Figure 1. Freedom from stroke and TIA after surgical aortic valve replacement with a bioprosthesis. TIA, transient ischemic attack.

Table 1. Subtypes of acute ischemic stroke after surgical aortic valve replacement with a bioprosthesis according to the TOAST classification.

TOAST classification	Proportion of strokes
Large-artery atherosclerosis (embolus/thrombosis)	5.6%
Cardioembolism (high-risk/medium-risk)	44.4%
Small-vessel occlusion (lacunar)	19.4%
Stroke of other determined etiology	8.3%
Stroke of undetermined etiology	22.2%

Note. TOAST, Trial of Org 10172 in Acute Stroke Treatment.

TOAST classification is detailed in Figure 2. Freedom from stroke in patients undergoing isolated SAVR with bioprosthesis is shown in Figure 3.

The baseline characteristics of patients with and without stroke or TIA are shown in Table 2. Patients with stroke or TIA were significantly older and more often had peripheral arterial disease, a history of heart failure and a previous marked limitation of physical activity due to heart failure. Patients with a stroke or TIA also more often had a prior stroke or TIA. Patients who suffered a stroke had a significantly lower prevalence of prior percutaneous coronary intervention. No differences in the pre- and postoperative laboratory values were detected. Preoperative and discharge drugs in patients with and without a stroke or TIA are detailed in Table 3. No differences in the medical therapies were detected except that patients with stroke or TIA were significantly more likely to be on insulin treatment at discharge. Notably, 47.2% of patients with stroke or TIA were on anticoagulation therapy at the time of the neurological event (TIA 48.6% and stroke 43.4%). Moreover, 40.9% of patients with cardioembolic stroke after 90 days were on anticoagulation treatment at the time of the event.

Predictors of stroke and TIA

A multivariable competing risk analysis identified the following variables as independent predictors of stroke or TIA: increased age (HR 1.03, 95%CI 1.00–1.06, $p = 0.022$), previous stroke or TIA (HR 1.75, 95%CI 1.14–2.70, $p = 0.010$), New York Heart Association (NYHA) class III or more (HR 1.51, 95%CI 1.01–2.24, $p = 0.044$) and insulin treatment at discharge (HR 1.20, 95%CI 1.09–3.64, $p = 0.024$). In multivariable competing risk analysis, increased age (HR 1.05, 95%CI 1.01–1.08, $p = 0.005$), history of heart failure (HR 2.22, 95%CI 1.37–3.59, $p = 0.001$), and insulin treatment at discharge (HR 2.56, 95%CI 1.27–5.19, $p = 0.009$) were independent predictors of stroke.

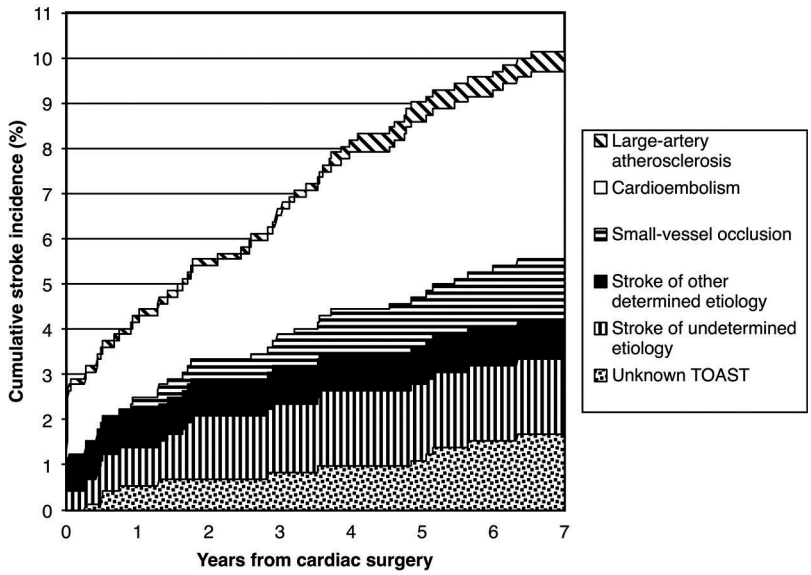

Figure 2. Cumulative stroke incidence according to TOAST classification of subtypes of stroke. TOAST, Trial of Org 10172 in acute stroke treatment.

