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Predictors of paravalvular regurgitation and permanent pacemaker implantation after TAVR with a next-generation self-expanding device

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Abstract

Aims To identify predictors of paravalvular regurgitation (PVR) and permanent pacemaker implantation (PPI) following TAVR with a next-generation self-expanding device.

Methods and results Device landing zone (DLZ) calcification, angiographic implantation depth, and baseline and procedural characteristics were analyzed in 212 patients being treated with the ACURATE *neo* aortic bioprosthesis. PVR was none/trace in 57.1% and ≥ mild in 42.9% (37% mild, 6% moderate). DLZ calcification (705 (IQR 240–624) vs. 382 (IQR 240–624) mm^3; $P < 0.001$) as well as absolute calcium asymmetry (233 ± 159 vs. 151 ± 151 mm^3; $P < 0.001$) was significantly higher in patients with PVR ≥ mild. On multivariate analysis, calcification of the aortic valve cusps (AVC) > 410.6 mm^3 was independently associated with PVR ≥ mild. PPI rate was 10.3% ($n = 20$). Patients with and without need for PPI had similar total DLZ calcium volume (740 (IQR 378–920) vs. 536 (IQR 315–822) mm^3; $P = 0.263$), but exhibited different calcium distribution patterns: LVOT calcium > 41.4 mm^3 in the sector below the left coronary cusp ($LVOT_{LC}$) was associated with increased PPI risk (26.9 vs. 7.7%; $P = 0.008$).

Conclusions The quantity of AVC calcium predicts residual PVR. Multivariable analysis identified $LVOT_{LC}$ calcium, preexisting RBBB, and age > 82.7 years as independent predictors of PPI. Based on these risk factors, a patient's individual PPI risk can be stratified ranging from 3.8 to 100%.

Keyword Transcatheter aortic valve replacement · Permanent pacemaker implantation · Paravalvular regurgitation · Prediction of risk · ACURATE *neo* TF · Calcium distribution

Introduction

Transcatheter aortic valve replacement (TAVR) has become the standard of care for the treatment of severe aortic stenosis in patients with a higher risk for conventional surgery [1]. Recently, first studies proved non-inferiority of interventional treatment compared to surgical aortic valve replacement (SAVR) in patients with intermediate risk [2–4].

This rapid extension of interventional therapy for aortic stenosis is fostered by significant improvements in the development of next-generation transcatheter devices resulting in lower rates of periprocedural complications such as new-onset conduction disturbances requiring permanent pacemaker implantation (PPI), paravalvular regurgitation (PVR), and vascular complications [5].

The next-generation self-expanding ACURATE *neo* (Symetis SA, Ecublens, Switzerland) transcatheter heart valve (THV) features a novel X-shaped stent with

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supra-annular located leaflets and an outer and inner pericardial anti-PVR skirt to provide optimal sealing (Supplementary Fig. 1). Flexible stabilization arches and an upper crown allow supra-annular anchoring and capture the native leaflets. Compared to other THV, the ACURATE *neo* exerts only intermediate radial force and only protrudes minimally into the left ventricular outflow tract (LVOT) to avoid excessive PPI. The THV is implanted in a top–down manner and can be implanted without rapid ventricular pacing [6]. In the context of the current extension of TAVR indication to lower risk populations, it is crucial to determine contributing factors of periprocedural complications to further improve patients' outcomes.

Extent and distribution of device landing zone calcium in conjunction with device specific features have been shown to be important contributing factors of annulus-associated complications such as PVR and PPI for several THV [7–11]. However, little is known about the predictive value for complications of these anatomical and device-related factors for the ACURATE *neo* THV.

The aim of this study was to determine predictors of PPI and PVR after TAVR with the ACURATE *neo* THV with a focus on calcification pattern within the device landing zone.

Methods

Study design

212 patients with severe aortic stenosis undergoing transfemoral TAVR with an ACURATE *neo* THV (Symetis SA, Ecublens, Switzerland) at two high-volume centers between March 2014 and February 2017 were retrospectively analyzed. Patients were considered not suitable for surgical aortic valve replacement by the local interdisciplinary heart team and consented for the procedure and data acquisition. All patients underwent a standardized pre-procedural work-up including echocardiography, coronary angiography, and contrast-enhanced multislice computed tomography (MSCT). The implantation procedure has been described previously [6]. Clinical and procedural data were collected in a dedicated database and analyzed in accordance with Valve Academic Research Consortium (VARC) II criteria [12]. Primary endpoints were (1) residual PVR ≥ mild and (2) new permanent pacemaker implantation. Residual PVR was evaluated pre-discharge by transthoracic echocardiography using a multiparametric approach [12] and classified by two independent observers as none, trace, mild, moderate, or severe who were unaware of results of CT assessment.

