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ORIGINAL RESEARCH

Late onset of new conduction disturbances requiring permanent pacemaker implantation following TAVI

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ABSTRACT

Background The timing of onset and associated predictors of late new conduction disturbances (CDs) leading to permanent pacemaker implantation (PPI) following transcatheter aortic valve implantation (TAVI) are still unknown, however, essential for an early and safe discharge. This study aimed to investigate the timing of onset and associated predictors of late onset CDs in patients requiring PPI (LCP) following TAVI.

Methods and results We performed retrospective analysis of prospectively collected data from five large volume centres in Europe. Post-TAVI electrocardiograms and telemetry data were evaluated in patients with a PPI post-TAVI to identify the onset of new advanced CDs. Early onset CDs were defined as within 48 hours after procedure, and late onset CDs as after 48 hours. A total of 2804 patients were included for analysis. The PPI rate was 12%, of which 18% was due to late onset CDs (>48 hours). Independent predictors for LCP were pre-existing non-specific intraventricular conduction delay, pre-existing right bundle branch block, self-expandable valves and predilation. At least one of these risk factors was present in 98% of patients with LCP. Patients with a balloon-expandable valve without predilation did not develop CDs requiring PPI after 48 hours.

Conclusions Safe early discharge might be feasible in patients without CDs in the first 48 hours after TAVI if no risk factors for LCP are present.

INTRODUCTION

Transcatheter aortic valve implantation (TAVI) is an established treatment for severe aortic stenosis in elderly people.[1–4] Due to technical advancements, the TAVI procedure has evolved into a standardised minimal invasive procedure with lower mortality and complication rates. Despite these improvements and the arrival of newer-generation devices, late onset conduction disturbances (CDs) requiring a permanent pacemaker implantation (LCP) after TAVI remain a serious complication, especially in view of an early discharge after TAVI.[5–7]

Identifying patients at risk for LCP is therefore an essential part for safe and early discharge. Predictors for permanent pacemaker implantation (PPI) after TAVI have been studied widely.[5 8] However, most studies did not assess predictors for LCP and the exact time window of the onset to these CDs, which is essential for safe early discharge.

The aim of the study was to investigate the timing of onset and associated predictors of late onset CDs in patients requiring PPI to identify patients suitable for safe early discharge following TAVI.

METHODS

Patient selection and data acquisition

All consecutive patients who underwent a TAVI in one of the five centres were included in this multi-centre study. Patients with a cardiac device implanted prior to TAVI or with periprocedural mortality were excluded from the analysis. Patients with a PPI more than 30 days post-TAVI were considered as patients without PPI related to the TAVI. Choice for treatment was made after evaluation by a Heart Team (cardiac surgeon and interventional cardiologist) and based on local guidelines. Baseline characteristics were collected from the TAVI registries and clinical records of all participating centres. Data of the onset of new CDs in patients with a PPI post-TAVI were collected prospectively. This study was approved by the medical ethics committee with a waiver. The study was performed in accordance with the local ethics committee of each centre.

Patient and public involvement

This research was done without patient involvement. Patients were not invited to comment on the study design and were not consulted to develop patient relevant outcomes or interpret the results.

Study definitions

The study population was divided into three groups: no PPI, PPI as a result of early onset CDs (ECP) and PPI as a result of late onset CDs (LCP). Early onset CDs were defined as onset of CDs within 48 hours after procedure and late onset CDs after 48 hours. The onset was defined as the time between the procedure and the first new sign of CDs eventually leading to PPI indication on the ECG or telemetry, for example, first-degree, second-degree or third-degree atrioventricular block (1d-AVB, 2d-AVB or 3d-AVB), prolongation of 1d-AVB, complete right bundle branch block (RBBB), sick sinus syndrome, alternating left bundle branch block (LBBB) and RBBB, or severe bradycardia with need for temporary pacemaker. An ECG was performed 1 day prior to TAVI in all patients. After the procedure, rhythm observation was performed by telemetry for at least 48 hours. When indicated, additional

ECGs were acquired. Both ECGs and telemetry registration of patients with a PPI post-TAVI were analysed by an independent reviewer. We defined LBBB as QRS duration of >120 ms with a dominant S wave in V1, broad monophasic R wave in lateral leads (I, aVL, V5-V6), absence of Q waves in lateral leads and prolonged R wave peak time >60 ms in left precordial leads (V5-6). We defined RBBB as QRS duration of >120 ms with RSR′ pattern in V1-3 and wide, slurred S wave in the lateral leads (I, aVL, V5-6). Patients with a QRS>110 ms without a LBBB/RBBB pattern were classified as non-specific intraventricular conduction delay (IVCD).

