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Can aortic valve calcium score predict a need for permanent pacemaker implantation after transcatheter aortic valve implantation?

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ABSTRACT

Introduction Conductive disturbances requiring permanent pacemaker (PPM) implantation remain a major concern after transcatheter aortic valve implantation (TAVI).

Aims To assess the impact of aortic valve calcium score (AVCS) on conductive disturbances requiring PPM after TAVI.

Methods All patients who underwent TAVI with accessible AVCS from the preprocedural CT scan report were included in this retrospective single-centre study. The primary endpoint was the occurrence of a conductive disturbance requiring PPM at 30 days. The association between PPM and AVCS, with its incremental prognostic value, was analysed using multivariable logistic regression, receiver operating characteristic curve analysis and likelihood ratio (LR) test.

Results We included 761 patients of which 125 (16%) required PPM at 30 days. AVCS score was significantly higher in patients requiring PPM (3788 (2487–5218) vs 3050 (2043–4367) AU, p<0.001). Using multivariable analysis, preprocedural right bundle branch block (RBBB) (OR 6.61, 95% CI 3.82 to 11.5, p<0.001), first atrioventricular block (OR 1.71, 95% CI 1.03 to 2.83, p=0.037), self-expanding valve (OR 3.25, 95% CI 1.17 to 9.09, p=0.025) and AVCS>4510 AU (OR 1.83, 95% CI 1.04 to 3.20, p=0.035) were independently associated with PPM. AVCS had an incremental discriminative value (C-index 0.79 vs 0.77, LR test p=0.036) over and above traditional PPM risk factors. An algorithm was proposed based on the initial presence of RBBB, AVCS and the type of implanted valve.

Conclusion Even if RBBB remained the strongest predictor of PPM post-TAVI, this study suggests that a high AVCS may help identifying patients at increased risk of PPM after TAVI, especially among those without pre-existing RBBB.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The impact of aortic valvular calcium score on conduction disturbances post-transcatheter aortic valve implantation (TAVI) remains incompletely elucidated.

WHAT THIS STUDY ADDS

⇒ This study shows that an aortic valve calcium score (AVCS) greater than 4510 AU is an independent predictor of post-TAVI conductive disorders requiring permanent pacemaker implantation.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This supports the routine use of this measurement for pre-TAVI assessment. Incorporating AVCS into the assessment report could significantly enhance the prediction and management of permanent pacemaker implantation risk.

INTRODUCTION

Transcatheter aortic valve implantation (TAVI) is increasingly used in the management of patients with severe aortic stenosis and has become the first-line treatment for patients over 75 years of age or at high surgical risk when femoral access is feasible.[1 2] Yet, its extension to younger patients is still limited by two main issues: the durability of percutaneous prosthesis and the higher rate of permanent pacemaker (PPM) compared with surgery. While the majority of complications have decreased over the past decade, the rate of PPM remains high and, according to registries, has even tended to increase.[3] Moreover, post-TAVI PPM is associated with an increased risk of hospitalisation for acute heart failure and mortality, thus leading to increased costs and resource utilisation.[4]

Several factors are known to increase this risk of PPM: depth of implantation,[5 6] presence of preprocedural right bundle branch block (RBBB),[7] overexpansion of the prosthesis in relation to the size of the aortic annulus,[8] extension of calcifications into the

left ventricular outflow tract (LVOT), especially near to the non-coronary cusp,[8 9] use of self-expanding valve (SEV)[10] and postdilatation.[11]

Aortic stenosis is characterised by progressive leaflet calcification. The extent of these calcifications is usually quantified by aortic valve calcium score (AVCS), usually measured by CT scan. Previous studies have already highlighted the performance of AVCS as a prognostic marker for aortic stenosis[12 13] as well as its interest to confirm the severity of aortic stenosis in case of discordant echocardiographic parameters, particularly in patients with paradoxical low-flow/low-gradient aortic stenosis.[1 2] Additionally, it has been demonstrated that AVCS is independently associated with the incidence of para-valvular leaks after TAVI, which are themselves associated with higher mortality risk.[14 15] Conversely, the literature is inconsistent regarding the impact of AVCS on the incidence of PPM after TAVI.[7 9 16–19]

The aim of this study was to assess the impact of AVCS on conductive disturbances requiring PPM after TAVI.

METHODS

Study population and outcomes

Between 1 January 2016 and 31 May 2022, 1487 patients were admitted to our centre for TAVI and were prospectively included in our local database. This prospective database collects clinical and paraclinical data from before the procedure, variables related to the procedure and hospitalisation and patient follow-up at 1 month and every year. The main complications were classified according to the Valve academic research consortium-3.[20] When AVCS was not accessible, patients referred for valve-in-valve procedures or for pure aortic regurgitation and those with a history of PPM before TAVI were excluded from this analysis. According to European guidelines, each case of aortic stenosis requiring TAVI was systematically reviewed and approved by our local valvular Heart Team.[1] For this study, the analysis of the initial (ie, preprocedure) ECG was carried out retrospectively by an investigator blinded to procedural results and pacemaker implantation.

CT scan and AVCS measurement

A non-contrast-enhanced acquisition of the aortic root was obtained before the pre-TAVI CT scan was performed according to European recommendations.[21] Studies were performed using a 256-slice multidetector CT scan (Revolution Apex, General Electric Healthcare, Milwaukee, Wisconsin, USA). The acquisition was performed with prospective ECG synchronisation, 120 kVp power, 25 cm field of view then 3 mm thick axial images was reconstructed. The AVCS was calculated using Smartscore V.4.0 software (General Electric Healthcare) derived from the Agatston and Janowitz method for coronary calcifications and adapted to the evaluation of the aortic valve during an injection-free sequence.[12 22] The software detects any structure greater than 1 mm^2 attenuating ≥130 Hounsfield units. Next, calcifications belonging to the aortic valve were manually selected, carefully avoiding the mitral annulus and coronary arteries. Each selected area was attributed a coefficient ranging 1–4 depending on its maximal attenuation. We also retrospectively analysed the distribution of calcifications in the aortic valve. Using contrast-enhanced sequences and multiplanar reconstruction, we positioned the imaging plane at the level of the aortic annulus. This entire plane was assessed from the aorta towards the LVOT to determine whether the distribution of calcifications at the valve level was homogeneous or heterogeneous, with predominance on the antero-left cusp, antero-right cusp or non-coronary cusp. The extension of calcifications into the LVOT was evaluated using multiplanar reconstruction with a dedicated incidence. Additionally, the overexpansion or underexpansion of the prosthesis relative to the aortic annulus was calculated by the ratio between the theoretical area of the prosthesis and the area of the aortic annulus measured on the CT scan. All these measurements and analyses were performed retrospectively by an investigator blinded to procedural results and pacemaker implantation.