MSCT data analysis

Quantification of device landing zone calcification was based on preoperative MSCT images routinely acquired for procedure planning on a dual source CT scanner (Siemens) with a slice thickness of 1 mm and 40 ml of intravenously administered contrast agent. The aortic annulus was defined as a virtual basal plane at the nadirs of the valve cusps. The device landing zone was defined as the composite of the aortic valve cusp (AVC) region and the LVOT. Thereby, the AVC region was defined as the area above the aortic annulus plane, measured from the basal plane to the lower coronary ostium. The LVOT was defined as the area below the aortic annulus plane, measured from the basal plane 10 mm into the left ventricle. The calcium volume in the THV landing zone was measured using an automated volume-scoring tool (3mensio Medical Imaging). Voxels above an empiric base threshold of 500 Hounsfield units (HU) were considered 'calcium'. If necessary, the threshold was adjusted manually depending on the patient's individual density of luminal contrast medium. Both AVC and LVOT were subdivided into three regions of interest along the aortic valve cusps (Fig. 1). The method has been validated by our group previously [10].

The cover index was calculated using the formula (THV area—annulus area)/THV area × 100 to assess relative sizing of the THV in relation with the annulus. Eccentricity of the aortic annulus was evaluated with an index calculated as 1 − (minimum diameter/maximum diameter). Asymmetry of calcium distribution was calculated as maximum absolute difference in calcium volume between leaflet sectors for both AVC and LVOT as well as for the complete DLZ.

THV implantation depth

The THV implantation depth was derived from post-implantation aortic root angiography and expressed as absolute implantation depth and as a ratio of ventricular part of the stent frame (measured from lower crown to the native aortic annulus) in relation with total stent frame length, as described previously [10]. Measurements were performed with OsiriX version 5.9 (Pixmeo SARL, Geneva, Switzerland).

Statistics

Categorical variables are reported as frequencies and percentages, whereas continuous variables are presented as mean ± SD. Depending on data distribution, Student *t* test or Mann–Whitney *U* test were applied. Categorical variables were analyzed with the Fisher exact test. The Kruskal–Wallis test was used to compare patients with