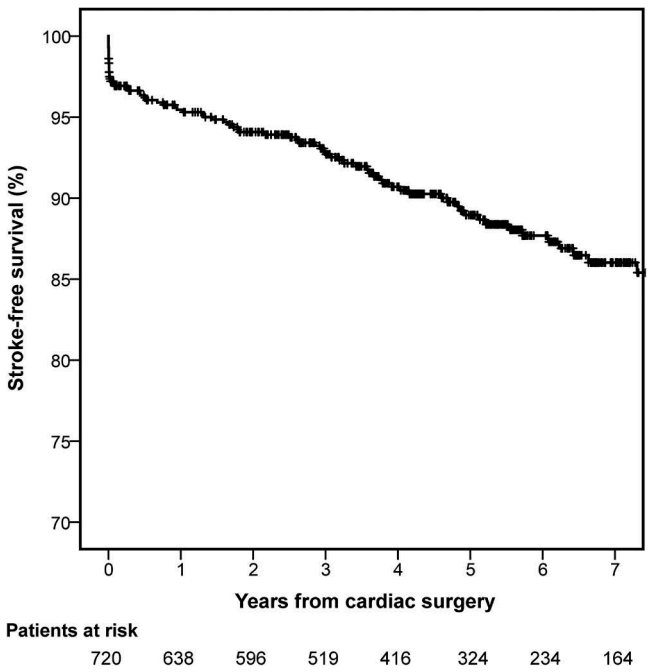

Figure 3. Freedom from stroke after surgical aortic valve replacement with a bioprosthesis.

Discussion

Main findings

The main findings in this study are: (1) the early event rate of stroke after bioprosthetic SAVR was higher than previously reported;[1–7] (2) almost half of the strokes (44.4%) were of cardioembolic etiology; (3) preoperative atrial fibrillation was not associated with a higher risk of stroke or TIA; (4) approximately half of the patients with cerebrovascular events (47.2%) were on anticoagulation therapy at the time of the event.

Clinical implications

This study has several clinical implications. This patient population is at high risk for ischemic cerebrovascular events and factors predisposing to postoperative stroke and TIA should be better understood in order to provide effective preventive strategies. In particular cardioembolic strokes were more frequent in this study population compared to earlier reports in the general population (Figure 2, Table 1, [13]), when evaluating the subtypes of stroke. It is likely that this is related to the prothrombotic state caused by the biological valve and surgery during the immediate postoperative period, and possibly, by the occurrence of atrial fibrillation and leaflet thrombosis later on. Such a high incidence of cardioembolic stroke suggests that some patients with bioprosthetic SAVR may need permanent anticoagulation therapy to prevent atrial fibrillation-related strokes as well as emboli arising from the leaflets of the bioprosthesis.[14] Strikingly, less than half of patients with new stroke were on warfarin therapy despite having AF previously. This implicates underuse of oral anticoagulation in this patient population.

Risk factors of cerebrovascular events

This study implicates that the risk of stroke is higher in patients who carry traditional risk factors for cerebrovascular events, and the risk is notably high in patients with a previous marked limitation of physical activity due to heart failure. Therefore, preventive strategies should be targeted in patients with multiple risk factors of stroke, with a special focus on patients with more severe symptoms of heart failure. Preventive measures include surgical closure of the left atrial appendage or a combination of anticoagulant and antiplatelet medications. The efficacy of left atrial appendage closure in these patients is currently under investigation in the LAA-CLOSURE trial (NCT02321137), which is testing whether prophylactic surgical closure of the left atrial appendage decreases strokes and cardiovascular mortality in patients undergoing SAVR.