Implantation depth of the prosthesis

The implantation depth of the prosthesis was retrospectively assessed by an investigator blinded to the clinical data, using the angiogram from the final procedure. Implantation depth was evaluated on the postimplant angiogram showing the prosthesis in an orthogonal view. Implantation depth (in mm) was defined as the distance from the virtual aortic annulus to the distal edge of the prosthesis. A deep implantation of the prosthesis was defined arbitrarily by a stent length >6 mm in the LVOT. All of these measurements and analyses were carried out retrospectively.

Primary endpoint

The primary endpoint was the incidence of PPM within 30 days post-TAVI. The indications for PPM were made individually after discussion between electrophysiologists and interventional cardiologists, in accordance with current guidelines.[23]

Statistical analysis

Continuous data were reported as the mean±SD for normally distributed data or the median and IQR (Q1–Q3) for non-normally distributed data. Categorical data were reported as counts and percentages. Comparisons were made with the χ^2 or Fisher's exact tests for categorical variables and the Student's t-test or Mann-Whitney-Wilcoxon test, as appropriate, for continuous variables.

To assess the association between AVCS and the primary outcome, a multivariable logistic regression analysis was performed, including into the model the variables associated with PPM and a $p<0.05$ in the univariable analysis or the variables consistently found in the literature. The capacity of AVCS to predict 30-day incidence of PPM was

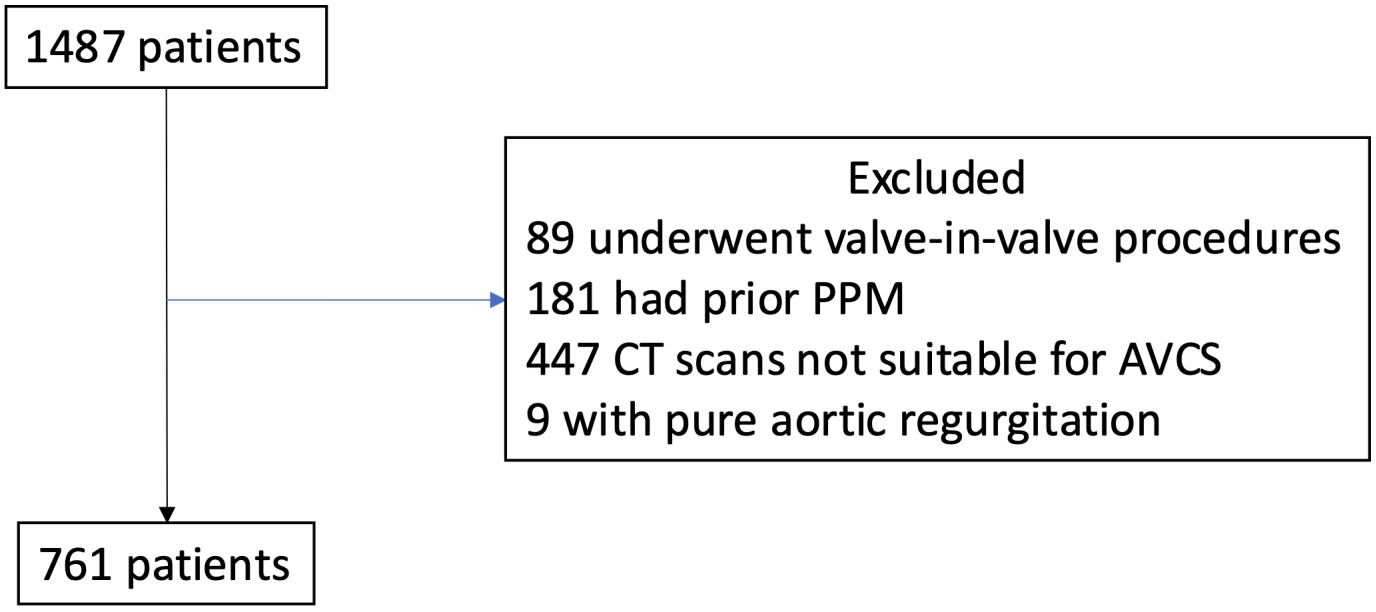


Figure 1 Flow chart of the selection process of the study population. During the study period, 1487 patients were admitted to our centre for TAVI. Among them, 726 patients were excluded from the study: 89 patients had valve-in-valve procedures, 181 patients had prior PPM, 447 patients had a CT scan that was not performed in our centre or that was not useable for AVCS and 9 patients underwent TAVI for pure aortic regurgitation. Our study, therefore, included a total of 761 patients. AVCS, aortic valve calcium score; PPM, permanent pacemaker; TAVI, transcatheter aortic valve implantation.

analysed using receiver operating characteristics (ROC) curve analysis. The best cut-off to be associated with the primary outcome was found afterwards using the Youden's index. In order to evaluate the incremental discriminative value of the AVCS over and above traditional PPM risk factors, we compared the Akaike information criterion (AIC) of two logistic regression models using an likelihood ratio (LR)-test as well as their C-index. The inter-reproducibility and intrareproducibility of AVCS measurement have been assessed using interclass and intraclass correlation coefficient and Bland-Altman analyses. A p<0.05 was considered as significant. All statistical analyses were made using R software (R Project for Statistical Computing, Vienna, Austria, V.4.0.2).

RESULTS

Baseline characteristics and procedural outcomes

Among 1487 patients admitted to our centre for TAVI, 761 patients were finally included in the study (figure 1). The sensitivity analyses are provided in online supplemental eTable 1.

During the study period, 125 (16%) patients with conductive disturbances required PPM after 30-day follow-up, including 123 patients during the in-hospital stay and 2 patients between discharge and 30-day follow-up. The median time to PPM implantation was 2 days post-TAVI, with an IQR of 1–4 days. Five patients (4%) were implanted for sinus node dysfunction, 85 patients (68%) for high-degree atrioventricular (AV) block and 35 patients (28%) were deemed at high risk for complete AV block with a PR interval >240 ms and/or QRS duration >150 ms and/or HV interval >70 ms.

Baseline and procedural characteristics are shown in tables 1 and 2. The median age was 84 years and the median logistic EuroSCORE was 8%.