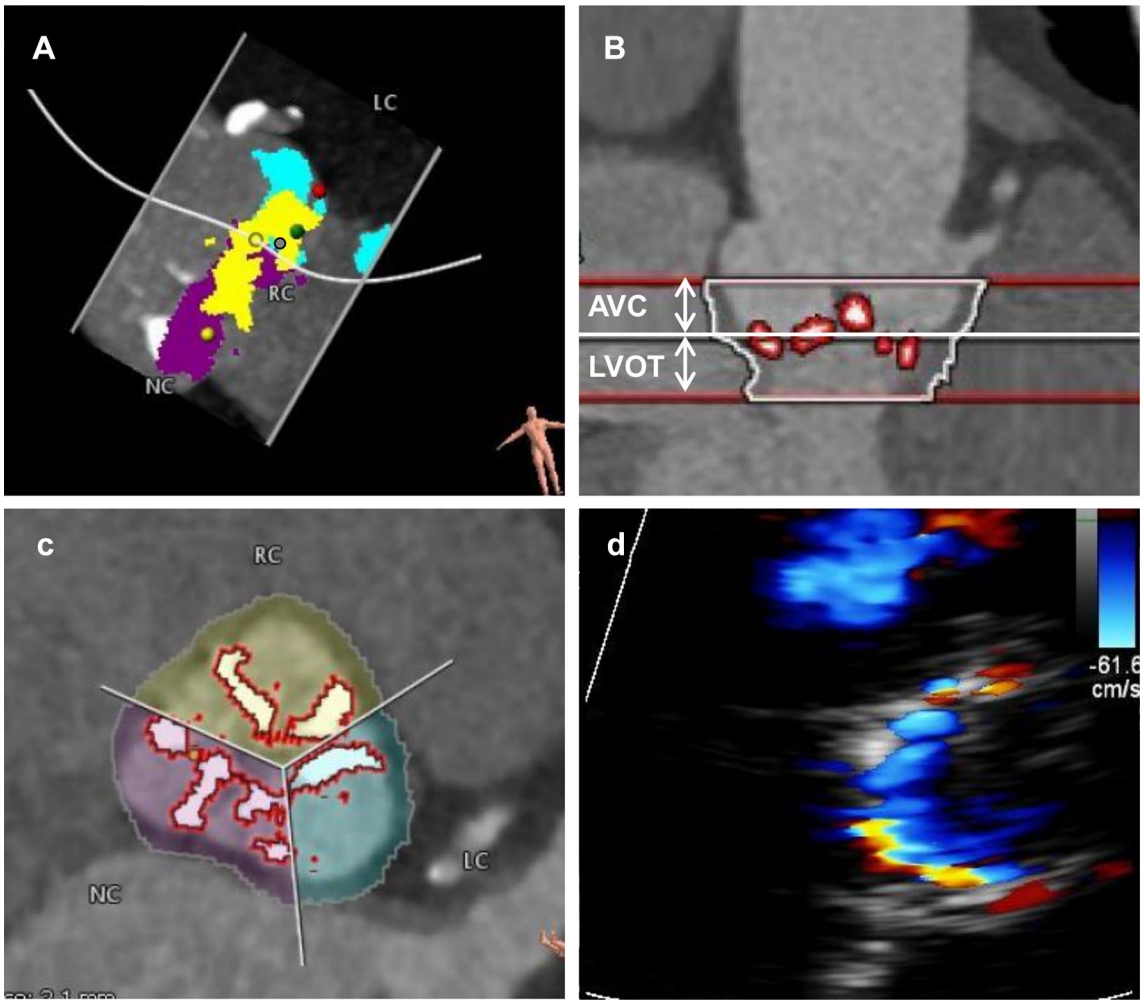

Fig. 1 Calcium quantification and PVR. **a** Three-dimensional reconstruction of total device landing zone calcium according to leaflet sector. **b** Calcium quantification of the aortic valve cusp (AVC) region and the LVOT. **c** Calcium quantification by leaflet sector at AVC level. **d** Moderate PVR in transthoracic parasternal short-axis view

different degrees of PVR. Due to substantially different group sizes of patients with and without need for PPI, differences in baseline variables were analyzed by calculating standardized mean differences (*d* values). Receiver-operating characteristic curve analysis was used to calculate best discriminatory thresholds in the calcification analysis and for continuous PPI risk factors. Two-sided *P* values < 0.05 were considered statistically significant. Multivariate logistic regression analysis was performed to investigate the independent influence of possible variables on PVR $\geq$ mild and PPI, respectively. Patients were binary grouped into patients with PVR none/trace or $\geq$ mild for logistic regression analysis.

All statistical analyses were performed using IBM SPSS Statistics version 22 (IBM, Armonk, New York).

Results

Patient population

212 patients treated with an ACURATE *neo* THV were included into the analysis. Baseline patient characteristics are presented in Table 1. Mean age was 82.1 ± 5.2 years, 74% were female, and patients had an intermediate to high risk for surgery (logistic EuroSCORE I 14.4 ± 10.4%) and relevant comorbidities. ACURATE *neo* THV in the sizes S (23 mm), M (25 mm), and L (27 mm) were implanted in 36, 45, and 19% of the patients, respectively. Pre-dilation was performed in 93%. In-hospital-mortality was 1.4%.

Table 1 Patient demographics, ECG findings, and calcium volume of patients with and without need for PPI

