Journal of Cardiovascular Computed Tomography 16 (2022) 215–221

Contents lists available at ScienceDirect

Journal of Cardiovascular Computed Tomography

journal homepage: www.JournalofCardiovascularCT.com

Clinical outcomes following transcatheter aortic valve implantation in patients with porcelain aorta

Masahiko Asami [a,1], Benedikt Bernhard [a,1], Caglayan Demirel [a], Taishi Okuno [a], Stefan Stortecky [a], Dik Heg [b], Daijiro Tomii [a], David Reineke [c], Fabien Praz [a], Jonas Lanz [a], Stephan Windecker [a], Christoph Gräni [a,2], Thomas Pilgrim [a,*,2]

[a] Department of Cardiology, Inselspital, Bern University Hospital, Bern, Switzerland
[b] Clinical Trials Unit, University of Bern, Bern, Switzerland
[c] Department of Cardiovascular Surgery, Inselspital, Bern University Hospital, Bern, Switzerland

ARTICLE INFO

Keywords:
Porcelain aorta
Aortic stenosis
Transcatheter aortic valve implantation
Computed tomography
Clinical outcomes

ABSTRACT

Background: Current guidelines favor transcatheter aortic valve implantation (TAVI) over surgical aortic valve replacement in patients with porcelain aorta (PAo). The clinical relevance of PAo in patients undergoing TAVI is however incompletely understood. The purpose of this study is to evaluate clinical outcome of patients with PAo undergoing TAVI.

Methods: Consecutive patients undergoing TAVI were enrolled in a prospective single-center registry. Presence of PAo was evaluated by ECG-gated multi-slice computed tomography prior to the intervention. The primary endpoint was disabling stroke.

Results: Among 2199 patients (mean age, 82.0 ± 6.3 years; 1135 females [51.6%]) undergoing TAVI between August 2007 and December 2019, 114 patients (5.2%) met VARC-2 criteria for PAo. Compared to individuals without PAo, patients with PAo were younger (79.4 ± 7.4 years vs. 82.1 ± 6.2 years; $p < 0.001$), had a lower left ventricular ejection fraction (51.8 ± 14.9% vs. 55.3 ± 14.2%; $p = 0.009$) and higher STS-PROM Scores (6.5 ± 4.3% vs. 4.9 ± 3.4%; $p < 0.001$). At 1 year, disabling stroke occurred more often in patients with PAo (7.2%) than in those without (3.0%) (HR_{adj}, 2.49; 95% CI, 1.12–5.55). The risk difference emerged within 30 days after TAVI (HR_{adj}, 3.70; 95% CI, 1.52–9.03), and was driven by a high PAo-associated risk of disabling stroke in patients with alternative access (HR_{adj}, 5.79; 95% CI, 1.38–24.3), not in those with transfemoral (HR_{adj}, 1.47; 95% CI 0.45–4.85).

Conclusions: TAVI patients with PAo had a more than three-fold increased risk of periprocedural disabling stroke compared to patients with no PAo. The difference was driven by a higher risk of stroke in patients treated by alternative access.

1. Introduction

Presence of porcelain aorta (PAo), defined as circumferential calcium deposition in the ascending aorta,[1] is considered a relative contraindication for surgical aortic valve replacement (SAVR) in patients with severe aortic stenosis (AS).[2] Transcatheter aortic valve implantation (TAVI) prevents the need for aortic cross-clamping and demonstrated feasible in patients with PAo.[3–5] Consequently, current European and American guidelines on valvular heart disease favor TAVI over SAVR in the presence of PAo.[6,7] However, available evidence of TAVI in patients with PAo is limited to cohorts modest in size, and anatomical determinants of clinical outcome are underappreciated in currently used risk scores.[8] Introduction of the transcatheter delivery system by retrograde approach interferes with PAo and may influence periprocedural outcomes. An antegrade, transapical approach foregoes crossing of the aortic arch with large-bore catheters, but comes at the expense of thoracotomy.

The aim of the present study was therefore to investigate the impact of PAo on rates of disabling stroke in patients undergoing TAVI.

* Corresponding author. Department of Cardiology, Inselspital, Bern University Hospital, CH-3010, Bern, Switzerland.
E-mail address: thomas.pilgrim@insel.ch (T. Pilgrim).
[1] Equally contributing first authors.
[2] Equally contributing last authors.

https://doi.org/10.1016/j.jcct.2021.10.006
Received 29 June 2021; Received in revised form 2 October 2021; Accepted 25 October 2021
Available online 28 October 2021

Abbreviation and acronyms

AS	aortic stenosis
ECG	electrocardiogram
MACCE	major adverse cardiac and cerebrovascular events
MSCT	multi-slice computed tomography
PAo	Porcelain aorta
SAVR	surgical aortic valve replacement
STS-PROM	Society of Thoracic Surgeons-Predicted Risk of Mortality
TAVI	transcatheter aortic valve implantation
TCEP	transcatheter cerebral embolic protection
VARC	Valve Academic Research Consortium

2. Methods

2.1. Study design and patient population

Consecutive patients undergoing TAVI at Bern University Hospital, Switzerland between August 2007 and December 2019 were prospectively enrolled into an institutional registry, which is a part of the Swiss TAVI registry (NCT01368250). The registry was approved by the local ethics committee and complied with the Declaration of Helsinki. Written informed consent for the intervention and the prospective follow-up was obtained from all subjects. Patients were eligible for the present analysis if they underwent electrocardiogram (ECG)-gated multi-slice computed tomography (MSCT) prior to the intervention. Patients not undergoing MSCT or with MSCT with poor image quality of the aortic window were excluded from the present analysis.