The different types of valves were divided into three groups: balloon-expandable valves (SAPIEN, SAPIEN XT and SAPIEN 3; Edwards Lifesciences, Irvine, CA, USA), self-expandable valves (CoreValve, CoreValve Evolut R and Engager (Medtronic, Minneapolis, MN, USA), JenaValve (JenaValve Technology, Munich, Germany), Portico (St Jude Medical, Saint Paul, Minnesota, USA), ACURATE neo (SYMETIS S.A., Ecublens, Switzerland)) and Other valves (Lotus (Boston Scientific, Marlborough, Massachusetts, USA), direct flow (Direct Flow Medical, Santa Rosa, CA, USA)). Implantation depth was defined as the distance between the annulus and ventricular end of the stent. To compensate for projection errors, the depth was calculated using the given prosthetic frame height of the expanded stent as reference.[9] Clinical and procedural characteristics were collected from the registries and clinical records.

Statistical analysis

Categorical variables are presented as frequencies and continuous data as mean±SD or as median and IQR, as appropriate. Between-group differences were compared using one-way analysis of variance or Kruskal–Wallis for numerical variables, depending on normality and homogeneity of variance. Tukey–Kramer post-hoc test for multiple comparisons and unequal sample size or Dunn's test with Benjamini–Hochberg correction was performed if statistical significance was achieved, respectively. Categorical variables were compared using χ^2 test, with Bonferroni post-hoc analysis when statistically significant. The multivariable models were constructed by including covariates with a p value less than 0.10 in univariate analyses, and using a stepwise backward elimination method. The accuracy of logistic regression model was tested using C-statistics. Missing data (11%) were assumed to be random and were handled by multiple imputation using chained equations. Covariates with missing values over 50%, for example, valve oversizing, were excluded for imputation and not available for analysis. Ten imputed datasets were created, and results were pooled according to Rubin's rule.[10] The difference in survival according to no PPI versus ECP versus LCP were assessed by Kaplan–Meier survival analysis and compared using the log-rank test. The impact of CDs requiring PPI on mortality was evaluated using a Cox proportional hazards model. Reported is adjusted HR (HRadj) with 95% CI, adjusted for age, sex, logistic EuroSCORE, valve type, procedural approach and moderate or severe paravalvular regurgitation pre-discharge. Proportional hazard assumption was assessed via Schoenfeld residuals.[11] After analysing the HRs of co-variates at different time-points, proportional hazard assumption was met. Influential observations were tested by estimating changes in the regression coefficients on deleting each observation in turn. None appeared to be of excessive influence. Non-linearity was tested and resolved by restricted cubic splines. For all analyses, a two-sided p value<0.05 was considered statistically significant. Analyses were performed in SPSS V.25.0 (IBM corporation, Chicago, IL, USA) and R (V.3.5.0, R Foundation for Statistical Computing, Vienna, Austria).

