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Original Research

Calcium Load in the Aortic Valve, Aortic Root, and Left Ventricular Outflow Tract and the Risk for a Periprocedural Stroke

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ABSTRACT

Background: Periprocedural stroke during transcatheter aortic valve implantation is a rare but devastating complication. The calcified aortic valve is the most likely source of the emboli in a periprocedural stroke. The total load and distribution of calcium in the leaflets, aortic root, and left ventricular outflow tract varies from patient to patient. Consequently, there could be patterns of calcification that are associated with a higher risk of stroke. This study aimed to explore whether the pattern of calcification in the left ventricular outflow tract, annulus, aortic valve, and ascending aorta can be used to predict a periprocedural stroke.

Methods: Among the 3282 consecutive patients who received a transcatheter aortic valve implantation in the native valve in Sweden from 2014 to 2018, we identified 52 who had a periprocedural stroke. From the same cohort, a control group of 52 patients was constructed by propensity score matching. Both groups had one missing cardiac computed tomography, and 51 stroke and 51 control patients were blindly reviewed by an experienced radiologist.

Results: The groups were well balanced in terms of demographics and procedural data. Of the 39 metrics created to describe calcium pattern, only one differed between the groups. The length of calcium protruding above the annulus was 10.6 mm (interquartile range 7-13.6) for patients without stroke and 8 mm (interquartile range 3-10) for stroke patients.

Conclusions: This study could not find any pattern of calcification that predisposes for a periprocedural stroke.

ABBREVIATIONS

CPD, cerebral protection device; CT, computed tomography; LCC, left coronary cusp; LVOT, left ventricular outflow tract; NCC, noncoronary cusp; RCC, right coronary cusp; SAVR, surgical aortic valve replacement; SWEDEHEART, Swedish Web-system for Enhancement and Development of Evidence-based care in Heart Disease Evaluated According to Recommended Therapies; SWENTRY, SWEdish traNscatheter cardiac intervention regisTRY; TAVR, transcatheter aortic valve replacement.

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Introduction

Treatment of aortic stenosis is changing rapidly as more evidence becomes available on the safety and efficacy of transcatheter aortic valve replacement (TAVR).[1-4] Despite the fact that TAVR is as safe as surgical aortic valve replacement (SAVR), and in some cases leads to improved outcome compared with SAVR, severe complications still occur.[1,2] The most prevalent complications are the need for a pacemaker, puncture site bleeding, renal impairment, and residual paravalvular leak. All these complications are manageable, often with little impact on patient outcome or quality of life. However, a periprocedural stroke is a potentially devastating complication that quickly offsets the benefits of the intervention. The frequency of periprocedural strokes during TAVR has been reported between 1% and 5%,[2,5-7] and the 1-year survival after stroke is 40% to 46%.[7,8] Given the negative impact of a periprocedural stroke on not only patient morbidity and mortality but also hospital systems, out-of-hospital care facilities, and emotional trauma to relatives, it is imperative to reduce the incidence of this complication.

Recently, different cerebral protection devices (CPDs) have been introduced[9-13] as a way to mitigate the risk of a periprocedural stroke. A reduction in stroke rate by CPD has only been shown in propensity-matched studies or meta-analyses.[11,14-16] Therefore, uncertainty exists as to whether CPD should be introduced to all patients, no patients, or to a subgroup of patients at high risk for periprocedural stroke. Several reports have found patient-specific risk factors for developing a stroke,[5-8] where the most frequent are previous stroke, age, reduced renal function, atrial fibrillation, high body mass index, and female sex. However, none of the studies have considered the calcium load and distribution in the aortic valve and left ventricular outflow tract (LVOT). Only a few studies have looked at the possible linkage between calcium distribution in the aortic root and the risk for stroke,[17,18] but these studies were performed on a small number of stroke patients.

Therefore, the aim of the present study was to determine whether radiological characteristics of the LVOT, annulus, and aortic valve can predispose patients to periprocedural stroke.

Material and Methods

Study Design

This is a retrospective, nationwide follow-up study of all patients who underwent TAVR in Sweden from January 2014 to September 2018. During this period, a CPD was not used in Sweden. The data set and data sources have been described earlier.[19] The initial data source was the national TAVR registry SWENTRY (SWEdish traNscatheter cardiac intervention regisTRY), which is a part of the SWEDEHEART registry (Swedish Web-system for Enhancement and Development of Evidence-based Care in Heart Disease Evaluated According to Recommended Therapies) and contains information on all TAVR procedures performed in the country.[20]

During the study period, a total of 3282 patients received a TAVR in a native valve (valve-in-valve procedures were excluded), and 52 (1.6%) of them developed a stroke during the procedure and were included in the stroke cohort (Table 1). A propensity score matching was performed based on 6 variables: age, gender, hypertension, peripheral vascular disease, atrial fibrillation, and myocardial infarction within the last 3 months; with the nearest neighbor method used to create a control group of 52 patients (Figure 1).