Decision for TAVI, prosthesis type, and size was made by consensus in a dedicated Heart Team, consisting of cardiac surgeons, interventional cardiologists, and cardiac imaging specialists. Default access route was transfemoral, but in patients with unfavorable vascular anatomy, alternative approaches were considered, including the transapical, subclavian, carotid, and transcaval access route. Post-procedural care included continuous rhythm monitoring, daily 12-lead ECG, and transthoracic echocardiography. Clinical follow-up was assessed at 30 days and one year after TAVI by standardized telephone interviews, documentation from referring physicians, and hospital discharge records. All adverse events were independently adjudicated by the local clinical events committee, according to the Valve Academic Research Consortium-2 (VARC-2) criteria.[1] Patients with PAo were compared to those without

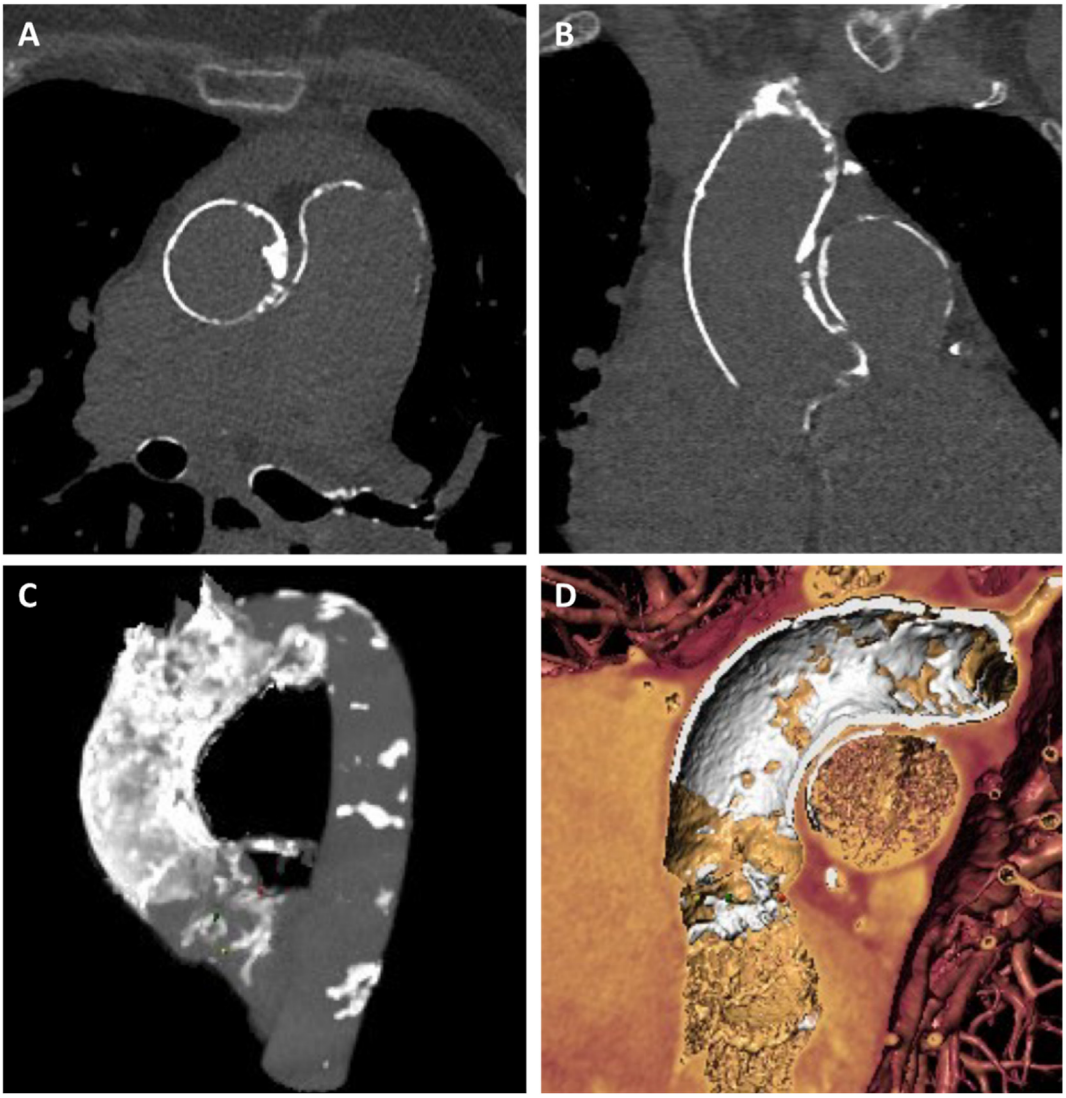

Fig. 1. Multi-slice native computed tomography images of porcelain aorta.
(A) Axial MPR, (B) coronal MPR, (C) MIP at LAO 45°, (D) Volume rendering. MIP = maximal intensity projection, MPR = multiplanar reformation.