Although the risk of stroke was highest in patients with traditional risk factors of cerebrovascular events, some differences require more detailed discussion. Preoperative heart failure was a major predictor for higher postoperative stroke incidence. This finding was not unexpected, since heart failure is a common cause of ischemic stroke.[15,16] Cardiac function may, however, improve after SAVR procedure, but the increased risk of stroke is most likely related to the permanent structural changes leading to increased thrombus formation.[17,18]

Surprisingly, preoperative atrial fibrillation was not associated with a higher risk of stroke or TIA—probably because of long-term anticoagulation after surgery. Nevertheless, most of the remaining traditional risk factors of cerebrovascular events, such as female gender, diabetes, hypertension, and vascular disease, had a non-significant trend towards a higher risk of stroke. When compared to previously known correlates of stroke in atrial fibrillation patients, the risk factors presented in this study were fairly similar. In fact, all risk factors included in the CHA_2DS_2-VASc score were either significant in the present study as well or had a non-significant trend toward higher stroke incidence. Therefore, the CHA_2DS_2-VASc score could be a useful tool, when estimating the risk of postoperative stroke.

In addition, our data shows that approximately half of the patients with ischemic cerebrovascular events were anticoagulated at the time of the event. This might be due to poor control of anticoagulation or non-adherence to the medication or both. However, in order to clarify this finding, we need to conduct a more detailed analysis of these events.

Incidence rate of cerebrovascular events

There was a clear-cut difference in the early event rates when compared to previous studies.[1–7] The discrepancy was most evident when compared to registry-based studies,[1–4] followed by other observational studies[6] as well as interventional studies.[7] In a previous large registry-based study, the reported freedom from stroke in similar patients population was 2.1% at one year and 7.3% at five years.[1] When compared to the

Table 2. Baseline characteristics and pre- and postoperative laboratory values in patients with or without stroke or TIA during follow-up.

	Stroke $n = 85$	$p1$ value	Stroke or TIA $n = 118$	$p2$ value	No stroke or TIA $n = 603$
Age (years)	76.8 [73.9–79.7]	0.002	76.8 [73.5–80.0]	0.007	75.8 [71.4–79.9]
Females	47 (58.0%)	0.944	70 (59.2%)	0.491	337 (55.9%)
Body mass index (kg/m^2)	26.6 [23.9–29.0]	0.384	27.5 [24.8–29.3]	0.440	27.0 [24.5–30.0]
Diabetes	18 (21.2%)	0.541	22 (18.6%)	0.775	120 (19.9%)
Dyslipidemia	46 (54.1%)	0.622	69 (58.5%)	0.501	339 (56.4%)
Hypertension	67 (78.8%)	0.462	88 (75.2%)	0.711	447 (74.1%)
Chronic lung disease	22 (25.9%)	0.379	27 (23.1%)	0.191	104 (17.3%)
Peripheral arterial disease	10 (11.8%)	0.040	13 (11.0%)	0.016	29 (4.8%)
Coronary artery disease	25 (29.4%)	0.807	31 (26.3%)	0.776	159 (26.4%)
Preoperative atrial fibrillation	21 (24.7%)	0.810	29 (24.6%)	0.873	154 (25.5%)
Chronic atrial fibrillation	13 (15.3%)	0.176	16 (13.6%)	0.452	71 (11.8%)
Paroxysmal atrial fibrillation	8 (9.4%)	0.324	13 (11.0%)	0.357	83 (13.8%)
Heart failure	53 (63.1%)	<0.001	70 (59.8%)	<0.001	245 (40.7%)
Active smoking	4 (5.7%)	0.189	5 (5.1%)	0.363	45 (8.3%)
Active or ex-smoker	21 (32.8%)	0.683	27 (29.4%)	0.986	154 (29.9%)
Previous stroke or TIA	18 (21.2%)	0.142	28 (23.7%)	0.013	79 (13.8%)
Previous myocardial infarction	4 (4.7%)	0.205	8 (6.8%)	0.737	42 (7.0%)
Previous percutaneous coronary intervention	1 (1.2%)	<0.001	5 (4.2%)	0.137	49 (8.1%)
Previous cardiac surgery	3 (3.5%)	0.221	4 (3.4%)	0.294	35 (5.8%)
EuroSCORE II (%)	1.8 [1.4–3.0]	0.936	1.8 [1.4–2.8]	0.631	1.7 [1.2–2.5]
NYHA class III or more	58 (68.2%)	0.002	75 (63.6%)	0.007	291 (48.3%)
Echocardiogram:					
Left ventricular ejection fraction (%)	60.0 [51.0–70.0]	0.715	61.0 [54.0–70.0]	0.539	60.0 [50.0–70.0]
Left atrium diameter (mm)	44.0 [38.0–48.0]	0.548	44.0 [38.0–48.0]	0.931	43.0 [38.0–47.0]
Aortic valve peak pressure gradient (mmHg)	81.0 [70.0–97.0]	0.124	81.0 [69.0–97.0]	0.497	78.0 [66.0–95.0]
Aortic valve regurgitation	44 (51.8%)	0.132	60 (50.9%)	0.123	334 (58.1%)
Mitral valve regurgitation	48 (56.5%)	0.911	67 (56.8%)	0.817	325 (55.9%)
Urgent, emergency or salvage procedure	3 (3.5%)	0.362	3 (2.5%)	0.295	30 (5.0%)
Preoperative laboratory values:					
eGFR	72.7 [57.8–81.6]	0.287	74.2 [58.5–83.1]	0.800	74.9 [59.8–87.9]
INR	1.2 [1.0–1.2]	0.618	1.2 [1.0–1.2]	0.625	1.2 [1.0–1.2]
Postoperative laboratory values:					
Troponin T max	795 [584–1070]	0.186	765 [530–1060]	0.220	645 [415–1087]
eGFR min	66.0 [55.0–82.0]	0.186	54.0 [54.0–83.0]	0.130	61.0 [46.5–78.0]
CK-MB max	28.9 [19.0–37.3]	0.892	26.0 [19.5–37.0]	0.686	24.0 [17.0–34.0]