The study was approved by the National Ethical Review Board in Sweden (registration number 2017/995 and EPN 2019/0584).

Radiological Analysis

We turned to all 8 centers performing TAVR in Sweden and asked for the multidetector computed tomography images of the heart and aorta performed before the TAVR for both the case and the control group. The images were electronically transferred to a local server in our hospital. Image analysis was performed by one (A.P.) thoracic radiologist blinded to the outcome (stroke/no stroke). Image storage, assessment, reconstruction, and semiquantitative analysis were performed for all cases using Sectra IDS7 (Sectra AB, Linköping, Sweden). Quantitative analysis of calcium burden was assessed using a modified routine within the cardiac workflow in Syngo.Via (Siemens Health, Erlangen, Germany).

Table 1
Distribution of strokes between centers during study period

Center	Cases	Stroke
1	443	3 (0.7%)
2	99	1 (1.0%)
3	386	3 (0.8%)
4	487	13 (2.7%)
5	931	21 (2.3%)
6	302	2 (0.7%)
7	433	5 (1.2%)
8	201	4 (2.0%)
Total	3282	52 (1.6%)

Relevant computed tomography (CT) series were identified: submillimeter slices of electrocardiogram-gated iodine contrast-enhanced imaging of the aorta root in 1 or 2 time points within the cardiac cycle, 3-mm thick slices of non-contrast-enhanced electrocardiogram-gated imaging of aorta root for standard calcium scoring according to Agatston, and submillimeter slices of imaging of the whole aorta.

Semiquantitative analysis of the device landing zone was performed on a 1 mm thick slice reconstructed to have the aortic annulus in axial projection. Presence, number, and size of calcifications; protrusion in the lumen; and central angle covered by calcium was recorded and attributed to respective parts of the sector of annulus for orientation (right coronary cusp [RCC], left coronary cusp [LCC], and noncoronary cusp [NCC], respectively; Figure 2). For the largest calcification, the extent above and under the annulus plane was measured on dedicated longitudinal reconstructions. Commissure calcifications were assessed on image series consisting of axial reconstructions of the aortic root (Figure 2).

Total calcium volume in the valve leaflets and LVOT were quantified using a modified calcium scoring protocol as described by Bettinger et al.[21] (Figure 3). Briefly, a threshold for separating calcium from the iodine was defined as 150 HU + the average attenuation in the lumen at annulus level, and the volume of voxels with higher attenuation was defined as calcium.

Statistical Analysis

A Shapiro–Wilk's test was performed to test distribution of data, and depending on the result, either a Student's t-test or Mann-Whitney U-test was performed for continuous data. For dichotomous data, a Fisher's exact test was used. Data are presented as mean ± SD, number (percentage), or median with interquartile range (interquartile range [IQR]). A p-value <0.05 was considered statistically significant. Data analyses were performed using Stata version 14.2 (StataCorp LLC, College Station, TX).

Results

Of the 104 patients included in the study, 2 did not undergo a CT examination of the heart, yielding 51 patients for both the case and the control group (Figure 1). The case and control groups were well balanced, with no significant differences in the demographic profile and comorbidities (Table 2). There were no significant