Table 1
Baseline characteristics.

	Overall	No-porcelain Aorta	Porcelain Aorta	p Value
	N = 2199	N = 2085	N = 114	
Age (years)	82.0 ± 6.3	82.1 ± 6.2	79.4 ± 7.4	**<0.001**
Female gender, n (%)	1135 (51.6)	1081 (51.8)	54 (47.4)	0.39
Body mass index (kg/m^2)	26.6 ± 5.3	26.6 ± 5.2	26.4 ± 5.7	0.59
NYHA classification III or IV, n (%)	1501 (68.4)	1417 (68.1)	84 (73.7)	0.26
Past medical history				
Diabetes mellitus, n (%)	554 (25.2)	514 (24.7)	40 (35.1)	**0.02**
Hypercholesterolaemia, n (%)	1454 (66.2)	1367 (65.6)	87 (77.0)	**0.01**
History of arterial hypertension, n (%)	1839 (86.1)	1797 (86.2)	96 (84.2)	0.58
History of coronary artery disease, n (%)	1317 (59.9)	1229 (58.9)	88 (77.2)	**<0.001**
Previous stroke or TIA, n (%)	251 (11.4)	232 (11.1)	19 (16.7)	0.09
Peripheral vascular disease, n (%)	293 (13.3)	257 (12.3)	36 (31.6)	**<0.001**
Chronic obstructive pulmonary disease, n (%)	266 (12.1)	235 (11.3)	31 (27.4)	**<0.001**
Renal failure (eGFR <60 mL/min/1.73m^2), n (%)	1440 (65.6)	1371 (65.9)	69 (60.5)	0.27
Permanent pacemaker, n (%)	185 (8.4)	171 (8.2)	14 (12.3)	0.16
History of atrial fibrillation, n (%)	1470 (66.8)	1403 (67.3)	67 (58.8)	0.07
Risk assessment				
Logistic EuroSCORE (%)	15.3 ± 13.2	14.8 ± 12.9	23.5 ± 16.3	**<0.001**
STS-PROM score (%)	5.0 ± 3.4	4.9 ± 3.4	6.5 ± 4.3	**<0.001**
Echocardiographic assessment				
Aortic valve area (cm^2)	0.7 ± 0.3	0.7 ± 0.3	0.7 ± 0.3	0.38
Mean gradient (mmHg)	40.2 ± 17.4	40.2 ± 17.3	39.8 ± 19.8	0.83
Left ventricular ejection fraction (%)	55.2 ± 14.2	55.3 ± 14.2	51.8 ± 14.9	**0.009**

Counts with percentages (%) or means ± standard deviations are shown.
Abbreviations: eGFR = estimated glomerular filtration rate; NYHA = New York Heart Association; STS-PROM = Society of Thoracic Surgeons-Predicted Risk of Mortality; TIA = Transient ischemic attack.

PAo with regards to the prespecified primary endpoint disabling stroke. Secondary endpoints included all-cause and cardiovascular mortality, a composite of major adverse cardiac and cerebrovascular events (MACCE), life-threatening bleeding events, and major access site complications.

2.2. Multi-slice computed tomography image acquisition and analysis

MSCT was performed as previously described,[9] using either a Siemens Somatom Sensation Cardiac 64 scanner with a slice collimation of 64 × 0.75 mm (Siemens Healthcare, Erlangen, Germany) or a Siemens Somatom Definition Flash Dual-Source scanner (Siemens Healthcare, Erlangen, Germany). In brief, MSCT was conducted with a collimation of 128 × 0.6 mm, a gantry rotation time of 280–370 ms, a tube voltage of 100 or 120 kV, and tube current according to patient size (Siemens Medical Solutions, Inc., Forchheim, Germany). All CT images were transmitted to a dedicated software customized for valve analysis (3mensio Valves, version 9.0, 3mensio Medical Imaging BV, Bilthoven, the Netherlands) and were blindly assessed by a board-certificated cardiologist. If available, a systolic phase was selected to assess the aortic valve dimension. Validated methodology was used to quantify the calcium volume in the aortic valvar complex and left ventricular outflow tract by contrast scan (850-Hounsfield unit threshold).[10] PAo was defined according to the VARC-2 criteria as presence of severe atheromatous plaques or heavy circumferential calcification of the ascending aorta extending to the aortic arch,1 as assessed by non-contrast axial CT (Fig. 1).

2.3. Statistical analysis

Statistical analyses were performed using Stata 16.1 (StataCorp, College Station, TX, USA).

Means and standard deviation are provided to describe continuous variables, while frequencies and percentages are provided for categorical variables. T-tests were used to compare means of continuous variables between groups. Categorical variables were analyzed using Chi-Square-test. Kaplan Meier estimators comparing PAo vs. no PAo were applied to analyze time-to-event data. Hazard ratios (HR) and 95% confidence intervals (CI) are from Cox regression models, crude and also adjusted for age, history of stroke or transit ischemic attack, New York Heart Association classification III or IV, peripheral artery disease, arterial hypertension, left ventricular ejection fraction, STS-PROM score, and femoral access. The two-tailed significance level was set at $\alpha < 0.05$.