Compared with patients without PPM, patients with PPM were more likely male and older (p=0.03 and p=0.012, respectively). Patients with PPM were more likely to have first-degree AV block and RBBB before the procedure (p<0.001 and p<0.001, respectively). In contrast, aortic stenosis severity and left ventricular ejection fraction were similar between groups (p=0.3 and p=0.4, respectively) as well as the distribution of calcifications in the aortic cusps (p=0.6). Interestingly, patients requiring PPM were more likely to have calcifications in the LVOT (p=0.002) and AVCS was significantly higher than in patients who did not require PPM (p<0.001). The ratio of prosthesis area to annulus area was also higher (p<0.001), indicating that oversizing was more common in patients who had PPM. SEV and postdilatation were also more frequently used in patients with PPM (both p<0.001 and p<0.001).

Pacemaker implantation rate according to AVCS quartiles

The impact of AVCS according to the distribution of PPM into quartiles is represented in figure 2. The incidence of PPM was similar in the first three quartiles, ranging from 12% to 15%. Interestingly, the incidence of PPM (26%) was significantly higher in the fourth quartile (ie, patients with AVCS>4510 AU) (p<0.001).

Considering the major known role of pre-existing RBBB[7] and the use of SEV[10] to predict PPM, we also assessed the impact of AVCS in patients with or without RBBB before TAVI and according to the type of valve

Table 1 Baseline characteristics of the population included (n=761)

Characteristics	Overall n=761	Patients without PPM within 30 days n=636	Patients with PPM within 30 days n=125	P value
Demographics				
Age, years	84 (80, 87)	84 (79, 87)	85 (81, 89)	**0.012**
Male, n (%)	377 (50)	304 (48)	73 (58)	**0.030**
Height, m	1.6 (1.6, 1.7)	1.6 (1.6, 1.7)	1.6 (1.6, 1.7)	0.4
Weight, kg	73 (63, 84)	73 (63, 84)	73 (65, 83)	0.9
BMI, kg/m^2	26.8 (23.9, 30.1)	26.8 (23.9, 30.1)	26.7 (24.0, 30.0)	0.8
Body surface area, m^2	1.82 (1.69, 1.99)	1.82 (1.69, 1.99)	1.81 (1.69, 1.99)	0.8
Comorbidities				
Logistic Euroscore (%)	8 (6, 13)	8 (6, 13)	9 (6, 14)	0.3
Hypertension, n (%)	599 (79)	502 (79)	97 (78)	0.7
Diabetes mellitus, n (%)	225 (30)	188 (30)	37 (30)	>0.9
Myocardial infarction, n (%)	58 (8.2)	48 (8.2)	10 (8.3)	>0.9
Stroke, n (%)	54 (12)	41 (11)	13 (17)	0.13
PAD, n (%)	73 (10)	62 (11)	11 (9.2)	0.6
COPD, n (%)	57 (7.6)	49 (7.8)	8 (6.5)	0.6
Previous BAV, n (%)	25 (3.3)	19 (3.0)	6 (4.8)	0.3
Coronary heart disease, n (%)	254 (33)	210 (33)	44 (35)	0.6
Previous CABG, n (%)	29 (3.8)	27 (4.2)	2 (1.6)	0.2
Previous PCI, n (%)	180 (24)	151 (24)	29 (23)	0.9
Previous dialysis, n (%)	14 (1.9)	12 (1.9)	2 (1.6)	>0.9
Symptoms				
NYHA functional class, n (%)				0.7
I–II	409 (53.7)	341 (53.6)	68 (54.4)	
III–IV	352 (46.3)	295 (46.4)	57 (45.6)	
CCS functional class, n (%)				0.2
I–II	738 (97)	619 (97.3)	119 (95.2)	
III–IV	23 (3)	17 (2.7)	6 (4.8)	
Syncope, n (%)	45 (5.9)	33 (5.2)	12 (9.6)	0.056
Hospitalisation for AHF, n (%)	183 (24)	147 (23)	36 (29)	0.2
Biology				
GFR, mL/min/1.73 m^2	54 (41, 71)	55 (41, 72)	53 (40, 64)	0.11
NTproBNP, ng/mL	1266 (500, 3528)	1234 (496, 3308)	1536 (540, 5135)	0.12
Previous treatment				
Beta blocker, n (%)	141 (48)	117 (48)	24 (49)	0.9
Preprocedural ECG				
First AV block, n (%)	203 (33)	153 (30)	50 (49)	**<0.001**
RBBB, n (%)	105 (14)	60 (9.4)	45 (36)	**<0.001**
LBBB, n (%)	83 (11)	70 (11)	13 (10)	0.9
TTE characteristics				
Aortic valve area, cm^2	0.76 (0.63, 0.90)	0.75 (0.63, 0.90)	0.79 (0.63, 0.90)	0.7
Mean aortic gradient, mm Hg	44 (38, 53)	44 (37, 52)	46 (38, 54)	0.3
LVEF, %	61 (55, 67)	62 (55, 67)	60 (52, 67)	0.4
CT scan characteristics				
AVCS, AU	3106 (2098, 4510)	3050 (2043, 4367)	3788 (2487, 5218)	**<0.001**

Continued

Table 1 Continued

Characteristics	Overall n=761	Patients without PPM within 30 days n=636	Patients with PPM within 30 days n=125	P value
Calcification extensions to the LVOT, n (%)	240 (32)	186 (29)	54 (43)	**0.002**
Distribution of aortic valve calcifications, n (%)				0.6
Homogenous, n (%)	570 (75)	474 (75)	96 (77)	
Predominantly on the left coronary cusp, n (%)	23 (3.0)	18 (2.8)	5 (4.0)	
Predominantly on the right coronary cusp, n (%)	34 (4.5)	31 (4.9)	3 (2.4)	
Predominantly on the non-coronary cusp, n (%)	134 (18)	113 (18)	21 (17)	
Prosthesis area to annulus area ratio	1.08 (1.00, 1.18)	1.07 (1.00, 1.16)	1.15 (1.04, 1.39)	**<0.001**

Results are n (%) or median (Q1, Q3) when appropriate.
AHF, acute heart failure; AU, arbitrary unit; AV, atrioventricular; AVCS, aortic valve calcium score; BAV, balloon aortic valvuloplasty; BMI, body mass index; NT pro BNP, N-terminal pro-B-type natriuretic peptide; CABG, coronary artery bypass graft; CCS, Canadian Cardiovascular Society; COPD, chronic obstructive pulmonary disease; GFR, glomerular filtration rate; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; LVOT, left ventricular outflow tract; NYHA, New York Heart Association; PAD, peripheral arterial disease; PCI, percutaneous coronary intervention; PPM, permanent pacemaker; RBBB, right bundle branch block; TTE, transthoracic echocardiogram.