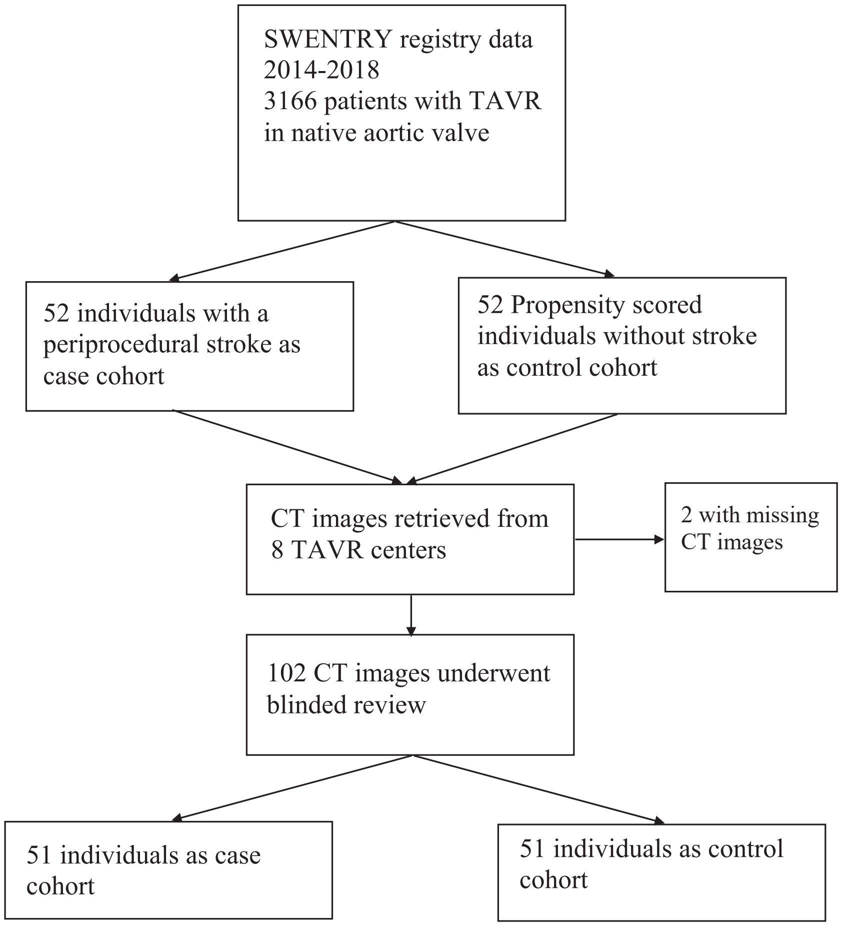

Figure 1. Flowchart of study design. Flowchart depicting study patient selection from SWENTRY registry. CT, computed tomography; SWENTRY, SWEdish traNscatheter cardiac intervention regisTRY; TAVR, transcatheter aortic valve replacement

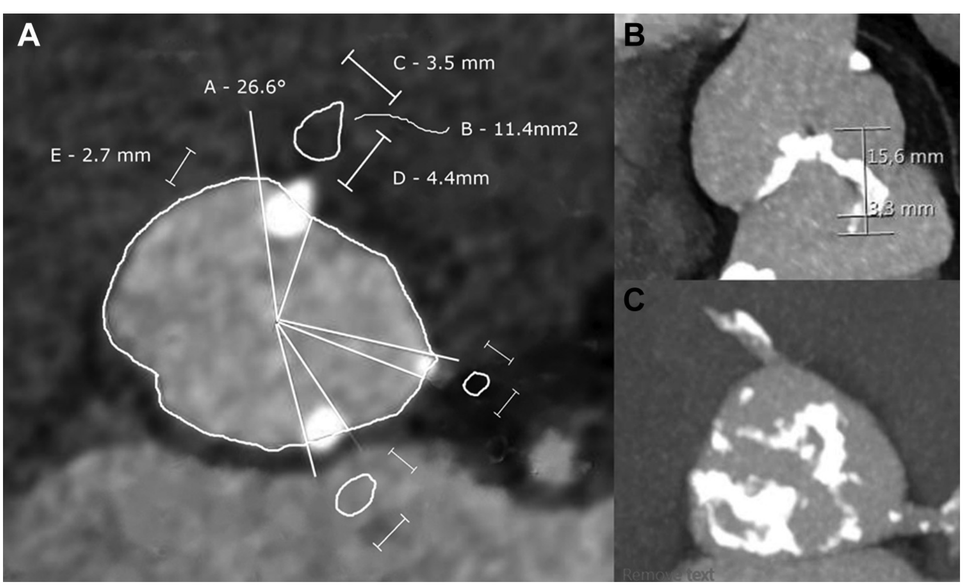

Figure 2. Example of measurements for calcifications in annulus and left ventricular outflow tract. (a) Annulus measurements where A = sector angle; B = area of calcification at measured level; C = width of calcification; D = thickness of calcification; E = protrusion of calcification into lumen. The total calcium volume (expressed in cubic millimeter) and sector engagement were calculated as the sum of NCC + RCC + LCC. (b) Maximum calcification length above and below annular plane. (c) Example of commissural bridge between RCC and LCC. Abbreviations: LCC, left coronary cusp; NCC, noncoronary cusp; RCC, right coronary cusp.

differences in intraprocedural relevant variables: access (transfemoral 92% for control group and 88% for stroke group), predilatation (49% for both groups), valve type (55% SEV for control group and 57% SEV for stroke group), and postdilatation (14% for control group and 16% for stroke group; Table 2). There were no differences between the groups for the postoperative outcome in terms of new permanent pacemaker, new dialysis, bleeding complications, infection, or new atrial fibrillation (Table 2). The group with stroke had, however, a higher 30-day mortality (17.3% vs. 3.8%; $p = 0.026$).