3. Results

3.1. Baseline characteristics

Among 2641 consecutive patients who underwent TAVI between August 2007 and December 2019, 2199 patients underwent MSCT and were considered for the present analysis. PAo according to VARC-2 criteria was documented in 114 individuals (5.2%). Demographic and clinical characteristics of the study participants are presented in Table 1. Patients with PAo were younger than patients with no PAo (79.4 ± 7.4 years vs. 82.1 ± 6.2 years; $p < 0.001$), and had higher STS-PROM scores (6.5 ± 4.3 vs. 4.9 ± 3.4; $p < 0.001$). Patients with PAo had lower left ventricular ejection fraction than patients without PAo (51.8 ± 14.9% vs. 55.3 ± 14.2%; $p = 0.009$), while transvalvular gradients were comparable between groups.

3.2. Imaging assessments and TAVI procedure

Imaging measurements as assessed by MSCT and procedural characteristics are summarized in Table 2. Patients with PAo had higher levels of calcium volume in the left ventricular outflow tract (31.4 ± 83.0 mm^3 vs. 14.1 ± 39.7 mm^3; $p < 0.001$) and the mitral valve (1083.3 ± 1936.1 mm^3 vs. 586.7 ± 1315.4 mm^3; $p = 0.001$) compared to patients with no PAo. Patients with PAo underwent TAVI by transfemoral access in 61.4% of cases, as compared to 92.6% of patients with no PAo ($p < 0.001$). The transapical route was the most common non-femoral approach in patients with PAo (84.1%). Furthermore, patients with PAo more frequently underwent concomitant percutaneous coronary intervention compared to patients with no PAo (14.9% vs. 7.6%; $p = 0.01$).

Table 2
Imaging and procedural characteristics.

	Overall	No-porcelain Aorta	Porcelain Aorta	p Value
	N = 2199	N = 2085	N = 114	
Imaging characteristics				
Mean aortic annulus diameter (mm)	24.1 ± 2.4	24.1 ± 2.4	24.0 ± 2.0	0.68
LVOT calcium volume (mm^3)	15.0 ± 43.2	14.1 ± 39.7	31.4 ± 83.0	**<0.001**
AVC calcium volume (mm^3)	315.9 ± 340.2	316.3 ± 344.9	309.1 ± 240.3	0.83
Mitral valve calcium volume (mm^3)	623.7 ± 1376.4	586.7 ± 1315.4	1083.3 ± 1936.1	**0.001**
Procedural characteristics				
Procedure time (min)	56.3 ± 32.8	55.5 ± 32.0	70.8 ± 41.7	**<0.001**
Hospital stay (days)	8.4 ± 4.7	8.3 ± 4.7	10.2 ± 5.7	**<0.001**
General anesthesia, n (%)	433 (19.7)	376 (18.1)	57 (50.0)	**<0.001**
Concomitant PCI, n (%)	176 (8.0)	159 (7.6)	17 (14.9)	**0.01**
Transcatheter cerebral embolic protection, n (%)	8 (0.4)	8 (0.4)	0 (0.0)	>0.999
Access route				
Transfemoral, n (%)	1999 (90.9)	1929 (92.6)	70 (61.4)	**<0.001**
Transapical, n (%)	173 (7.9)	136 (6.5)	37 (32.5)	**<0.001**
Subclavian, n (%)	15 (0.7)	8 (0.4)	7 (6.1)	**<0.001**
Carotid, n (%)	3 (0.1)	3 (0.1)	0 (0.0)	>0.999
Transcaval, n (%)	8 (0.4)	8 (0.4)	0 (0.0)	>0.999
Implanted device				0.40
Self-expanding, n (%)	1021 (50.2)	967 (50.3)	54 (48.6)	0.77
Balloon-expandable, n (%)	886 (43.6)	833 (43.3)	53 (47.7)	0.38
Mechanically-expanding, n (%)	127 (6.2)	123 (6.4)	4 (3.6)	0.31
Postprocedural specifications				
Post-TAVI AR moderate or severe, n (%)	145 (6.6)	137 (6.6)	8 (7.0)	0.85
Post-TAVI need for PPM within 30 days, n (%)	394 (17.9)	374 (17.9)	20 (17.5)	>0.999

Counts with percentages (%) or means ± standard deviations are shown. Abbreviations: AR = aortic regurgitation; AVC = aortic valvar complex; LVOT = left ventricular outflow tract; MSCT = multi slice computed tomography; PCI = Percutaneous coronary intervention; PPM = Permanent Pacemaker implantation; TAVI = Transcatheter aortic valve implantation.

Table 3
Short- and long-term clinical outcomes.