used (figure 3). In patients with preprocedural RBBB, although PPM rates were very high, we did not observe any significant difference according to AVCS quartiles (p=0.5). In contrast, the incidence of PPM was significantly increased in patients without preprocedural RBBB and with AVCS>4510 AU (p<0.001). In patients treated with SEV, there was a trend towards an increase in the incidence of PPM according to AVCS quartiles (p=0.069). In patients treated with a balloon-expandable valve (BEV), the incidence of PPM was low and similar in the first three quartiles and was significantly higher in patients with ACVS>4510 AU. Finally, the incidence of PPM was similar between SEV and BEV in patients with AVCS in the first quartile (ie, <2098 AU). In contrast, the

Table 2 Procedural and postprocedural characteristics of the population included (n=761)

Characteristics	Overall n=761	Patients without PPM within 30 days n=636	Patients with PPM within 30 days n=125	P value
Procedural characteristics				
Transfemoral access, n (%)	713 (95)	591 (94)	122 (98)	0.5
Predilatation, n (%)	333 (44)	272 (43)	61 (49)	0.2
Postdilatation, n (%)	39 (5.1)	25 (3.9)	14 (11)	**<0.001**
Valve size, mm				
20	7 (1)	7 (1)	0 (0)	
23	213 (28)	194 (31)	19 (15)	
26	315 (41)	274 (43)	41 (33)	
29	184 (24)	136 (21)	48 (38)	
34	42 (6)	25 (4)	17 (14)	
Valve type, n (%)				**<0.001**
BEV	617 (81)	538 (85)	79 (63)	
SEV	144 (19)	98 (15)	46 (37)	
Deep prosthesis implantation, n (%)	139 (18)	110 (17)	29 (23)	0.12
Post procedural follow-up				
Telemetry monitoring, days	1.00 (1.00, 2.00)	1.00 (1.00, 2.00)	2.00 (1.00, 3.00)	**<0.001**
Length of stay, days	2.00 (2.00, 4.00)	2.00 (2.00, 4.00)	4.00 (2.00, 6.00)	**<0.001**

Results are n (%) or median (Q1, Q3) when appropriate.
BEV, balloon-expandable valve; PPM, permanent pacemaker; SEV, Self-expanding valve.

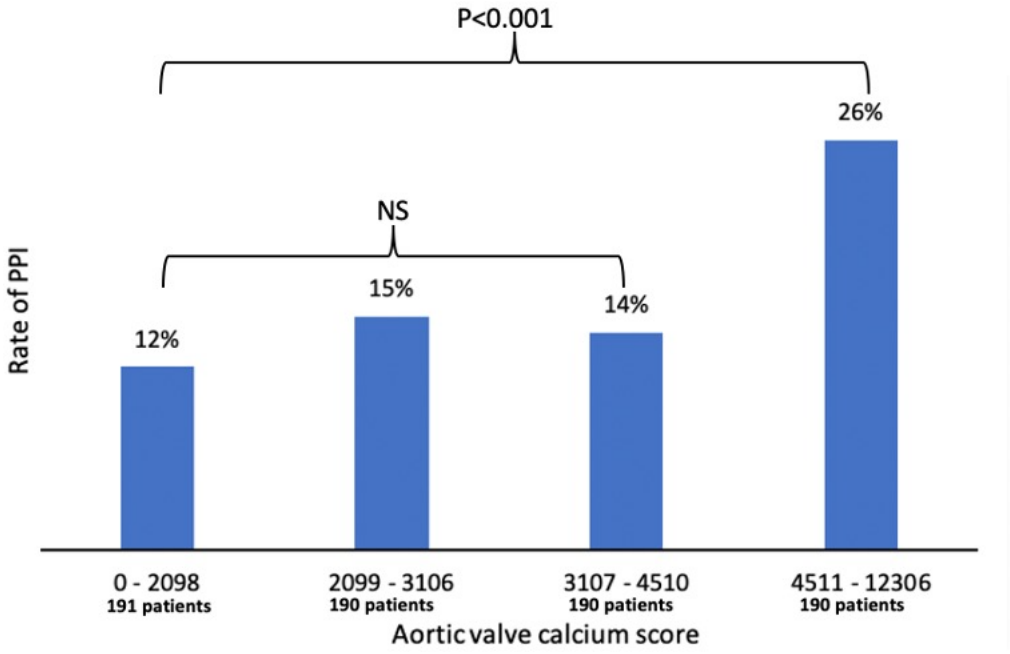


Figure 2 Pacemaker implantation rate according to AVCS quartiles for the overall population (n=761). This histogram represents the distribution of PPM according to AVCS quartiles. PPM rates were similar in the first three quartiles and ranged between 12% and 15%. However, we observed a significant increase in PPM rate in patients with AVCS>4510 AU (26%, p<0.001). AU, arbitrary unit; AVCS, aortic valve calcium score; PPM, permanent pacemaker.

incidence of PPM was significantly higher in the last three quartiles when SEV was used.

Intraclass and interclass correlation coefficients were excellent for AVCS measurement: 0.992, 95% CI (0.976 to 0.997) and 0.976, 95% CI (0.982 to 0.996), respectively (see online supplemental figure S1 for the Bland-Altman analysis).

Univariable and multivariable logistic regression analysis for PPM implantation within 30 days

Univariable and multivariable logistic regression analyses are shown in table 3. AVCS (as a continuous variable or >4510 AU), pre-existing conductive disturbances (first AV block and RBBB) and SEV were independently associated with conductive disturbances requiring PPM. The best cut-off to be associated with the primary outcome was 3622 AU. In another multivariable logistic regression analysis, an AVCS score >3622 AU remained independently associated with the primary outcome (online supplemental eTable 3).

ROC curve analysis

The discrimination of AVCS to predict PPM, using ROC curve analysis, is represented in figure 4. The area under the ROC curve was 0.60 (95% CI 0.55 to 0.66), indicating poor discrimination. The same analysis was performed in patients without preprocedural RBBB, in patients implanted with SEV, or with BEV. The areas under the ROC curve were 0.64 (95% CI 0.57 to 0.70), 0.61 (95% CI 0.51 to 0.71) and 0.59 (95% CI 0.52 to 0.66), respectively.