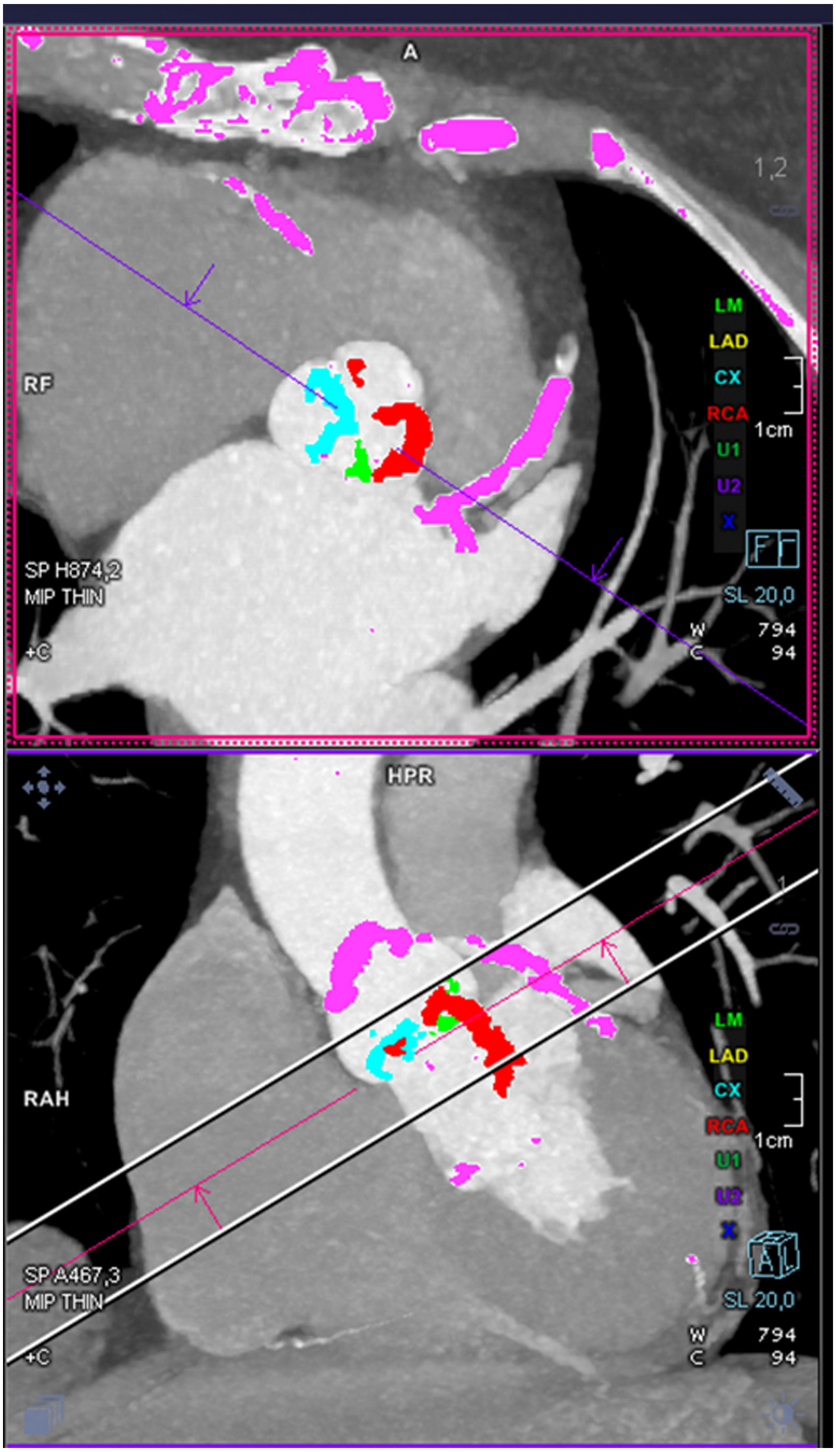

Figure 3. Measurement of calcium volume. Twenty-millimeter thick maximum intensity projections at annulus level (axial image, above) and longitudinal projection along the longest calcification. An attenuation cutoff value of 498 HU (150 HU + average HU/annulus; see Figure 2) was used to discriminate between iodine contrast and calcium; all voxels with attenuation above the threshold value were color-coded automatically to pink (as part of the standard workflow for calcium scoring using syngo.via CaScoring algorithm). Afterward, on an axial reconstruction of the aortic root, the structures with attenuation above threshold and connected to aortic valve cusps, anulus, and left ventricular outflow tract were manually color-coded according to the anatomic sector (red for right coronary cusp, green for left coronary cusp, and blue for noncoronary cusp).

Total Calcium Load

There were no differences in total calcium load of the aortic valve described as volume (867.5 [IQR 628-1272] mm^3 for the no stroke group vs. 798.5 [IQR 488-1365] mm^3 for the stroke group, $p = 0.53$; Table 3).

Annular Calcium Load

In the comparison of all annuli in both groups, there were no differences in the amount of calcium (Table 3). When the annuli with calcification were analyzed separately, only the length that calcium was protruding above the annulus differed with 10.6 mm [IQR 7-13.6] for patients without stroke and 8 mm [IQR 3-10] for stroke patients ($p = 0.012$; Table 4).