RESULTS
Baseline and procedural characteristics

The study included 2993 patients who underwent TAVI in five centres in the Netherlands and Spain between August 2008 and January 2018, of which 2804 patients were included for analysis (figure 1). Baseline characteristics and procedural features are presented in tables 1 and 2. The median age was 82 (77–85) and 56% was women. The majority of patients received a balloon-expandable valve (56%), and in 37% and 7% of the cases a self-expandable or other valves were implanted, respectively. The PPI rate post-TAVI was 12% (341/2804 patients), of which 10% (280/2804) developed early onset CDs and 2% (61/2804) late. The PPI rate was for the balloon-expandable
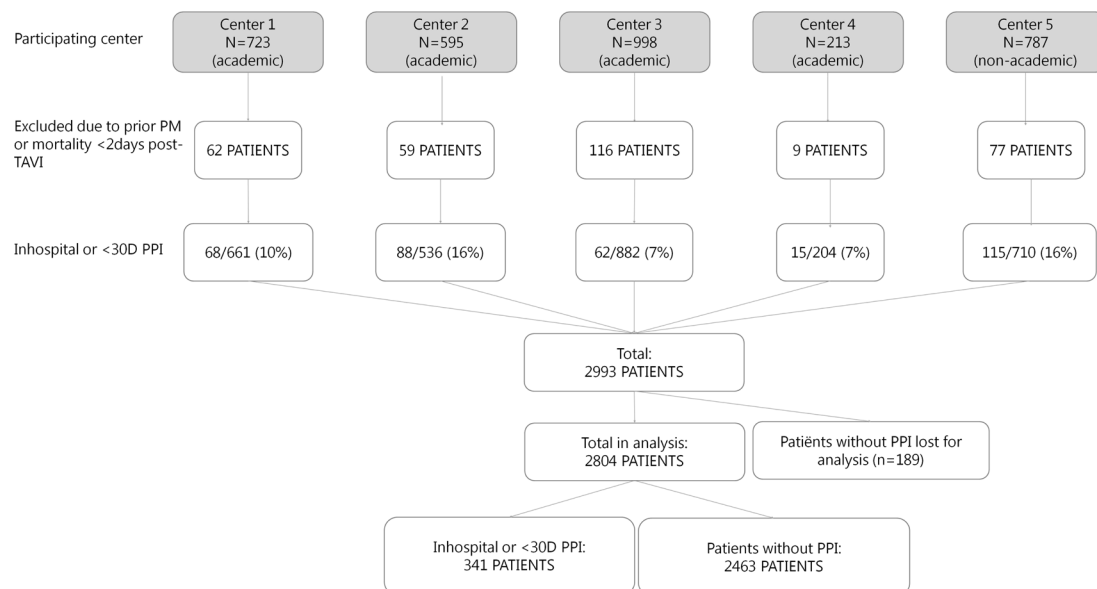
Figure 1 Study flow diagram of patients who underwent transcatheter valve implantation of each participating centre.

Table 1 Baseline characteristics

	Overall (n=2804)	No PPI (n=2463)	PPI group ECP (n=280)	PPI group LCP (n=61)	P value
Clinical characteristics					
N	2804 (100)	2463 (88)	280 (10)	61 (2)	
Age (n=2804)	82 (77 to 85)	82 (77 to 85)	82 (77 to 86)	83 (80 to 85)	0.130
Female (n=2804)	1556 (55.5)	1380 (56.0)	146 (52.1)	30 (49.2)	0.280
Logistic EuroSCORE (%) (n=2802)	15 (10 to 24)	15 (10 to 24)	16 (10 to 23)	15 (10 to 26)	0.641
Comorbidities					
Diabetes mellitus (n=2804)	804 (28.7)	709 (28.8)	80 (28.6)	15 (24.6)	0.773
Hypertension (n=2803)	1895 (67.6)	1681 (68.3)	168 (60.0)	46 (75.4)	0.008*
CAD (n=2801)	1363 (48.7)	1194 (48.5)	134 (47.9)	35 (57.4)	0.379
Prior CABG (n=2803)	499 (17.8)	437 (17.7)	46 (16.4)	16 (26.2)	0.190
Chronic pulmonary disease (n=2804)	742 (26.5)	657 (26.7)	68 (24.3)	17 (27.9)	0.670
Prior aortic valve replacement (n=2615)	83 (3.2)	81 (3.6)	1 (0.4)	1 (1.6)	0.012*
Medication					
- Beta-blocker (n=1954)	1128 (57.7)	945 (58.3)	148 (54.4)	35 (58.3)	0.491
- Anti-arrhytmica (n=1760)	75 (4.3)	61 (4.3)	11 (4.0)	3 (4.9)	0.940
- Digoxin (n=1910)	193 (10.1)	166 (10.2)	20 (8.7)	7 (12.1)	0.677
Baseline ECG					
Atrial fibrillation (n=2804)	969 (34.6)	841 (34.1)	102 (36.4)	26 (42.6)	0.305
Prior 1d AVB (n=1928)	438 (22.7)	364 (22.4)	64 (24.9)	10 (20.4)	0.632
PQ time (ms) (n=1634)	180 (160 to 200)	178 (160 to 200)	185 (163 to 212)	178 (157 to 200)	0.029*
QRS width (ms)(n=2088)	102 (92 to 122)	102 (90 to 118)	110 (94 to 144)	108 (96 to 127)	<0.001*
Intraventricular conduction disturbances (n=2544)					
- No CDs	1761 (69.2)	1577 (71.6)	149 (53.2)	35 (57.4)	<0.001*‡
- IVCD	188 (7.4)	162 (7.4)	15 (5.4)	11 (18.0)	0.003‡†
- LBBB	316 (12.4)	288 (13.1)	22 (7.9)	6 (9.8)	0.037*§
- RBBB	279 (11.0)	176 (8.0)	94 (33.6)	9 (14.8)	<0.001*†
Echocardiography/CT					
AVA (cm²) (n=2547)	0.8 (0.6 to 0.9)	0.8 (0.6 to 0.9)	0.7 (0.6 to 0.9)	0.8 (0.6 to 0.9)	0.423
Aortic peak gradient (mm Hg) (n=2616)	67.7±23.1	67.5±23.0	69.9±23.4	67.4±26.9	0.258
Left ventricle ejection fraction<30% (n=2769)	171 (6.2)	150 (6.2)	16 (5.7)	5 (8.2)	0.770
Functionally bicuspid valve (n=1731)	26 (1.5)	20 (1.4)	6 (2.2)	0 (0.0)	0.382
Ratio Min/Max diameter annulus (n=1610)	0.80±0.07	0.80±0.08	0.79±0.07	0.79±0.08	0.170