Analysis of the incremental discriminative value of AVCS

To evaluate the incremental discriminative value of AVCS in relation to the usual risk factors for PPM, we compared two logistic regression models (figure 5). The AIC of the model without AVCS was 464, while the AIC of the model with AVCS was 459, with an LR test p value of 0.036. The model with AVCS had a significantly higher c-index compared with the model without AVCS (0.79 vs 0.77, p=0.036), indicating greater incremental value.

Proposal of a preprocedural algorithm to assess the risk of PPM implantation after TAVI

Based on these findings, we propose a preprocedural algorithm to assess the risk of PPM post-TAVI (figure 6). Initially, the presence of RBBB identified a very high-risk population whereas AVCS did not provide additional information (p=0.98). Conversely, in the absence of initial RBBB, AVCS provided additional information (p<0.001). An AVCS of <4510 AU indicated a low risk of PPM, whereas an AVCS of >4510 AU indicated a high risk. Finally, in these different scenarios, the implantation of SEV compared with BEV resulted in a higher rate of PPM (p=0.0003 and p=0.07).

DISCUSSION

We aimed to assess the impact of AVCS on conductive disturbances requiring PPM after TAVI. The main results of our study may be summarised as follows: (1) AVCS was higher in patients presenting with conductive disturbances requiring PPM, particularly when its value was greater than 4510 AU; (2) AVCS was independently

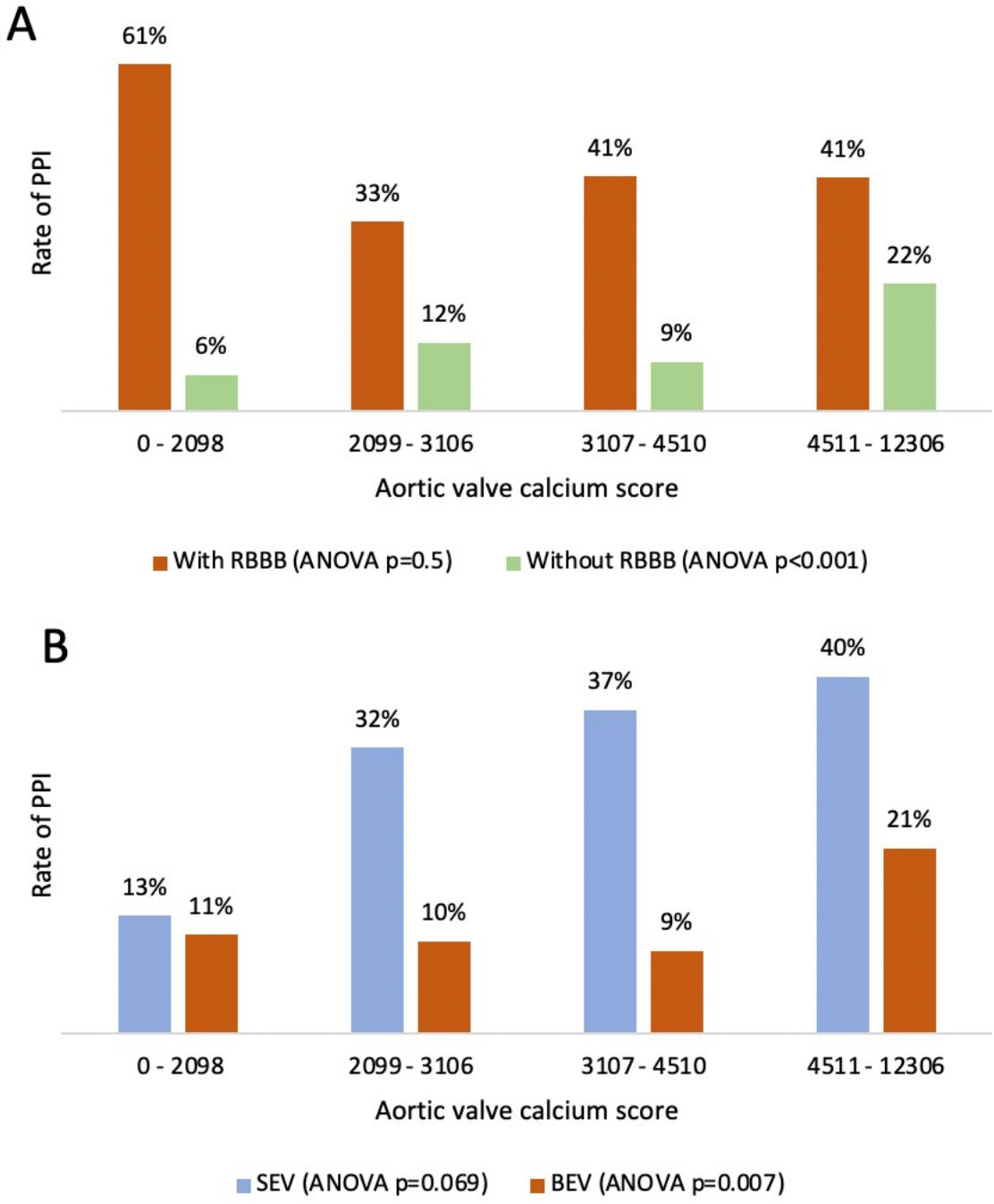


Figure 3 Pacemaker implantation rate according to AVCS quartiles. (A) In patients with or without preprocedural RBBB. (B) In patients with SEV or with BEV. This histogram represents the distribution of PPM according to AVCS quartiles in patients with or without preprocedural RBBB and according to valve type. In patients with preprocedural RBBB, PPM rates were very high, but we did not observe a significant impact of AVCS (p=0.5). Yet, patients without preprocedural RBBB and with AVCS>4510 AU had a significant increase in PPM (p<0.001). In patients with SEV, we did not observe a significant impact of AVCS (p=0.069). Conversely, patients with BEV and AVCS>4510 AU had a significant increase in PPM rate (p=0.007). ANOVA, analysis of variance; AU, arbitrary unit; AVCS, aortic valve calcium score; BEV, balloon-expandable valve; PPM, permanent pacemaker; RBBB, right bundle branch block; SEV, self-expanding valve.

associated with PPM over traditional risk factors; (3) AVCS poorly predicted the risk of PPM but provided a significant incremental discriminative value compared with the usual risk factors for PPM, (4) AVCS appears particularly useful in the absence of initial RBBB, allowing to differentiate between high-risk and low-risk populations for PPM (online supplemental central illustration).