Note. Continuous variables are reported as median [25th, 75th percentiles]. Values in parentheses are percentages.
$p1$ value, stroke vs. no stroke or TIA; $p2$ value, stroke or TIA vs. no stroke or TIA; CK-MB, creatine kinase-myocardial band isoenzyme; eGFR, estimated glomerular filtration rate using modification of diet in renal disease formula; INR, international normalized ratio; NYHA, New York Heart Association Functional Classification; TIA, transient ischemic attack.

present results, the event rates were notably higher in the present study in the early post-operative period (Figure 2). This difference also remained in subpopulations of men, women, ejection fraction <50%, ejection fraction ≥50% and different age groups.[1]

When it comes to reliability of endpoints, registry-based studies have multiple challenges. Incomplete data capture, heterogeneity between different systems and coding errors, may affect data quality.[19] Nevertheless, it is unlikely that these would explain the lower incidence in other observational studies and interventional studies. Another challenge relating to both observational and interventional studies is that symptoms related to cerebrovascular events are often perceived as unavoidable surgery-related factors rather than complications. As a consequence, the events may remain unreported.

In the present study the estimated incidence of stroke at 5 years was 11.0%, giving an average incidence of 2.2% per year. As a comparison, the long-term stroke risk of atrial fibrillation is 4.1% per year without anticoagulation and approximately 1.5% per year with anticoagulation.[20] Thus the incidence of stroke is markedly higher after bioprosthetic SAVR when compared to patients with atrial fibrillation on anticoagulation therapy.

Strengths and limitations

Methodologically, this study has several strengths. A validated, structured case report form was used at all study sites. As a quality control, a professional third party monitored the data. This patient population is from regional catchment areas where cerebrovascular events are treated exclusively at the participating centers. Moreover, to the authors' knowledge, this is the first study assessing the cumulative stroke incidence according to subtypes of stroke after cardiac surgery.

Table 3. Medication before surgery and at discharge in patients with or without stroke or TIA during follow-up.