	All ($n=212$)	No PPI ($n=174$)	PPI ($n=20$)	*d* value
	Mean/median	Mean/median	Mean/median	
Demographics				
Age (years)	82.1 ± 5.2	81.8 ± 5.2	84.6 ± 4.8	0.56
Female sex	156 (73.6)	132 (75.9)	13 (65.0)	0.24
BSA (m^2)	1.79 ± 0.19	1.79 ± 0.19	1.85 ± 0.18	0.31
BMI (kg/m^2)	27.6 ± 5.5	27.4 ± 5.1	28.9 ± 5.4	0.29
Logistic EuroSCORE I (%)	14.3 ± 10.4	13.9 ± 9.6	14.8 ± 8.6	0.10
Comorbidities				
CAD	136 (64)	109 (62.6)	12 (60.0)	0.05
Previous cardiac surgery	21 (10)	13 (7.5)	2 (10.0)	0.09
COPD	33 (16)	28 (16.1)	4 (20.0)	0.10
PAD	33 (16)	28 (16.1)	1 (5.0)	0.37
Diabetes mellitus	69 (33)	54 (31.0)	10 (50.0)	0.39
Hypertension	197 (93)	159 (91.4)	20 (100.0)	0.43
Pacemaker at baseline	18 (8.5)	n/a	n/a	–
ECG findings				
Atrial fibrillation	72 (34.0)	58 (33.3)	7 (35.0)	0.04
AVB grade I	14 (7.2)	10 (5.7)	4 (20.0)	0.44
RBBB	14 (7.2)	9 (5.2)	5 (25.0)	0.58
LBBB	15 (7.7)	15 (8.6)	0 (0.0)	0.43
LAHB	8 (4.1)	8 (4.6)	0 (0.0)	0.31
MSCT measurements				
Diameter (mm)	24.3 ± 5.7	24.3 ± 6.2	24.2 ± 2.5	0.04
Area (mm^2)	425.3 ± 79.7	424.6 ± 79.9	424.3 ± 83.5	0.00
Perimeter (mm)	74.4 ± 6.5	74.3 ± 6.4	75.6 ± 6.9	0.19
Eccentricity Index	0.2 ± 0.1	0.2 ± 0.1	0.2 ± 0.1	0.14
Calcium quantification				
AVC calcium volume (mm^3)	512 (295–723)	502 (302–743)	555 (315–367)	0.14
NCC	212 (121–342)	210 (124–342)	264 (132–456)	0.19
RCC	128 (59–219)	130 (58–239)	106 (70–197)	0.05
LCC	130 (60–230)	128 (58–225)	149 (79–248)	0.20
LVOT calcium volume (mm^3)	18 (2–75)	14 (2–64)	30 (5-159)	0.24
$LVOT_{NC}$	3 (0–32)	2 (0–30)	3 (0–26)	0.01
$LVOT_{RC}$	0 (0–5)	0 (0–5)	0 (0–6)	0.12
$LVOT_{LC}$	3 (0–14)	2 (0–11)	5 (0-108)	0.36
Total DLZ calcium volume (mm^3)	552 (326–829)	536 (315–822)	740 (376–920)	0.18
Procedural details				
Pre-dilation	194 (93.3)	158 (93)	19 (95.0)	0.09
Post-dilation	77 (36.8)	61 (36)	7 (35.0)	0.01
Implantation depth				
Absolute (mm)	5.7 ± 2.0	5.8 ± 2.0	5.3 ± 1.9	0.24
Relative (%)	30.7 ± 10.7	31.3 ± 10.6	28.7 ± 10.0	0.25
Cover Index	11.4 ± 11.1	12.0 ± 10.5	9.5 ± 14.7	0.20

Values are presented as mean ± SD, median (IQR) or *n* (%)

AVB atrioventricular block, *AVC* aortic valve cusps, *BMA* body mass index, *BSA* body surface area, *CAD* coronary artery disease, *COPD* chronic obstructive pulmonary disease, *DLZ* device landing zone, *LAHB* left anterior hemiblock, *LBBB* left bundle branch block, *LCC* left coronary cusp, *LVOT* left ventricular outflow tract, *MSCT* multislice computed tomography, *NCC* non-coronary cusp, *PAD* peripheral artery disease, *PPI* permanent pacemaker implantation, *RBBB* right bundle branch block, *RCC* right coronary cusp

Residual paravalvular regurgitation

Residual PVR at discharge was classified as none in 24.5%, trace in 32.5%, mild in 36.8%, and moderate in 6.1% of patients (Fig. 2a). No patient exhibited severe PVR. Degree of PVR was significantly related to AVC, LVOT and total DLZ calcification. Total device landing zone calcium volume was 389 (IQR 207–699) mm^3, 371 (IQR 248–610) mm^3, 690 (IQR 508–943) mm^3, and 777 (555–1486) mm^3 in patients with none, trace, mild, and moderate PVR, respectively ($P < 0.001$; Fig. 2b). The rate of PVR ≥ mild was 7.5, 45, 55, and 64% in the four quartiles of total DLZ calcium volume ($P < 0.001$). Patients were dichotomized in patients with none/trace and PVR ≥ mild for further analysis. Calcium volume in all regions was significantly lower comparing patients with none/trace PVR to patients with PVR ≥ mild (AVC 370 (IQR 209–587) vs. 619 (IQR 483–905) mm^3; LVOT 8 (IQR 0–48) vs. 30 (IQR 8 -141) mm^3; and total DLZ 382 (240–624) vs. 705 (512–958) mm^3; Fig. 2c). In addition, absolute asymmetry was significantly higher in patients with PVR ≥ mild in all examined regions (Table 2). There was no association of PVR ≥ mild with device implantation depth (range 1.2–10.9 mm; $P = 0.941$), cover index ($P = 0.259$), or eccentricity of the aortic annulus ($P = 0.062$). Further ROC-curve analysis was performed to identify best cut-off values for AVC, LVOT, and total DLZ calcium volume as well as sector asymmetry to predict PVR ≥ mild, as presented in supplementary Fig. 2.