	No-porcelain Aorta	Porcelain Aorta	Crude hazard ratio		Adjusted hazard ratio	
	N = 2084	N = 114	HR (95% CI)	p Value	HR_{adj} (95% CI)	p Value
30 days follow-up						
All-cause death, n (%)	54 (2.6)	6 (5.3)	2.06 (0.89-4.78)	0.09	1.18 (0.47-2.94)	0.72
Cardiovascular death, n (%)	46 (2.2)	4 (3.6)	1.61 (0.58-4.47)	0.36	0.93 (0.31-2.76)	0.90
Disabling stroke, n (%)	36 (1.7)	7 (6.2)	3.59 (1.60-8.06)	0.002	3.70 (1.52-9.03)	**0.004**
Myocardial infarction, n (%)	15 (0.7)	1 (0.9)	1.22 (0.16-9.26)	0.85	0.80 (0.10-6.78)	0.84
MACCE, n (%)	83 (4.0)	10 (8.8)	2.23 (1.16-4.31)	0.02	1.52 (0.75-3.09)	0.25
Life-threatening bleeding event, n (%)	115 (5.5)	15 (13.2)	2.44 (1.42-4.17)	0.001	1.55 (0.86-2.79)	0.15
Major access site complications, n (%)	234 (11.3)	12 (10.6)	0.94 (0.53-1.68)	0.84	0.78 (0.43-1.43)	0.43
One-year follow-up						
All-cause death, n (%)	237 (11.5)	20 (17.8)	1.59 (1.01-2.50)	0.047	0.94 (0.57-1.53)	0.80
Cardiovascular death, n (%)	153 (7.5)	16 (14.6)	1.96 (1.17-3.28)	0.01	1.18 (0.67-2.06)	0.57
Disabling stroke, n (%)	61 (3.0)	8 (7.2)	2.48 (1.19-5.18)	0.02	2.49 (1.12-5.55)	**0.03**
Myocardial infarction, n (%)	35 (1.8)	1 (0.9)	0.53 (0.07-3.87)	0.53	0.53 (0.07-4.07)	0.54
MACCE, n (%)	221 (10.9)	23 (20.8)	2.00 (1.30-3.08)	0.002	1.39 (0.87-2.21)	0.17

Hazard ratios were determined by Cox regression for time-to-event data and adjusted for age, history of stroke or TIA, NYHA III or IV, peripheral artery disease, arterial hypertension, LVEF, STS-PROM score, and femoral access.
Abbreviations: MACCE = Major adverse cardiovascular and cerebrovascular events (composite of cardiovascular death, disabling stroke, and myocardial infarction); LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; STS-PROM = Society of Thoracic Surgeons-Predicted Risk of Mortality; TIA = Transient ischemic attack.

3.3. Clinical outcomes

Event rates for clinical outcomes are presented in Table 3. The incidence of disabling stroke at one year was higher in patients with PAo (n = 8, 7.2%) compared to those without PAo (n = 61, 3.0%) (HR_{adj}, 2.49; 95% CI, 1.12–5.55; p = 0.03) (Graphical abstract). This difference emerged within 30 days after TAVI (PAo: n = 7, 6.2% vs. no PAo: n = 36, 1.7%; HR_{adj}, 3.70; 95% CI, 1.52–9.03; p = 0.004) (Fig. 2A), and was driven by high stroke rates in patients with PAo undergoing TAVI by alternative access route, while no association of PAo to strokes was observed in patients treated by femoral access (Online Table 1). Clinical outcomes stratified by device types were provided in Online Table 2. In patients with PAo balloon-expandable valves were primarily used in patients with transapical access and have been associated with higher rates of stroke compared to those without. Furthermore, similar rates of disabling stroke were observed in patients treated with early versus newer generation devices (Online Table 3). In a multivariable model, presence of PAo was identified as an independent predictor of disabling stroke at one year (HR_{adj}, 2.47; 95% CI, 1.17–5.19; p = 0.02) (Table 4).

The one-year cardiovascular and all-cause mortality did not differ between groups (all-cause mortality: HR_{adj}, 0.94; 95% CI, 0.57–1.53; p = 0.80; cardiovascular mortality: HR_{adj}, 1.18; 95% CI, 0.67–2.06; p = 0.57) (Fig. 2B).

4. Discussion

The pertinent findings of the present analysis can be summarized as follows. PAo was documented in 5.2% of patients undergoing TAVI and