LVOT Calcium Load

In the analysis of LVOT, there was no difference in calcium load between patients. When the patients with LVOT calcifications were compared, there also was no noted difference (Table 5).

Table 2
Demographics and intraprocedural variables

Demographics	All (n = 102)	Control (n = 51)	Stroke (n = 51)	*p* level
Age	84.3 ± 5.3	84.7 ± 4.4	83.9 ± 6.1	0.448
Female gender	62.7% (64)	62.7% (32)	62.7% (32)	1.000
Length (cm)	164.1 ± 9.5	163.7 ± 10.4	164.4 ± 8.5	0.716
Weight (kg)	70.9 ± 13.5	70.0 ± 12.8	71.8 ± 14.3	0.510
Hypertension	84.3% (86)	84.3% (43)	84.3% (43)	1.000
Diabetes	16.7% (17)	17.6% (9)	15.7% (8)	1.000
Atrial fibrillation	30.4% (31)	33.3% (17)	27.5% (14)	0.667
PVD	14.7% (15)	13.7% (7)	15.7% (8)	1.000
Previous AMI	Able	7.8% (4)	9.8% (5)	1.000
Previous stroke	14.7% (15)	15.7% (8)	13.7% (7)	1.000
Previous cardiac surgery	11.8% (12)	11.8% (6)	11.8% (6)	1.000
BAV	2.9% (3)	0% (0)	5.9% (3)	0.243
PCI	30.4% (31)	27.5% (14)	33.3% (17)	0.667
COPD	18.6% (19)	11.8% (6)	25.5% (13)	0.126
Critical preop state	2.9% (3)	3.9% (2)	2% (1)	1.000
Reduced mobility	16.7% (17)	9.8% (5)	23.5% (12)	0.109
NYHA				1.000
NYHA I	1% (1)	0% (0)	2% (1)	
NYHA II	9.8% (10)	9.8% (5)	9.8% (5)	
NYHA III	71.6% (73)	72.5% (37)	70.6% (36)	
NYHA IV	17.6% (18)	17.6% (9)	17.6% (9)	
Porcelain aorta	6.9% (7)	3.9% (2)	9.8% (5)	0.436
Chest deformity	4.9% (5)	0% (0)	9.8% (5)	0.056
Radiation	2% (2)	0% (0)	3.9% (2)	n/a
Malignancy	15.7% (16)	19.6% (10)	11.8% (6)	0.415
Dialysis before	1% (1)	0% (0)	2% (1)	1.000
Creatinine (μmol/L)	96.5 ± 41.0	95.9 ± 45.7	97.2 ± 36.2	0.873
eGFR (mL/min/1.73 m^2)	58.1 ± 17.6	59.2 ± 17.5	56.9 ± 17.9	0.523
Declined SAVR	84.2% (85)	88.2% (45)	80% (40)	0.288
AVA	0.65 ± 0.16	0.64 ± 0.1	0.67 ± 0.1	0.296
Mean gradient	47.6 ± 13.4	48.0 ± 15.0	47.2 ± 11.8	0.759
LVEF				0.151
Normal	64.7% (66)	66.7% (34)	62.7% (32)	
Slightly reduced	14.7% (15)	7.8% (4)	21.6% (11)	
Moderately reduced	13.7% (14)	17.6% (9)	9.8% (5)	
Severely reduced	4.9% (5)	3.9% (2)	5.9% (3)	
Intraprocedural	**All**	**Control**	**Stroke**	***p* level**
Predilatation	49% (50)	49% (25)	49% (25)	1.000
Postdilatation	14.7% (15)	13.7% (7)	15.7% (8)	1.000
Access type				0.523
Transfemoral	90.2% (92)	92.1% (47)	88.2% (45)	
Transapical	4.9% (5%)	5.9% (3)	3.9% (2)	
Direct aortic	1.0% (1)	0% (0)	2.0% (1)	
Subclavian	3.9% (4)	2.0% (1)	5.9% (3)	
Rapid pacing	57.8% (59)	58.8% (30)	56.9% (29)	1.000
Second valve	0% (0)	0% (0)	0% (0)	n/a
SEV	55.9% (57)	54.9% (28)	56.9% (29)	0.842
Amount of contrast (mL)	77.7 ± 56.5	67.9 ± 46.0	87.5 ± 64.2	0.079
Flouro time (min)	23.0 ± 14.2	21.4 ± 12.7	24.5 ± 15.5	0.271
Postprocedural	**All**	**Control**	**Stroke**	***p* level**
New permanent pacemaker	5.8% (6)	7.7% (4)	3.8% (2)	0.339
New dialysis	0% (0)	0% (0)	0% (0)	n/a
Bleeding complications	3.8% (4)	1.9% (1)	5.8% (3)	0.310
Infection	5.8% (6)	3.8% (2)	7.7% (4)	0.339
New atrial fibrillation	1% (1)	0% (0)	1.9% (1)	0.500
30-d mortality	10.6% (11)	3.8% (2)	17.3% (9)	0.026