Values are mean±SD, n (%), or median (IQR).
*P<0.05 No PPI versus ECP.
†P<0.05 ECP versus LCP.
‡P<0.05 No PPI versus LCP.
§Post-hoc analyses not significant.
AVA, aortic valve area; AVB, atrioventricular block; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CDs, conduction disturbances; ECP, early onset conduction disturbances requiring PPI; IVCD, intraventricular conduction disorder; LBBB, left bundle branch block; LCP, late onset conduction disturbances requiring PPI; PPI, permanent pacemaker implantation; RBBB, right bundle branch block.

valve 8%, and for the self-expandable and other valve type 17% and 22%, respectively. The main access route was transfemoral (76%).

Pre-existing LBBB was less frequent in ECP group compared with no PPI (8% vs 13%), whereas pre-existing RBBB was more frequent (34% vs 8%). PQ time and QRS width were significantly larger among patients with ECP versus without PPI (185 (163, 212) ms vs 178 (160, 200) ms, and 110 (94, 144) ms vs 102 (90, 118) ms, respectively). The rate of transfemoral approaches and the ratio of prosthesis size to annulus size were higher among patients with ECP compared with patients without PPI (89% vs 74%, and 1.08 (1.04, 1.15) vs 1.06 (1.02, 1.11), respectively). In the LCP group, we found pre-existing non-specific IVCD and periprocedural postdilation to be more frequent than in the no PPI group (18% vs 7%, and 25% vs 14%, respectively). Indications for PPI are shown in table 3.

Onset of CDs requiring PPI

CDs leading to PPI were in 82% early onset CDs (figure 2). Within 4 days, 94% of all new CDs requiring PPI were identified. The CDs after 4 days account for one-third of the LCP. Although clear differences in incidence of PPI were observed between the different valve types, no significant difference for the valve types was noted with respect to early versus late onset of CDs requiring PPI.

Predictors for onset of CDs requiring PPI

A multivariable analysis (figure 3) was performed to evaluate predictors for both ECP and LCP. Independent predictors for ECP were PQ time (OR: 1.01 (1.00–1.01)), pre-existing RBBB (OR: 6.6 (4.7–9.1)) and predilation (OR: 1.5 (1.1–2.0)) (figure 3A). Prior aortic valve replacement (OR: 0.1 (0–0.7)), transapical approach (vs transfemoral) (OR: 0.4 (0.3–0.7)) and