Anticipating conduction disturbances requiring PPM implantation after TAVI

TAVI is a cornerstone in the management of aortic stenosis, with a steadily increasing number of procedures.[24] Conversely, hospital resources, both human and financial, are limited. It is, therefore, essential to optimise

Table 3 Univariable and multivariable logistic regression analysis for permanent pacemaker implantation within 30 days after transcatheter aortic valve implantation

	Univariable			Multivariable					
				Model 1*			Model 2†		
Variables	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
AVCS	1.00	1.00 to 1.00	**<0.001**	1.00	1.00 to 1.00	**0.03**			
AVCS>4510 AU	2.26	1.50 to 3.39	**<0.001**				1.83	1.04 to 3.20	**0.035**
Age	1.04	1.01 to 107	**0.026**	1.01	0.97 to 1.05	0.7	1.01	0.97 to 1.05	0.7
Male sex	1.53	1.04 to 2.27	**0.031**	0.87	0.49 to 1.54	0.6	0.92	0.53 to 1.59	0.8
Initial first AV block	2.28	1.48 to 3.51	**<0.001**	1.71	1.03 to 2.83	**0.037**	1.76	1.06 to 2.91	**0.027**
Initial RBBB	5.47	3.47 to 8.60	**<0.001**	6.61	3.82 to 11.5	**<0.001**	6.49	3.75 to 11.3	**<0.001**
SEV	3.20	2.09 to 4.87	**<0.001**	3.25	1.17 to 9.09	**0.025**	3.36	1.22 to 9.36	**0.02**
Deep prosthesis implantation	1.44	0.90 to 2.27	0.12	1.41	0.79 to 2.46	0.2	1.43	0.80 to 2.50	0.2
Prosthesis area to annulus area ratio	4.70	2.16 to 10.1	**<0.001**	0.52	0.08 to 3.26	0.5	0.5	0.07 to 3.12	0.5
Postdilatation	3.08	1.52 to 6.04	**0.001**	2.15	0.90 to 4.90	0.074	2.15	0.90 to 4.91	0.074
Extension of calcifications to the LVOT	1.84	1.24 to 2.72	**0.002**	1.34	0.79 to 2.22	0.3	1.38	0.83 to 2.29	0.2

*Model 1 included AVCS, age, male sex, initial AV block, initial RBBB, SEV, deep prosthesis implantation, prosthesis area to annulus area ratio, postdilatation and extension of calcifications to the LVOT.
†Model 2 included AVCS>4510 AU, age, male sex, initial AV block, initial RBBB, SEV, deep prosthesis implantation, prosthesis area to annulus area ratio, postdilatation and extension of calcifications to the LVOT.
AU, arbitrary unit; AV, atrioventricular; AVCS, aortic valve calcium score; LVOT, left ventricular outflow tract; RBBB, right bundle branch block; SEV, self-expanding valve.

the procedure by encouraging short hospital stays and anticipating complications as far as possible. The main complication post-TAVI is conduction disturbance requiring pacemaker implantation. This complication leads to increased lengths of hospital stay.[25] A strategy to prevent this complication is therefore crucial, taking into account all the parameters associated with it.

Several factors increase the risk of PPM post-TAVI, notably pre-existing conductive disturbances such as preprocedural RBBB. Two meta-analyses reported a 4-fold increase in PPM risk with RBBB (RR 4.17, 95% CI 3.07 to 5.66, p<0.0001).[26 27] In our study, RBBB was the strongest predictor of PPM post-TAVI (OR 6.61, 95% CI 3.82 to 11.5, p<0.001) and pre-existing first-degree AV block also correlated with increased PPM risk (OR 1.71, 95% CI 1.03 to 2.83, p=0.037).

Although deep prosthesis implantation has been associated with higher PPM rates due to potential His bundle damage,[26 27] our study found no significant association (OR 1.41, 95% CI 0.79 to 2.46, p=0.2). Differences in our results may be related to adjustments for patient-specific factors, the low proportion of deep implantations in our cohort, or variations in the definition of deep implantation. Other factors previously linked to PPM, such as prosthesis overexpansion,[8] postdilatation[11] and LVOT calcification extension,[8 9] were not significant in our multivariable analysis (OR 0.52, 95% CI 0.08 to 3.26, p=0.5; OR 2.15, 95% CI 0.90 to 4.90, p=0.074; OR 1.34, 95% CI 0.79 to 2.22, p=0.3, respectively).

The use of SEV, known for their deeper LVOT extension and subannular tissue compression,[10] showed a consistent association with higher PPM rates in both univariable and multivariable analyses (OR 3.25, 95% CI 1.17 to 9.09, p=0.025).

There are conflicting data regarding the impact of aortic valve calcification on PPM. While some studies did not find significant associations,[28] others showed a correlation between AVCS and PPM,[19] and specific cusp calcification patterns were also implicated.[8 9] In our larger cohort, we found no significant differences based on calcification distribution.

In our study, the PPM rate was higher in patients with an AVCS of >4510 AU. After multivariable analysis, AVCS remained independently associated with PPM but with a low discriminatory power (area under the ROC curve 60.3%). Nevertheless, AVCS>4510 AU provided a significant incremental discriminative value compared with the usual risk factors for PPM.

The increased need for PPM in patients with high AVCS can be attributed to several factors. A high calcium burden often extends into the LVOT near the membranous septum and the AV conduction system, including the His bundle and left bundle branch. Excessive calcification in these regions may cause mechanical compression, leading to direct injury of the conduction pathways during valve deployment. Additionally, extensive calcification might necessitate more aggressive predilation or postdilation, further increasing the risk of injury to the conduction system.