Notes. Comparison between patients who developed an intraprocedural stroke and a propensity-matched control cohort. Data are presented as mean ± SD or % (n). Abbreviations: AMI, acute myocardial infarction; AVA, aortic valve area; BAV, bicuspid aortic valve; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; SAVR, surgical aortic valve replacement; SEV, self-expandable valve (compared with balloon-expandable valve and mechanically expandible valve).

Discussion

In this study, we sought to find a pattern of calcification in the aortic valve and aortic root that predisposed patients to a periprocedural stroke. Despite a detailed analysis of calcium distribution, the study failed to find any radiological signs that could help us categorize patients as high risk or low risk for a periprocedural stroke.

Only one significant finding was made in our comparison, and it was the length that the calcium extended above the aorta annulus. Interestingly, this metric was higher in the control group than in the stroke group. Our interpretation of this finding is that it is a type I error, especially because we did not adjust for multiple testing in this study, and the finding has no clinical relevance. The presence of calcium in the LVOT was found in 55% of stroke patients and 37% in the control group

Table 3
Total calcium volume in the aortic valve

Measurement	All		No stroke		Stroke		p level
	Mean ± SD	Median [IQR]	Mean ± SD	Median [IQR]	Mean ± SD	Median [IQR]	
Total calcium load mm^3	1106 ± 1028	840.5 [552-1329]	1079 ± 865	867.5 [628-1272]	1132 ± 1178	798.5 [488-1365]	0.527

Notes. Calcium volume presented for the entire cohort and the 2 groups expressed as mm^3.
IQR, interquartile range.

Table 4
Measurements of annular calcifications

Measurement	All (n = 102)		No stroke (n = 51)		Stroke (n = 51)		p level
	Mean ± SD	Median [IQR]	Mean ± SD	Median [IQR]	Mean ± SD	Median [IQR]	
Commissural Ca bridge	21% (21)		25% (13)		16% (8)		0.327
Ca in annulus	53% (54)		51% (26)		55% (28)		0.843
No. of calcifications							
Annulus	0.53 ± 0.5	1 [0-1]	0.78 ± 1.22	1 [0-1]	0.88 ± 1.03	1 [0-1]	0.447
RCC	0.14 ± 0.37	0 [0-0]	0.18 ± 0.43	0 [0-0]	0.1 ± 0.3	0 [0-0]	0.554
LCC	0.41 ± 0.63	0 [0-1]	0.31 ± 0.55	0 [0-1]	0.51 ± 0.7	0 [0-1]	0.269
NCC	0.28 ± 0.59	0 [0-0]	0.29 ± 0.67	0 [0-0]	0.27 ± 0.49	0 [0-1]	1.000
Patients with calcification in annulus							
Measurement	All (n = 54)		No stroke (n = 26)		Stroke (n = 28)		p level
	Mean ± SD	Median [IQR]	Mean ± SD	Median [IQR]	Mean ± SD	Median [IQR]	
Sector with Ca (arc degree)							
RCC	4.4 ± 9.3	0 [0-0]	5.7 ± 10.8	0 [0-9.3]	4.4 ± 9.3	0 [0-0]	0.321
LCC	15.8 ± 18.8	12.1 [0-20.8]	13 ± 17.2	11 [0-20.3]	15.8 ± 18.8	13.2 [0-27.1]	0.256
NCC	10.6 ± 16.4	0 [0-15]	10.5 ± 17.7	0 [0-10.6]	10.6 ± 16.4	0 [0-15.9]	0.721
Area of Ca per cusp (mm^2)							
RCC	2.4 ± 5.4	0 [0-0]	3.2 ± 6.8	0 [0-5.8]	2.4 ± 5.4	0 [0-0]	0.310
LCC	9.1 ± 15.3	4.9 [0-11.3]	7.1 ± 9.4	4.25 [0-13.7]	9.1 ± 15.3	5.15 [0-11.3]	0.472
NCC	4.4 ± 7.4	0 [0-5.5]	3.9 ± 6.5	0 [0-3.6]	4.4 ± 7.4	0 [0-5.7]	0.749
Largest ca block							
Area (mm^2)	12 ± 13.7	7.75 [4.8-14.8]	10.9 ± 8.3	6.7 [5-16.8]	12 ± 13.7	8.5 [4.8-12.9]	0.856
Protrusion (mm)	1.4 ± 1	1.15 [0.7-2]	1.4 ± 0.8	1.2 [0.7-1.9]	1.4 ± 1	0.95 [0.7-2.2]	0.972
Width (mm)	4.4 ± 2.9	3.55 [2.4-4.9]	4.3 ± 2.7	3.55 [2.2-5.8]	4.4 ± 2.9	3.65 [2.7-4.7]	0.762
Thickness (mm)	3.1 ± 1.6	2.7 [2-4.1]	2.9 ± 1.1	2.8 [2.1-3.5]	3.1 ± 1.6	2.65 [2-4.4]	0.665
Length above (mm)	8.4 ± 4.6	9.3 [5.9-11.2]	10 ± 4.6	10.6 [7-13.6]	6.9 ± 41	8 [3-10]	**0.012**
Length under (mm)	6.1 ± 6.5	2.5 [3.8-7.8]	6.5 ± 5.7	2.1 [4.4-9.2]	6.1 ± 6.5	7.1 [2.5-7.1]	0.709