Table 2   Procedural characteristics

	Overall (n=2804)	No PPI (n=2463)	PPI group ECP (n=280)	LCP (n=61)	P value
Procedural characteristics					
Valve implantation<2014 (n=2804)	1530 (54.6)	1345 (54.6)	148 (52.9)	37 (60.7)	0.537
Valve type (n=2794)					<0.001*
Self-expandable	1028 (36.8)	850 (34.6)	148 (52.9)	30 (50)	
Balloon-expandable	1564 (56.0)	1446 (58.9)	92 (32.9)	26 (43.3)	
Other	202 (7.2)	158 (6.4)	40 (14.3)	4 (6.7)	
Approach (n=2803)					<0.001*
Transfemoral	2122 (75.7)	1824 (74.1)	248 (88.6)	50 (82.0)	
Transapical	428 (15.3)	401 (16.3)	19 (6.8)	8 (13.1)	
Direct transaortic	253 (9.0)	237 (9.6)	13 (4.6)	3 (4.9)	
Predilation (n=2577)	1934 (75.0)	1698 (75.4)	186 (69.4)	50 (86.2)	0.014†
Postdilation (n=2561)	369 (14.4)	315 (13.9)	39 (16.4)	15 (24.6)	0.043‡§
Single valve implantation (n=2104)	2050 (97.4)	1833 (97.7)	164 (94.3)	53 (100.0)	0.012*
Implantation depth LCC in mm (n=221)	7.37±3.54	NA	7.39±3.53	7.32±3.63	0.901
Implantation depth NCC in mm (n=223)	7.86±3.30	NA	7.85±3.18	7.89±3.67	0.929
Prosthesis size (n=2705)	26.35±2.39	26.26±2.35	27.10±2.57	26.85±2.37	<0.001*
Ratio of prosthesis size to annulus size (diameter based) (n=1310)	1.06 (1.02 to 1.12)	1.06 (1.02 to 1.11)	1.08 (1.04 to 1.15)	1.09 (1.01 to 1.13)	0.001*

Values are mean±SD, n (%), or median (IQR).
*P<0.05 No PPI versus ECP.
†P<0.05 ECP versus LCP.
‡P<0.05 No PPI versus LCP.
§Post-hoc analyses not significant.
ECP, early onset conduction disturbances requiring PPI; LCC, left coronary cusp; LCP, late onset Conduction disturbances requiring PPI; NA, not available; NCC, non coronary cusp; PPI, permanent pacemaker implantation.

balloon-expandable valve (vs self-expandable) (OR: 0.3 (0.2–0.5)) were associated with lower rates of ECP.

Independent risk factors for LCP were pre-existing IVCD (OR: 3.3 (1.6–6.7)), pre-existing RBBB (OR: 2.6 (1.2–5.6)), self-expandable valves (OR: 2.5 (1.7–5.0)) and predilation (OR: 3.3 (1.4–7.9)) (figure 3B). The predictive value of the multivariate analysis was confirmed by c-statistics (0.69, 95% CI: 0.63 to 0.76). Most of the patients with LCP (58 out of 59 patients with no missing value of these risk factors, 98%) did have one of these risk factors. Of the patients without ECP and with complete data of these risk factor, none of the risk factors

were present in 219 out of the 2425 patients (9%). The nomogram (online supplementary figure 1) shows the predicted individual risk of developing late CDs requiring PPI. The total score is the sum of the points obtained for each risk factor in the nomogram. For patients with a total score of 98 points or lower (corresponding to a risk of 1.46% or lower), a sensitivity of 90% was achieved for identifying patients with late CDs requiring PPI. Subanalysis of patients including only patients with a strong PPI recommendation according to European guidelines (n=308) revealed size prosthesis as an additional predictor for ECP (OR: 1.1 (1–1.1)), while the predictors for LCP remained unchanged.

Differences per valve type

In a subanalysis of 341 patients requiring PPI, independent predictors for LCP were evaluated per valve type with respect to timing of onset of CDs (figure 4A,B). As shown in figure 4A, patients requiring PPI and with pre-existing IVCD developed CDs after 48 hours in 50% of the cases. In case of a self-expandable valve, these CDs developed relatively late with an onset rate of 30% (n=3) after day four. No significant differences in onset of CDs with respect to pre-existing RBBB or LBBB were observed among valve types. The effect of predilation on patients with LCP is shown in figure 4B. Of 158 patients with a balloon-expandable valve without predilation, only seven patients (4%) needed a PPI. Among these seven, none developed LCP. These 151 patients with a balloon-expandable valve without predilation and without ECP appeared to be not at risk for LCP. In comparison, patients with a balloon-expandable valve in combination with predilation developed LCP after 48 hours in 25% of cases. Patients with an other valve type in combination with predilation developed in all cases the CDs within 48 hours; nevertheless, this subgroup consisted of only 41 patients in total.