In multivariate regression analysis including AVC and LVOT calcification, AVC and LVOT absolute asymmetry, and cover index to control for relative sizing, only AVC calcium > 410.6 mm^3 (OR 6.9, CI 3.0–15.8; $P < 0.001$) emerged as independent predictor of PVR ≥ mild (Supplementary table 1A). There were no significant differences in PVR for the different sizes of the device.

Predictors of permanent pacemaker implantation

After exclusion of patients with pre-existing pacemaker ($n = 18$), 194 patients remained for further analysis. PPI was performed in 10.3% of patients ($n = 20$). The baseline characteristics of patients with and without new-onset conduction disturbances requiring PPI were similar regarding sex, logistic EuroSCORE I, and comorbidities (Table 1). However, patients requiring PPI were significantly older (84.6 ± 4.8 vs. 81.8 ± 5.2 years; $P = 0.017$). Pre-existing

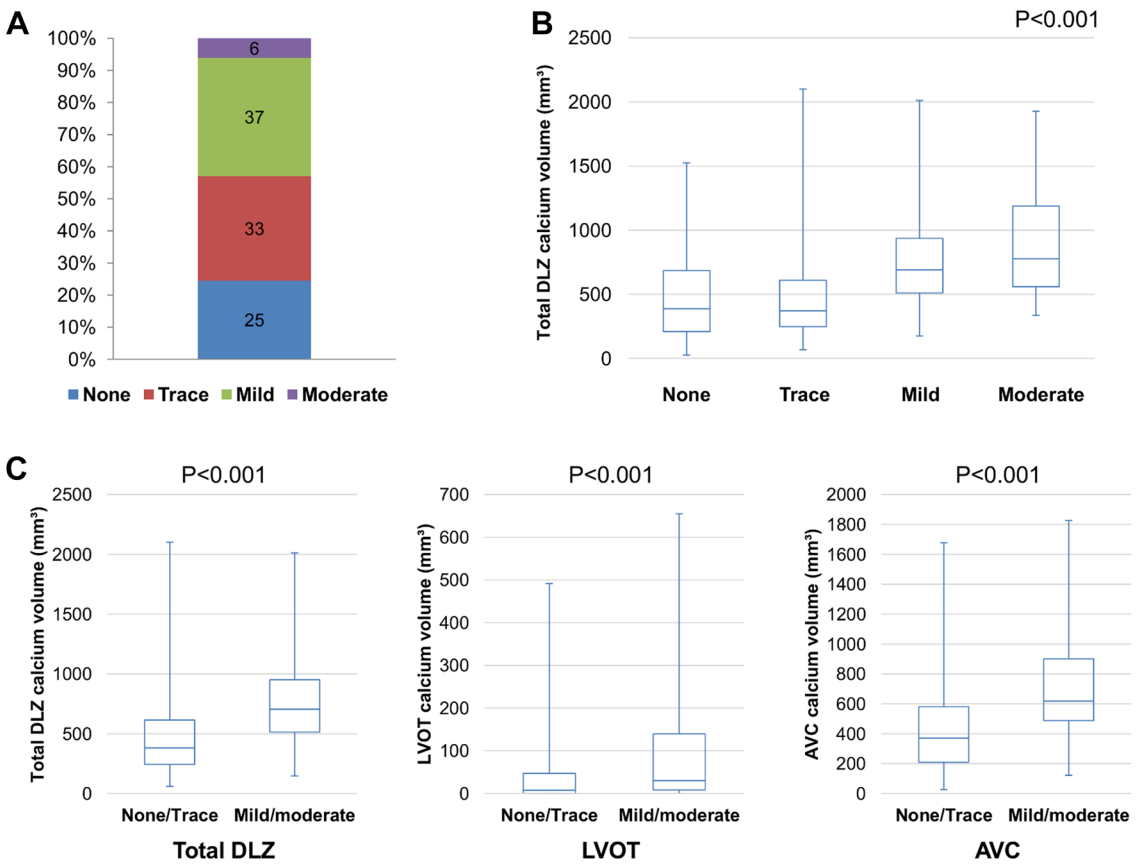

Fig. 2 Residual paravalvular regurgitation and calcium volume. **a** Degree of PVR; **b** Degree of PVR increases with calcium volume ($P < 0.001$); **c** Calcium volume according to residual PVR by sector of interest