Notes. Upper part all 102 CT examinations. Lower part only the 54 examinations with calcifications in the annulus.
IQR, interquartile range; LCC, left coronary cusp; NCC, noncoronary cusp; RCC, right coronary cusp.

($p = 0.074$). It could be argued that this is type II error and that a larger cohort would have detected a difference. But the absolute difference is 18%, so it would not be a strong predictor that could be useful in determining whether to use a CPD or not.

Relation to Previous Studies

At least 2 other studies have tried to explore a relation between aortic valve morphology and the risk for a periprocedural stroke. Pollari et al.[18] found that the amount of calcium in LVOT of RCC correlated with stroke. However, in their study, they analyzed all in-hospital strokes, not only periprocedural strokes. Moreover, the study covered only 9 cases of stroke and 572 patients without stroke, making it challenging to draw conclusions regarding high-risk anatomical features. Spaziano et al.[17] found that LVOT calcium predisposed patients for a composite outcome of death and stroke at 1 year in women. Aggarwal et al.[22] used transcranial doppler in a series of 63 patients and found a correlation between the number of high-intensity transient signals and calcium load of the aortic valve and aortic root measured as Agatston score. A similar finding was done by Vlastra et al.[23] when they correlated magnetic resonance imaging findings with calcium burden. They found that aortic valve calcium volume correlated to new cerebral white matter hyper-intensity. However, no such correlation was found for calcium burden in the ascending aorta and LVOT. To summarize these findings, one study found that LVOT calcium correlated with clinical stroke, whereas 2 studies found a correlation between embolic load and aortic valve calcium but not with LVOT calcium. Given the disparate results of these studies with different designs and weaknesses, no clear pattern can be established between calcium burden in the aorta/aortic valve/LVOT and the risk of periprocedural stroke. The findings of the present study further strengthen the notion that no strong correlation exists.

Clinical Perspective

The main driver and rationale for this study were to identify anatomical signs in CT imaging that could help us identify patients at high risk for a periprocedural stroke and who would benefit most from a CPD. The scientific data supporting the adoption rate of CPD in practice is currently limited. Although randomized studies have shown no or even negative effects[24,25] of CPD, meta-analysis and pooled data have been able to find a benefit in terms of stroke reduction.[16,24] Therefore, the question of if and when to use CPD is still unanswered. This question is being addressed in 2 smaller ongoing studies (Clinicaltrials registration numbers: NCT02895737 and NCT04704258) and 1 larger ongoing study (Clinicaltrials registration number: NCT04149535). The large study includes a wide selection of TAVR patients and will include 3000 patients and have any type of stroke as its primary endpoint.

Table 5
Measurements of LVOT calcifications

Measurement	All (n = 102)		No stroke (n = 51)		Stroke (n = 51)		p level
	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)	
Ca in LVOT	46% (47)		37% (19)		55% (28)		0.074
Number of calcifications							
Annulus	0.61 ± 0.82	0 [0-4]	0.49 ± 0.73	0 [0-3]	0.55 ± 0.5	1 [0-4]	0.114
RCC	0.05 ± 0.22	0 [0-1]	0.06 ± 0.24	0 [0-1]	0.73 ± 0.9	0 [0-1]	0.648
LCC	0.34 ± 0.59	0 [0-3]	0.25 ± 0.48	0 [0-2]	0.04 ± 0.2	0 [0-3]	0.171
NCC	0.22 ± 0.41	0 [0-1]	0.18 ± 0.39	0 [0-1]	0.43 ± 0.67	0 [0-1]	0.338