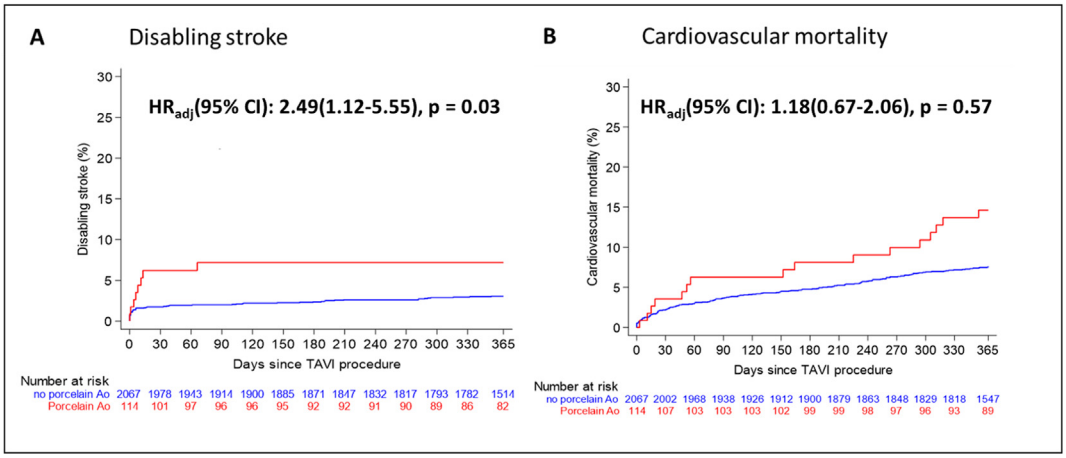

Fig. 2. Cumulative incidence of disabling stroke (A) and cardiovascular death (B) at one year after TAVI.
Adjusted Hazard ratios (HR_{adj}) and 95% confidence intervals (CI) from Cox regressions for time-to-event data, after adjusting for diabetes mellitus, age, history of stroke or TIA, NYHA III or IV, peripheral artery disease, arterial hypertension, LVEF, STS PROM score.

Table 4
Predictive factors for disabling stroke at one year.

Variables	Univariate analysis		Multivariable analysis		Final included variables	Multivariable analysis	
	HR (95% CI)	p Value	HR_{adj} (95% CI)	p Value		HR_{adj} (95% CI)	p Value
Porcelain Aorta	2.50 (1.20-5.23)	**0.02**	2.47 (1.11-5.53)	**0.03**	Porcelain Aorta	2.47 (1.17-5.19)	**0.02**
Age (years)	1.02 (0.98-1.06)	0.42	1.01 (0.96-1.05)	0.74	History of CVEs	1.81 (1.00-3.28)	**0.049**
History of CVEs	2.01 (1.12-3.61)	**0.02**	1.83 (1.00-3.36)	0.051	Post AR moderate/severe	3.07 (1.64-5.72)	**<0.001**
Post AR moderate/severe	3.11 (1.67-5.80)	**<0.001**	3.09 (1.64-5.83)	**<0.001**	Atrial fibrillation	1.64 (1.02-2.66)	**0.04**
Gender (female)	1.07 (0.67-1.72)	0.78	0.91 (0.54-1.54)	0.73			
Renal failure (eGFR<60)	1.13 (0.68-1.88)	0.63	1.02 (0.56-1.86)	0.95			
Body mass index (kg/cm^2)	0.98 (0.94-1.03)	0.40	1.01 (0.96-1.06)	0.75			
Coronary artery disease	0.93 (0.58-1.50)	0.77	0.88 (0.53-1.48)	0.64			
NYHA (III or IV)	1.32 (0.77-2.25)	0.32	1.29 (0.74-2.26)	0.37			
Peripheral artery disease	1.14 (0.58-2.23)	0.70	1.03 (0.49-2.17)	0.93			
Hypertension	0.73 (0.39-1.35)	0.31	0.75 (0.40-1.43)	0.38			
LVEF (%)	1.01 (0.99-1.03)	0.34	1.01 (1.00-1.03)	0.13			
STS-PROM score	1.02 (0.95-1.08)	0.61	1.00 (0.92-1.09)	0.93			
Femoral access	0.64 (0.32-1.28)	0.21	0.76 (0.35-1.65)	0.49			
Atrial fibrillation	1.69 (1.05-2.71)	**0.03**	1.67 (1.02-2.72)	**0.04**			

AR = aortic regurgitation; COPD = chronic obstructive pulmonary disease; CVEs = cerebrovascular events; eGFR = estimated glomerular filtration rate; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; STS-PROM = Society of Thoracic Surgeons-Predicted Risk of Mortality.
Final multivariable model retains covariates with $p < 0.2$.

was associated with an increased risk of periprocedural disabling stroke. The difference was driven by higher PAo-associated rates of disabling stroke in patients treated by alternative access route. PAo was identified as an independent predictor of disabling stroke at one year. Cardiovascular- and all-cause mortality, as well as rates of access site complications and life-threatening bleedings were comparable in patients with and without PAo at 30 days and one year.

Previous studies using various definitions of PAo indicated a prevalence among TAVI patients ranging from 4.2 to 19.0%,[3,11–15] and reported an incidence of stroke in these patients between 1.6 and 16.1%.[3,12–14] In an analysis of 52 matched pairs of patients with severe AS and PAo, TAVI was associated with a borderline lower periprocedural mortality compared to SAVR, while rates of stroke were comparable.[4] The largest prospective cohort study in patients with PAo undergoing TAVI included 147 patients (82% with transfemoral access) and documented a significantly higher rate of myocardial ischemia and a trend towards an increased risk of periprocedural stroke in patients with as compared to those without PAo.[15] The study was limited to in-hospital outcomes, used no standardized definition of PAo, and clinical events were not independently adjudicated. In the present study, transfemoral access was performed in 61% of patients with PAo. While we found no difference in myocardial infarction in patients with vs. without PAo, we documented a significantly increased risk of disabling stroke in patients with PAo.