Table 2 MSCT measurements and implantation depth in patients with PVR none/trace and ≥ mild

	PVR none/trace ($n=93$) Mean/median	PVR ≥ mild ($n=57$) Mean/median	P value
AVC calcium volume (mm^3)	370 (209–587)	619 (483–905)	< 0.001
NCC	161 (88–293)	255 (183–426)	< 0.001
RCC	96 (40–174)	174 (96–280)	< 0.001
LCC	87 (41–167)	177 (111–274)	< 0.001
LVOT calcium volume (mm^3)	8 (0–48)	30 (8–141)	< 0.001
$LVOT_{NC}$	1 (0–14)	11 (0–62)	< 0.001
$LVOT_{RC}$	0 (0–4)	0 (0–16)	0.070
$LVOT_{LC}$	2 (0–11)	4 (0–22)	0.062
Total DLZ calcium volume (mm^3)	382 (240–624)	705 (512–958)	< 0.001
Absolute asymmetry (mm^3)			
AVC asymmetry	135.5 ± 107.3	202.0 ± 146.8	< 0.001
LVOT asymmetry	31.2 ± 56.3	57.8 ± 83.5	< 0.001
DLZ asymmetry	151.0 ± 115.1	232.7 ± 159.3	< 0.001
Implantation depth			
Absolute (mm)	5.7 ± 2.0	5.7 ± 1.9	0.948
Relative (%)	30.7 ± 11.0	30.8 ± 10.2	0.941
Eccentricity Index	0.20 ± 0.08	0.20 ± 0.06	0.062
Cover Index	12.30 ± 10.91	10.31 ± 11.20	0.259

Values are presented as mean ± SD or median (IQR). Abbreviations as in Table 1

RBBB (25 vs. 5%; $P=0.008$) and first degree atrioventricular block (AVB; 20 vs. 6%; $P=0.042$) were more frequent in patients eventually requiring PPI. Indication for PPI was complete atrioventricular block (AVB) in the majority of cases ($n=18$), and symptomatic bradyarrhythmia in two patients.

The total DLZ calcium volume as well as the calcification of the three cusps was similar in patients with and without need for PPI (Total DLZ calcium: 740 (IQR 376–740) vs. 536 (IQR 315–822) mm^3, $P=0.263$; Table 1). However, further evaluation of calcification pattern using ROC-curve analysis identified an $LVOT_{LC}$ calcium volume above a threshold of 41.4 mm^3 as a risk factor for PPI (PPI rates above and below the threshold: 26.9 vs. 7.7%, $P=0.008$). Calcification of all other examined sectors was not predictive. In addition, absolute asymmetry was not a predictor of PPI. However, asymmetry between the sectors $LVOT_{LC}$ (high burden) and $LVOT_{NC}$ (low burden) calcium was significantly higher in patients requiring PPI (15.6 ± 76 vs. − 5.4 ± 62 mm^3; $P=0.012$).

THV implantation depth was similar in patients with and without need for PPI (5.3 ± 1.9 vs. 5.8 ± 2.0 mm; $P=0.332$), as was the cover index (9.5 ± 14.7 vs. 12.0 ± 10.5; $P=0.334$), and annular eccentricity (0.21 ± 0.06 vs. 0.20 ± 0.07; $P=0.581$). The rates of pre- and post-dilation were similar in both groups (Table 1).

In multivariate analysis (Supplementary table 1B) including pre-existing RBBB, pre-existing first degree AVB, $LVOT_{LC}$ calcium volume > 41.4 mm^3, and age > 82.7 years (as assessed by ROC-curve analysis) only pre-existing RBBB (OR 5.0, CI 1.1–22.6; $P=0.035$), $LVOT_{LC}$ calcification (OR 5.0, CI 1.5–17.1; $P=0.010$), and age (OR 6.9, CI 2.0–24.1; $P=0.003$) emerged as independently associated with PPI, whereas first degree AVB did not ($P=0.154$).