Patients with calcification in LVOT

	All (n = 47)		No stroke (n = 19)		Stroke (n = 28)		p level
	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)	
Sector with Ca (arc degree)							
RCC	1.6 ± 5.5	0 [0-0]	2.7 ± 7.8	0 [0-0]	0 ± 0	0 [0-0]	0.373
LCC	13.5 ± 14.6	10.1 [0-18.2]	14.3 ± 15.1	10.3 [0-21.4]	0.8 ± 3	9.95 [0-15.9]	0.722
NCC	8.1 ± 10.5	0 [0-14.5]	10 ± 12.5	0 [0-18.4]	13 ± 14.4	0 [0-13.5]	0.424
Area of Ca per cusp (mm^2)							
RCC	0.9 ± 3.2	0 ± 0-0]	1.5 ± 4.6	0 [0-0]	6.9 ± 9	0 [0-0]	0.331
LCC	7.3 ± 10.1	3.5 [0-8.7]	7.3 ± 8.9	6 [0-9]	0.4 ± 1.8	3.4 [0-7.5]	0.747
NCC	3.3 ± 4.3	0 [0-6.4]	3.2 ± 4.3	0 [0-6.4]	7.2 ± 10.9	0 [0-6.55]	0.906
Largest Ca block							
Area (mm^2)	10.3 ± 9.8	6.9 [4.3-10.9]	10.2 ± 7.9	7.9 [3.7-13.7]	3.3 ± 4.5	6.8 [4.3-9.95]	0.618
Protrusion (mm)	1.2 ± 0.9	1 [0.7-1.4]	1.3 ± 0.9	1.1 [0.8-1.6]	10.3 ± 11.1	1 [0.55-1.3]	0.259
Width (mm)	4 ± 2.2	3.5 [2.3-5.1]	4.4 ± 2.1	3.8 [2.6-6.1]	1.1 ± 0.9	3.35 [2.15-4]	0.162
Thickness (mm)	2.9 ± 1.5	2.4 [1.7-3.3]	2.9 ± 1.6	2.4 [1.6-3.9]	3.7 ± 2.3	2.4 [1.75-3.3]	0.983

Notes. Upper part all 102 CT examinations. Lower part only the 47 examinations with calcifications in the LVOT.
IQR, interquartile range; LCC, left coronary cusp; LVOT, left ventricular outflow tract; NCC, noncoronary cusp; RCC, right coronary cusp.

Limitations and Strengths

The present study has both some limitations and strengths. Among the limitations, the use of propensity score matching to create a control group could be discussed. Despite being well-balanced, a better alternative would be to use the entire cohort as a control group. However, it would be an almost insurmountable task to review more than 3000 CT examinations with the granularity used in this study. Another limitation is the relatively small cohort of 52 patients with a periprocedural stroke. A larger cohort could potentially detect differences that we could not find in the current cohort. However, we could not discern any obvious trend in this study, and therefore, even if a larger cohort would yield a positive result, the difference between the groups would be small. As we did not have CT of the brain for stroke patients, we could not discern between calcific and thrombotic emboli, where the former presumably originates from the aortic valve and the latter from the aorta and delivery system. This is a registry-based study and reporting of the occurrence of cerebral events or not was performed by the clinicians responsible for the care of the patients. A structured neurological examination with a CT would have increased the accuracy of the stroke diagnosis but would need to be assessed in the same manner for the entire cohort to yield equal groups and thus impossible to have as a clinical routine. But as it is a all-comers study for all TAVR patients treated in Sweden, this is not possible. The quality of the CT images had a variability because of the use of different types of hardware (computer tomographs) as well as various site-specific and patient-adapted study protocols (electric potential [kV]), resulting in different settings for image acquisition parameters. This has an impact on the accuracy of setting the threshold to discern between calcium and iodine contrast, which in turn influences the way the total calcium volume in the landing zone was calculated. However, this affects both study groups and, therefore, does not influence the comparison between the groups. Only a few patients had a CT examination, including an unenhanced series that allowed a formal calculation of calcium score according to Agatston. A prospective study design could benefit from having standard machine parameters and including a noncontrast series for a better objective quantification of calcium. One strength of the present study is that we used nationwide all-comers material. The cohort also came from an era where CPD was not used, and therefore, none of the 102 patients studied had CPD used for their procedure.

Conclusion

In this study, we could not find any patterns of calcium load on CT imaging that predisposes patients to periprocedural stroke and, consequently, were unable to identify a population at higher risk for a periprocedural stroke.

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Ethics Statement

The study followed the Declaration of Helsinki for studies in human subjects and was approved by the National Ethical Review Board in Sweden (registration number 2017/995 and EPN 2019/0584).

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Disclosure statement

H. Bjursten has served as a consultant for Boston Scientific and Edwards Lifesciences. N. Samano received honorarium from Edwards Lifesciences. A. Rück has served as a consultant and received research support from Boston Scientific and Edwards Lifesciences. S. James received proctoring fees from Medtronic. M. Settergren has served as a consultant and advisory boards for Boston Scientific, Edwards

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