Small case series advocated for a transapical approach as a default strategy for TAVI in patients with PAo based on the rationale to forego manipulation with the delivery catheter in the calcified aorta.[3] Intriguingly, in our cohort, rates of disabling stroke were particularly high among patients treated by transapical or transsubclavian access, while rates of disabling stroke in PAo patients treated by transfemoral route were comparable to the rates in patients without PAo. Given the modest numbers and the non-randomized treatment allocation, these results must be interpreted with caution. Data from the PARTNER 2 trial showed disabling stroke at 30 days in 2.3% of patients treated by transfemoral route as compared to 6.0% of patients treated by transthoracic route.[16] In contrast, propensity score matched analyses from the PARTNER I trial and the National Inpatient Sample in the United States indicated comparable risks of stroke in patients treated by transfemoral vs. transapical approach, respectively.[17,18] In line, there was no difference in stroke among patients undergoing TAVI as a function of transfemoral, transapical or transsubclavian approach in the FRANCE 2 registry.[19] Our findings challenge the notion, that a transapical approach is preferred over transfemoral access for TAVI in patients with PAo. Localization, extent, and distribution of calcification in the ascending aorta and the

aortic arch warrant an informed decision on the preferred access route on an individual basis. In the present analysis, moderate or greater post-TAVI aortic regurgitation was identified as a strong predictor of disabling stroke. This finding may be confounded by the association of left ventricular outflow tract calcification with both aortic regurgitation and stroke. In addition, balloon-expandable valves have been associated with higher rates of stroke compared to self-expanding valves and were primarily used in patients with transapical access.

The risk of stroke continues to be of relevant concern in TAVI patients, in particular in those with PAo. Strategies to mitigate the risk of stroke include the use of transcatheter cerebral embolic protection (TCEP) devices. Previous studies indicated that the use of TCEP devices was independently associated with a lower risk of ischemic strokes after TAVI.[20–22] Two ongoing prospective randomized outcome trials (NCT02895737 and NCT02536196) are anticipated to provide concluding evidence on the effectiveness of TCEP. Nevertheless, careful patient selection for implantation of TCEP devices remains crucial.[23] The present study provides evidence that patients with PAo have an increased risk of stroke compared to patients with no PAo, and may therefore particularly benefit from such devices.

4.1. Study limitations

The findings of our analysis have to be interpreted in light of several limitations. Our analysis is based on a relatively modest number of patients from a single center. However, our prospective registry is considerably larger than the cohorts of previous analyses and adheres to high standards of data quality in terms of data collection, standardized follow-up, and independent event adjudication at regular time intervals. Furthermore, exclusion of patients who did not undergo MSCT might lead to sample bias, as this might apply particularly to patients with indications for urgent and emergency TAVI. Additionally, our endpoints are limited to events with high impact on the patient's well-being. Occult strokes, also affecting the clinical outcome, were not systematically assessed. Confounders, such as the higher rate of balloon-expandable valves in patients undergoing transapical TAVI might have contributed to the worse outcomes in these patients, since balloon-expandable valves have been associated with a higher risk of stroke.[24] Randomized comparison of different therapeutic approaches in patients with PAo like access routes or prostheses types was beyond the scope of our study and could be addressed in future studies.

4.2. Conclusions and clinical implications

Patients with PAo are more likely to suffer from disabling stroke after TAVI, while presence of PAo was not associated with cardiovascular- and all-cause mortality within one year. Our findings challenge the notion that a transapical approach should be preferred in patients with PAo.

Funding

None.

Disclosures

Dr. Windecker reports research and educational grants to the institution from Abbott, Amgen, BMS, Bayer, Boston Scientific, Biotronik, Cardinal Health, CardioValve, CSL Behring, Daiichi Sankyo, Edwards Lifesciences, Johnson&Johnson, Medtronic, Querbet, Polares, Sanofi, Terumo, Sinomed. He serves as unpaid advisory board member and/or unpaid member of the steering/executive group of trials funded by Abbott, Abiomed, Amgen, Astra Zeneca, BMS, Boston Scientific, Biotronik, Cardiovalve, Edwards Lifesciences, MedAlliance, Medtronic, Novartis, Polares, Sinomed, V-Wave and Xeltis, but has not received personal payments by pharmaceutical companies or device manufacturers. He is also member of the steering/executive committee group of several investigated-initiated trials that receive funding by industry without impact on his personal remuneration. He is an unpaid member of the Pfizer Research Award selection committee in Switzerland. Dr. Stortecky reports having received research grants to the institution by Edwards Lifesciences, Medtronic, Abbott, and Boston Scientific, and speaker fees from Boston Scientific, Teleflex, and BTG. Dr. Praz has received travel expenses from Edwards Lifesciences, Abbott Medical, and Polares Medical. Dr. Pilgrim reports having received research grants to the institution from Boston Scientific, Biotronik, and Edwards Lifesciences and speaker fees from Boston Scientific and Biotronik, and consultancy from HighLife SAS; he is a proctor for Boston Scientific and Medtronic. All other authors have no relationships relevant to the contents of this article to disclose.

Acknowledgements

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcct.2021.10.006.