Therefore, we believe that AVCS may be used to predict the risk of PPM after TAVI in combination with other known traditional risk factors. In our study, AVCS

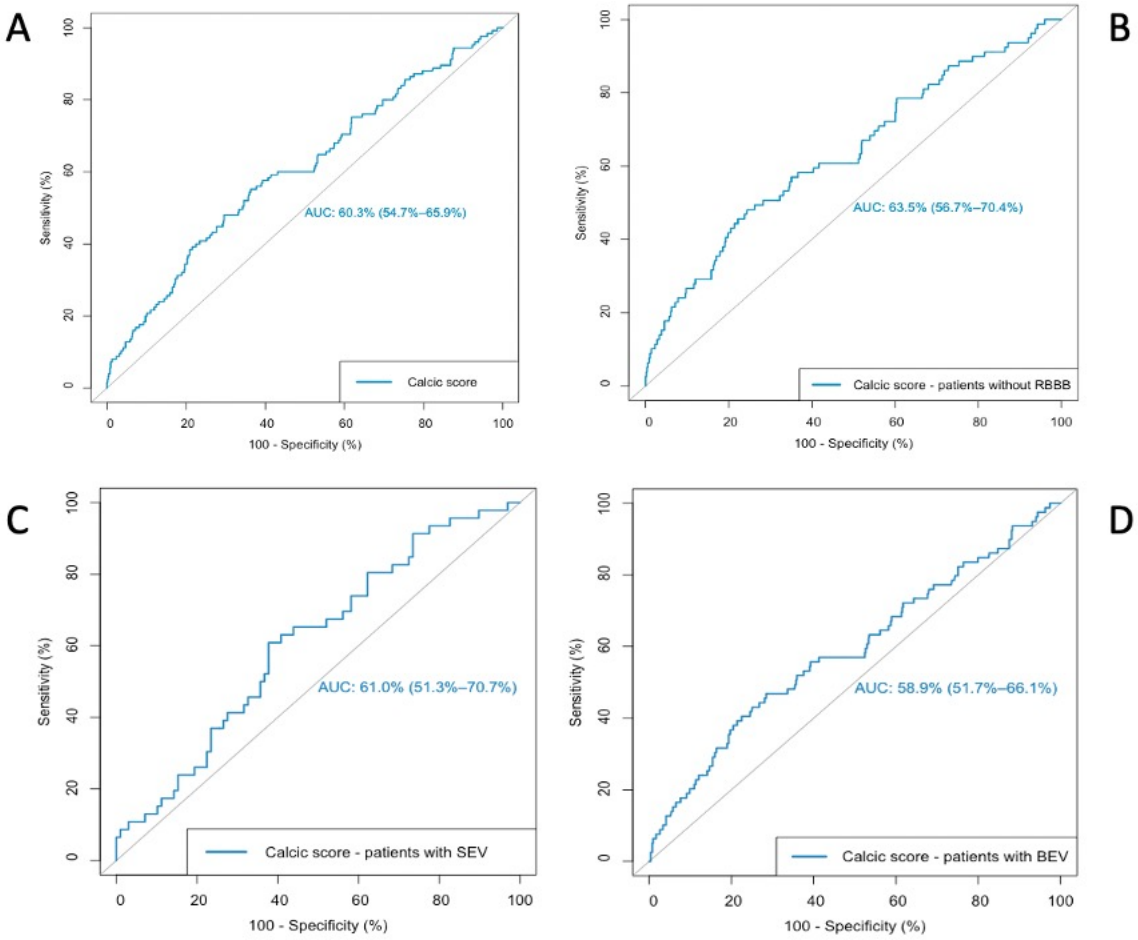


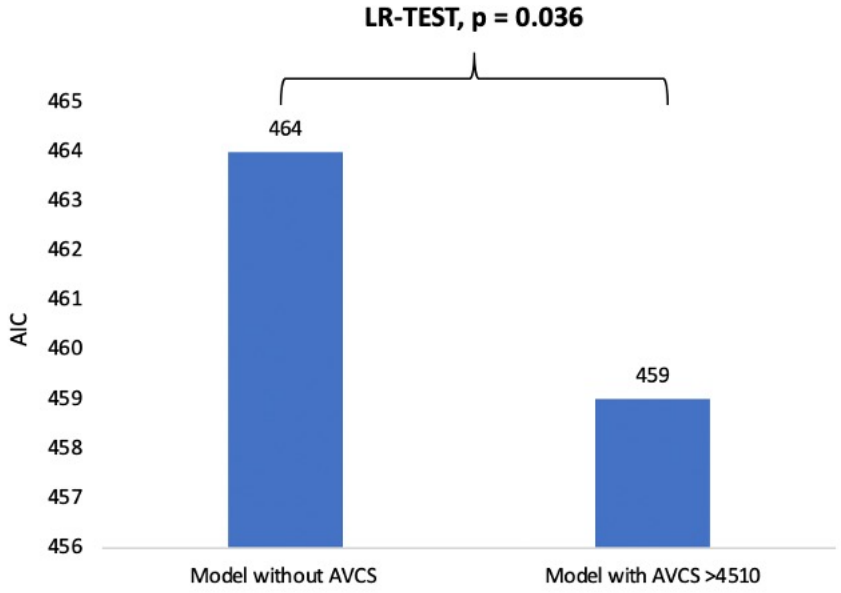
Figure 4 (A) Receiver-operating characteristic (ROC) curve analysis for AVCS to predict PPM implantation. (B) ROC curve for AVCS to predict PPM implantation in patients without RBBB. (C) ROC curve for AVCS to predict PPM implantation in patients with SEV. (D) ROC curve for AVCS to predict PPM implantation in patients with BEV. Graphical representation of the relationship between the sensitivity and specificity of AVCS to predict the risk of PPM. The area under the ROC curve was 60.3% (95% CI 54.7% to 65.9%), indicating poor predictive performance of PPM risk after TAVI. Graphical representation of the relationship between the sensitivity and specificity of AVCS to predict the risk of PPM in patients without RBBB. The area under the ROC curve was 63.5% (95% CI 56.7% to 70.4%). Graphical representation of the relationship between the sensitivity and specificity of AVCS to predict the risk of PPM in patients with SEV. The area under the ROC curve was 61% (95% CI 51.3% to 70.7%). Graphical representation of the relationship between the sensitivity and specificity of AVCS to predict the risk of PPM in patients with BEV. The area under the ROC curve was 58.9% (95% CI 51.7% to 66.1%). AUC, area under the curve; AVCS, aortic valve calcium score; BEV, balloon-expandable valve; PPM, permanent pacemaker; RBBB, right bundle branch block; SEV, self-expanding valve.

appears to provide information primarily in the absence of initial RBBB, differentiating between patients at high risk versus low risk of PPM. Conversely, in the presence of initial RBBB, AVCS does not seem to add value to risk stratification. The relative lack of added value of AVCS in the presence of RBBB could be due to the fact that RBBB itself already signals a higher risk of conduction issues, which may overshadow the contribution of AVCS in these patients. Based on these data, we propose an algorithm for classifying patients in terms of PPM risk, considering the presence of initial RBBB, AVCS and the type of valve used.