A risk stratification model based on the three risk factors determined in the multivariate model identified several groups with differing risk for PPI. The PPI rate was 3.8, 9.0, 42, and 100% in patients with 0 (3 out of 79 patients), 1 (9/100), 2 (5/12), and 3 (3/3) risk factors, respectively ($P<0.001$, Fig. 3).

Post-dilation

Post-dilation was performed frequently (36.8%) due to relevant PVR or elevated transvalvular gradient caused by incomplete stent frame expansion. Patients requiring post-dilation had significantly higher DLZ calcium volume (766 ± 500 vs. 557 ± 368 mm^3; $P=0.002$). This was driven by a significantly higher AVC calcium volume (692 ± 442 vs. 501 ± 319 mm^3; $P=0.002$), whereas LVOT calcification was similar (74 ± 108 vs. 56 ± 99 mm^3; $P=0.101$). The rate of post-dilation was 25, 30, 42, and 57% in the four quartiles of total DLZ calcium volume ($P=0.001$; supplementary Fig. 3).

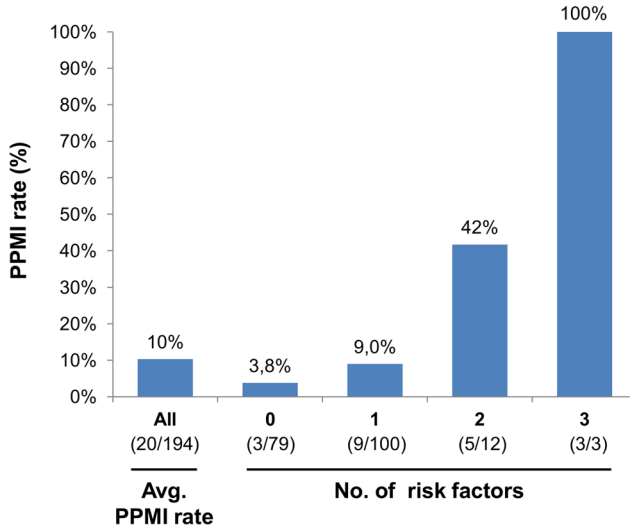

Fig. 3 PPI rate dependent on presence of risk factors. The PPI risk could be stratified by combination of the three risk factors age, elevated $LVOT_{LC}$ calcification, and pre-existing right bundle branch block

Discussion and limitations

The present study sought to investigate predictors of PVR and PPI after TAVR with a novel self-expanding THV, the ACURATE *neo*, thereby focusing on the impact of DLZ calcification pattern. Key findings of our work are the following (1) the burden of DLZ calcium predicts residual PVR and the need for post-dilation; (2) age, pre-existing RBBB and calcification pattern of the LVOT are predictors for PPI; and (3) the patient's individual PPI risk can be stratified on the basis of the identified risk factors.

Paravalvular regurgitation

PVR is a major limitation of TAVR, being associated with increased mortality in numerous studies [13, 14]. Previous studies have analyzed the impact of DLZ calcification on PVR with various valve systems, thereby using different methods for calcium quantification [8, 15–20]. While most studies conclude, that DLZ calcium is predictive for PVR, there is variable data regarding the distribution of calcium. Several studies demonstrated the influence of calcium asymmetry on PVR [8, 15], which was contradicted in another study [18, 20]. Ewe and colleagues suggested calcium at the aortic wall of each valve cusp as most important factor [17]. Several authors pointed out the importance of LVOT calcification [8, 16, 19], which might influence infra-annular sealing mechanisms, whereas others emphasized the role of AVC calcification [20].

The present study analyzed both quantity and distribution pattern of DLZ calcification. Both the amount and distribution of LVOT and AVC calcium predicted PVR in univariate regression analysis, but in multivariate analysis the burden of AVC calcium was the only factor independently associated with PVR ≥ mild. Due to the stent design of the ACURATE *neo* with its unique anchoring mechanism (superior crown, low radial force with minimal annular oversizing) calcification of the AVC seems to be more important in predicting PVR compared to other balloon- and self-expandable valve systems.

In addition to DLZ calcification, THV undersizing and implantation depth have been identified as risk factors for PVR after TAVR with first-generation THV [13]. In contrast, we did not observe any influence of implantation depth on PVR that—again—may be attributed to the design of the stent frame which only protrudes minimally into the LVOT. In addition, relative sizing was not related to the degree of PVR in our study. Besides PVR, degree of calcification also predicted the rate of post-dilation as reported previously [8]. Of note, no aortic root injury or annulus rupture was observed in our cohort.