	Stroke $n = 85$	$p1$ value	Stroke or TIA $n = 118$	$p2$ value	No stroke or TIA $n = 603$
Preoperative drugs:					
Warfarin	17 (20.0%)	0.523	25 (21.2%)	0.488	113 (18.8%)
Low molecular weight heparin	7 (8.2%)	0.397	8 (6.8%)	0.823	36 (6.0%)
Acetylsalicylic acid	43 (51.2%)	0.940	62 (52.9%)	0.823	305 (51.0%)
ADP receptor inhibitor	0 (0.0%)	—	3 (2.6%)	0.148	7 (1.2%)
Beta blocker	53 (63.4%)	0.669	74 (62.7%)	0.720	380 (63.6%)
ACE inhibitor	47 (55.3%)	0.479	61 (51.7%)	0.741	307 (51.2%)
Statin	45 (52.9%)	0.987	67 (56.8%)	0.311	315 (52.5%)
Oral antidiabetic drug	13 (15.3%)	0.479	16 (13.6%)	0.997	84 (14.0%)
Insulin	8 (9.4%)	0.147	10 (8.5%)	0.284	35 (5.8%)
NSAID	1 (1.2%)	0.592	2 (1.7%)	0.738	15 (2.5%)
Proton-pump inhibitor	15 (17.7%)	0.683	18 (15.3%)	0.823	99 (16.5%)
Digoxin	6 (7.1%)	0.714	7 (6.0%)	0.582	45 (7.5%)
Discharge drugs:					
Warfarin	78 (96.3%)	0.645	110 (96.5%)	0.763	569 (96.8%)
Low molecular weight heparin	21 (26.9%)	0.651	29 (26.1%)	0.357	190 (32.7%)
Acetylsalicylic acid	10 (12.6%)	0.322	13 (11.6%)	0.313	91 (15.9%)
ADP receptor inhibitor	0 (0.0%)	—	1 (0.9%)	0.133	1 (0.2%)
Beta blocker	67 (82.7%)	0.853	93 (81.6%)	0.357	504 (85.1%)
ACE inhibitor	44 (54.3%)	0.759	57 (52.3%)	0.765	311 (52.4%)
Statin	45 (56.3%)	0.635	64 (56.6%)	0.483	321 (54.3%)
Oral antidiabetic drug	11 (13.8%)	0.728	12 (10.6%)	0.399	82 (13.9%)
Insulin	9 (11.3%)	0.029	12 (11.2%)	0.043	36 (6.1%)
NSAID	0 (0.0%)	—	1 (0.9%)	0.315	15 (2.5%)
Proton-pump inhibitor	29 (36.3%)	0.217	37 (33.0%)	0.319	177 (30.0%)
Digoxin	9 (11.3%)	0.260	10 (8.9%)	0.795	50 (8.5%)

Note. Values in parentheses are percentages.
$p1$ value, stroke vs. no stroke or TIA; $p2$ value: stroke or TIA vs. no stroke or TIA; ACE, angiotensin-converting-enzyme; ADP, adenosine diphosphate; NSAID, non-steroidal anti-inflammatory drug; TIA transient ischemic attack.

The main limitation of this study is its retrospective nature. However, data are from electronic patient records and data on baseline, operative and outcomes are reported in detail at each of the participating hospitals. Second, diagnoses were made by treating physicians, which might have affected the sensitivity of registering the end points. On the other hand as a result of the retrospective nature and physicians' diagnoses, there is a problem with false negative cerebrovascular events rather than false positives. This strengthens further the conclusion of the problem of underdiagnosing early cerebrovascular events in previous studies. In addition, the subtypes of stroke were classified by the treating physicians. The decision regarding the use of imaging methods in the etiological assessment of stroke or TIA was at the discretion of the treating neurologist. However, especially in the case of cardioembolic stroke, the categorization is always an educated guess made by the treating physician instead of an absolute medical finding. In practice this means that the treating neurologists used the imaging methods needed (e.g. computer tomography, carotid ultrasound imaging, echocardiogram) to exclude large artery atherosclerosis, small vessel occlusion and other determined etiologies and to evaluate the probability of cardioembolic etiology. Based on these findings, the treating neurologists classified the events as of cardioembolic or other etiologies. Neurological events were defined as "Unknown TOAST" when not otherwise categorized by the treating neurologists. The small size of this study is another limitation of this analysis, and therefore, these findings should be viewed as hypothesis generating.

Conclusion

The present results suggest that the incidence of stroke in the early postoperative period after isolated bioprosthetic SAVR is higher than previously documented. More severe symptoms of heart failure preoperatively were associated with a markedly increased risk of cerebrovascular events. Almost a half of the strokes were of cardioembolic origin. These findings highlight the need for better prevention of cardioembolic events after SAVR.

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