Finally, in the current technical recommendations on CT prior to TAVI, a non-contrast CT scan of the aortic root is only considered as an option[21 29]; our data support the routine performance of this acquisition prior to TAVI and the inclusion of the calcium score in the report in order to improve the risk assessment for PPM.

Limitations

Our study has several limitations. First, it was a retrospective, single-centre study, and it is possible that other variables not included in the analysis may have influenced our results. Second, the analysis of the distribution of calcifications was performed semiquantitatively. Therefore, different results might have been obtained using a quantitative analysis. Third, in our study, there were 447 patients for whom an AVCS was not calculated. This is because the scoring process requires additional image acquisition and detailed contouring of calcifications. Apart from specific indications, such as low-flow, low-gradient aortic stenosis where the score has a



C-INDEX	0.77	0.79

Figure 5 Analysis of the incremental discriminative value of AVCS. Histogram representing the AICs of two logistic regression models. The AIC of model 1 (age, male sex, initial AV block, initial RBBB, SEV, deep prosthesis implantation, prosthesis area to annulus area ratio, postdilatation, extension of calcifications to the LVOT) was 464. The AIC of model 2 (age, male sex, initial AV block, initial RBBB, SEV, deep prosthesis implantation, prosthesis area to annulus area ratio, postdilatation, extension of calcifications to the LVOT and AVCS>4510 AU) was 459. Model 2 had a significantly greater incremental value (LR test p=0.036) with c-indexes of 0.77 for model 1 and 0.79 for model 2. AIC, Akaike information criterion; AU, arbitrary unit; AV, atrioventricular; AVCS, aortic valve calcium score; LR, likelihood ratio; LVOT, left ventricular outflow tract; RBBB, right bundle branch block; SEV, self-expanding valve.

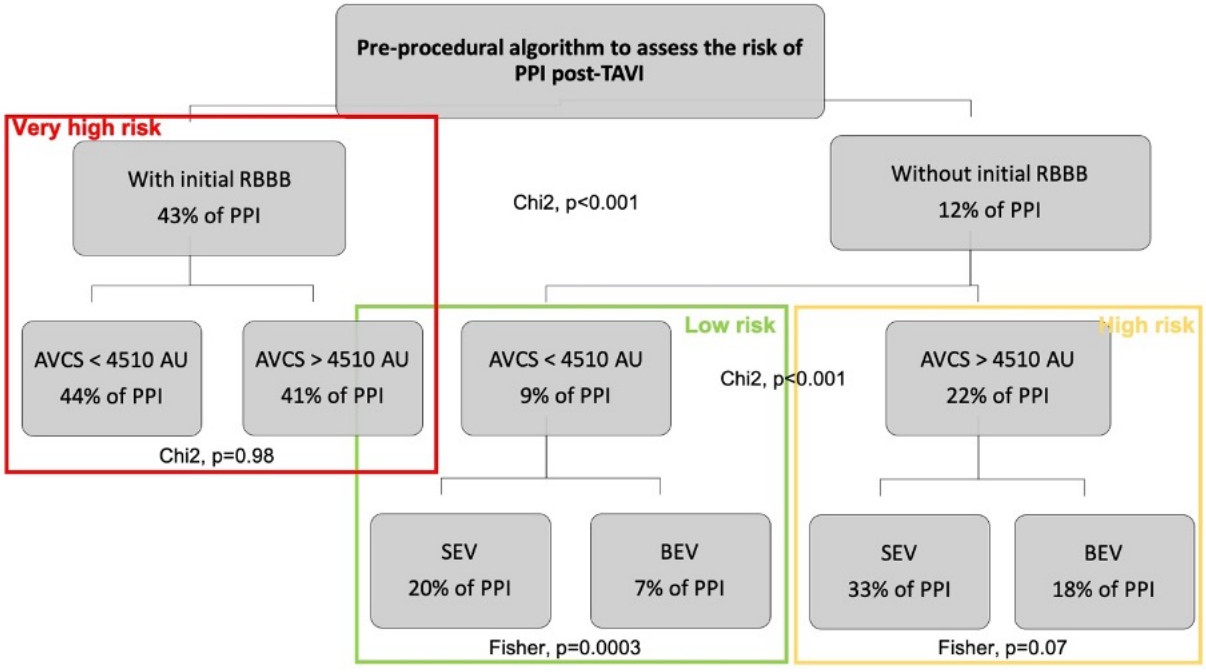


Figure 6 Proposal of a preprocedural algorithm to assess the risk of PPM implantation after TAVI. Proposal of a preprocedural algorithm to assess the risk of PPM post-TAVI, considering the presence of RBBB, AVCS and the type of valve. This algorithm allows the identification of three populations: very high risk, high risk and low risk of PPM. AVCS, aortic valve calcium score; BEV, balloon expanding valve; PPM, permanent pacemaker; RBBB, right bundle branch block; SEV, self-expanding valve; TAVI, transcatheter aortic valve implantation.

well-established utility, for other patients, the decision to perform this assessment was at the discretion of the radiologist or cardiologist performing the examination. Fourth, some patients received PPM in response to the occurrence of a high-grade conduction disturbance, while others were implanted for 'preventive' purposes in the presence of conduction disturbances judged to be high risk (QRS >150 ms, PR interval >240 ms and HV interval >70 ms during electrophysiology study). Fifth, we did not have data on the ventricular pacing rates of the implanted pacemakers. Some patients may have required a pacemaker only temporarily.

CONCLUSION

The results of our study suggest that AVCS could be an interesting additional parameter to predict post-TAVI conductive disorders requiring PPM. Indeed, an AVCS greater than 4510 AU is an independent predictive factor of PPM and has incremental discriminative value over and above traditional risk factors. AVCS appears to provide information primarily in the absence of initial RBBB by differentiating between patients at high and low risk of PPM. By better stratifying PPM, we could direct patients towards shorter care pathways, thereby optimising resource utilisation. Further studies are needed to confirm our results in a larger sample and in a multicentre study.

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Competing interests None declared.

Patient consent for publication Consent obtained directly from patient(s).

Ethics approval This study involving human participants was approved by the Comité de Qualification des Projets de Recherche (members: Fabienne Tamion, Gilles Gargala, Marie-Pierre Tavolacci, Thierry Lequerre, Guillaume Savoye, Jeremy Bellien; permanent DRCI members: Julien Blot, Delphine Picoche), with registration number 1124. Participants gave informed consent to participate in the study before taking part.

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