Predictors of PPI

New-onset conduction disturbances after TAVR are the result of direct mechanical interaction between the THV stent frame and the AV conduction system located in the membranous part of the interventricular septum in the area under the right and the non-coronary aortic cusp [21]. A variety of factors have been suggested to increase the risk for PPI, including baseline conduction disturbances, use of a self-expandable THV and procedure-related factors such as oversizing, post-dilation, and implantation depth [22, 23]. PPI rates from 22 to 38% have been reported for the first-generation self-expandable CoreValve THV and 25.5% for its successor, the Evolut R, in the recently published SURTAVI trial [3, 24, 25]. In our study with the ACURATE *neo*, the PPI rate was 10.3% and thus substantially lower than previously reported for self-expandable devices. Similar PPI rates have been reported recently [26]. This might be due to the fact that the ACURATE *neo* features an X-shaped stent which avoids excessive pressure on the conduction system. Moreover, the applied radial force is only intermediate compared to other devices [6]. The respective stent design and the lower radial force seem also to be the reason that we did not observe any influence of implantation depth on PPI rate which has been described as a risk factor of PPI for a variety of THV systems, including the CoreValve, the SAPIEN 3 and the Lotus THV [10, 27, 28]. Of note, other procedural factors such as pre- and post-dilation strategy and sizing were not associated with PPI in our study.

However, our study showed a significant influence of the DLZ calcification pattern on PPI risk, whereas absolute calcium volume was not different between groups. An

elevated calcium burden of the LVOT in the area below the left coronary cusp was associated with an increased risk of PPI. Similar results have been reported previously in the context of TAVR with the CoreValve, SAPIEN XT, and the SAPIEN 3 THV [7, 10]. A shift of the expanded stent frame away from the calcified area towards the area below the right and non-coronary cusp might exert a locally increased pressure on the AV conduction system. This explanation has been postulated before by other investigators [7, 10]. Hence, the pattern of calcium distribution seems to be more relevant than the absolute calcium volume, particularly with regard to the absolute asymmetry between $LVOT_{LC}$ and $LVOT_{NC}$. Finally, a pre-existing RBBB was a significant predictor of PPI which is a well-known risk factor for PPI after TAVR [23]. In patients with pre-existing RBBB a new LBBB which is a frequent complication after TAVR is sufficient to cause clinically complete AVB. In contrast to previous studies, other baseline ECG abnormalities such as first grade atrioventricular block or atrial fibrillation were not significantly related to PPI.

Last but not least, age emerged as predictor of PPI which has previously been suggested as a considerable factor for PPI [29, 30], most likely reflecting age-related alterations of the conduction system in general.

Study limitations

Limitations of the study are (1) the limited number of retrospectively analyzed patients, (2) the non-randomized inclusion of patients in only two centers, serving (3) an all-comer patient population, which was chosen to be treated with this specific device by the best clinical knowledge of the respective heart team. Due the low number of patients requiring PPI, our risk stratification model has to be interpreted with caution and warrants validation in a larger, prospective patient cohort.

Conclusions

From our data, we conclude that the amount and the distribution of DLZ calcium are important factors for both degree of PVR and risk of PPI. Interestingly, other than previously described for several THV, the PPI rate seems not to be affected by operator-depending factors such as implantation depth or balloon-dilation strategy after TAVR with the ACU RATE *neo*. In contrast, only patient-depending characteristics, i.e. age, RBBB at baseline, and $LVOT_{LC}$ calcification, were predictors for PPI in our study. PVR ≥ moderate was observed in 6.1% of patients, which is a higher rate compared to other current THV like the SAPIEN 3 or the LOTUS valve. On the other side, substantially higher PPI rates were reported for those devices. Although no direct comparison to other available THV was performed in our study, clinicians should keep in mind the tradeoff between low PVR rates and high risk for PPI. Careful pre-procedural planning may identify patients at risk for those TAVR-related complications and subsequently help to select the optimal prosthesis for the individual patient to reduce both PVR and PPI.

Compliance with ethical standards

Conflict of interest Lenard Conradi, Tanja Rudolph, and Ulrich Schäfer are proctors for Symetis. Hamburg Heart Center is a training site for transfemoral and transapical Symetis TAVI training. All other authors report no conflict of interest.

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