References

1. Kappetein AP, Head SJ, Généreux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. *J Am Coll Cardiol*. 2012;60:1438–1454.
2. Carrel T. Should the porcelain aorta be revisited in the era of transcatheter aortic valve replacement? *Eur J Cardio Thorac Surg*. 2019;55:1010–1011.
3. Useini D, Haldenwang P, Schlömicher M, et al. Mid-term outcomes after transapical and transfemoral transcatheter aortic valve implantation for aortic stenosis and porcelain aorta with a systematic review of transfemoral versus transapical approach. *Thorac Cardiovasc Surg*. 2020;68:623–632.
4. Ramirez-Del Val F, Hirji SA, Yammine M, et al. Effectiveness and safety of transcatheter aortic valve implantation for aortic stenosis in patients with "porcelain" aorta. *Am J Cardiol*. 2018;121:62–68.
5. Zahn R, Schiele R, Gerckens U, et al. Transcatheter aortic valve implantation in patients with "porcelain" aorta (from a Multicenter Real World Registry). *Am J Cardiol*. 2013;111:602–608.
6. Writing Committee Members, Otto CM, Nishimura RA, et al. ACC/AHA guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American heart association Joint committee on clinical Practice guidelines. *J Am Coll Cardiol*. 2020;77:450–500, 2021.
7. Baumgartner H, Falk V, Bax JJ, et al. ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J*. 2017;38:2739–2791, 2017.
8. Thourani VH, Suri RM, Gunter RL, et al. Contemporary real-world outcomes of surgical aortic valve replacement in 141,905 low-risk, intermediate-risk, and high-risk patients. *Ann Thorac Surg*. 2015;99:55–61.
9. Okuno T, Asami M, Khan F, et al. Does isolated mitral annular calcification in the absence of mitral valve disease affect clinical outcomes after transcatheter aortic valve replacement? *Eur Heart J Cardiovasc Imag*. 2020;21:522–532.
10. Jilaihawi H, Makkar RR, Kashif M, et al. A revised methodology for aortic-valvar complex calcium quantification for transcatheter aortic valve implantation. *Eur Heart J Cardiovasc Imag*. 2014;15:1324–1332.
11. Nakasu A, Greason KL, Nkomo VT, et al. Transcatheter aortic valve insertion in patients with hostile ascending aorta calcification. *J Thorac Cardiovasc Surg*. 2018;156:1028–1034.
12. Buz S, Pasic M, Unbehaun A, et al. Trans-apical aortic valve implantation in patients with severe calcification of the ascending aorta. *Eur J Cardio Thorac Surg*. 2011;40:463–468.

13. Kempfert J, Van Linden A, Linke A, et al. Transapical aortic valve implantation: therapy of choice for patients with aortic stenosis and porcelain aorta? *Ann Thorac Surg*. 2010;90:1457–1461.
14. Rodés-Cabau J, Webb JG, Cheung A, et al. Transcatheter aortic valve implantation for the treatment of severe symptomatic aortic stenosis in patients at very high or prohibitive surgical risk: acute and late outcomes of the multicenter Canadian experience. *J Am Coll Cardiol*. 2010;55:1080–1090.
15. Zahn R, Schiele R, Gerckens U, et al. Transcatheter aortic valve implantation in patients with "porcelain" aorta (from a Multicenter Real World Registry). *Am J Cardiol*. 2013;111:602–608.
16. Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med*. 2010;363:1597–1607.
17. Blackstone EH, Suri RM, Rajeswaran J, et al. Propensity-matched comparisons of clinical outcomes after transapical or transfemoral transcatheter aortic valve replacement: a placement of aortic transcatheter valves (PARTNER)-I trial substudy. *Circulation*. 2015;131:1989–2000.
18. Kumar N, Khera R, Fonarow GC, Bhatt DL. Comparison of outcomes of transfemoral versus transapical approach for transcatheter aortic valve implantation. *Am J Cardiol*. 2018;122:1520–1526.
19. Gilard M, Eltchaninoff H, Iung B, et al. Registry of transcatheter aortic-valve implantation in high-risk patients. *N Engl J Med*. 2012;366:1705–1715.
20. Seeger J, Kapadia SR, Kodali S, et al. Rate of peri-procedural stroke observed with cerebral embolic protection during transcatheter aortic valve replacement: a patient-level propensity-matched analysis. *Eur Heart J*. 2019;40:1334–1340.
21. Megaly M, Sorajja P, Cavalcante JL, et al. Ischemic stroke with cerebral protection system during transcatheter aortic valve replacement. *JACC Cardiovasc Interv*. 2020;13:2149–2155.
22. Giustino G, Sorrentino S, Mehran R, Faggioni M, Dangas G. Cerebral embolic protection during TAVR: a clinical event meta-analysis. *J Am Coll Cardiol*. 2017;69:465–466.
23. Bagur R, Solo K, Alghofaili S, et al. Cerebral embolic protection devices during transcatheter aortic valve implantation: systematic review and meta-analysis. *Stroke*. 2017;48:1306–1315.
24. Thiele H, Kurz T, Feistritzer HJ, et al. Comparison of newer generation self-expandable vs. balloon-expandable valves in transcatheter aortic valve implantation: the randomized SOLVE-TAVI trial. *Eur Heart J*. 2020;41:1890–1899.