Table 3   Indications for 30-day PPI

Indication for PPI	Overall (n=341)	No PPI (n=0)	PPI group ECP (n=280)	LCP (n=61)	P value
3d AVB	256 (75.1)	–	219 (78.2)	37 (60.7)	0.007
Other high-grade AVB	51 (15.0)		36 (12.8)	15 (24.6)	0.033
		–			
1d AVB, LBBB	7		4	3	
AF+LBBB	4		2	2	
Alternating LBBB/RBBB	6		6	0	
Bifascicular block (symptomatic)	3	–	2	1	
2d AVB type 2	4		1	3	
2d AVB type 1+LBBB	2		2	0	
2d AVB type 1+AF	1		0	1	
Trifascicular block	8		7	1	
Unspecified	16		12	4	
Sick-sinus syndrome	34 (10.0)	–	25 (8.9)	9 (14.8)	0.25

Values are n (%)
AF, atrial fibrillation; AVB, atrioventricular block; ECP, early onset conduction disturbances requiring PPI; LBBB, left bundle branch block; LCP, late onset conduction disturbances requiring PPI; PPI, permanent pacemaker implantation; RBBB, right bundle branch block.
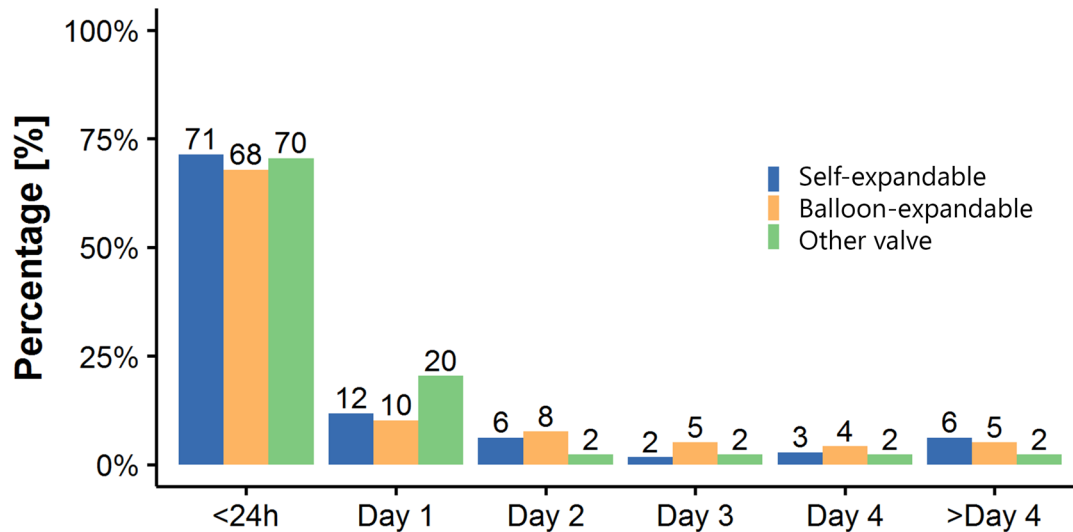
Figure 2 Timing and frequency of onset of conduction disturbances leading to permanent pacemaker implantation, per valve.

Mortality

At 5 year follow-up, all-cause mortality was not statistically significant between the no PPI, ECP and LCP groups (p=0.086, figure 5). HRadj for 5-year mortality were also comparable: ECP versus no PPI; 0.84 (0.67–1.05), p=0.13. LCP versus no PPI; HRadj: 0.69; 95% CI (0.44 to 1.10); p=0.12. LCP versus early onset CDs; HRadj: 0.83; 95% CI (0.50 to 1.36); p=0.45.

DISCUSSION

To our knowledge, we present one of the largest multicentre cohort studies evaluating the timing of onset and associated predictors of LCP after TAVI. Currently, early discharge opportunities are limited by the risk of LCP and evidence regarding onset and risk factors is scarce. The main findings of the present study are that[1] LCP (>48 hours) occurred in 18% of all patients
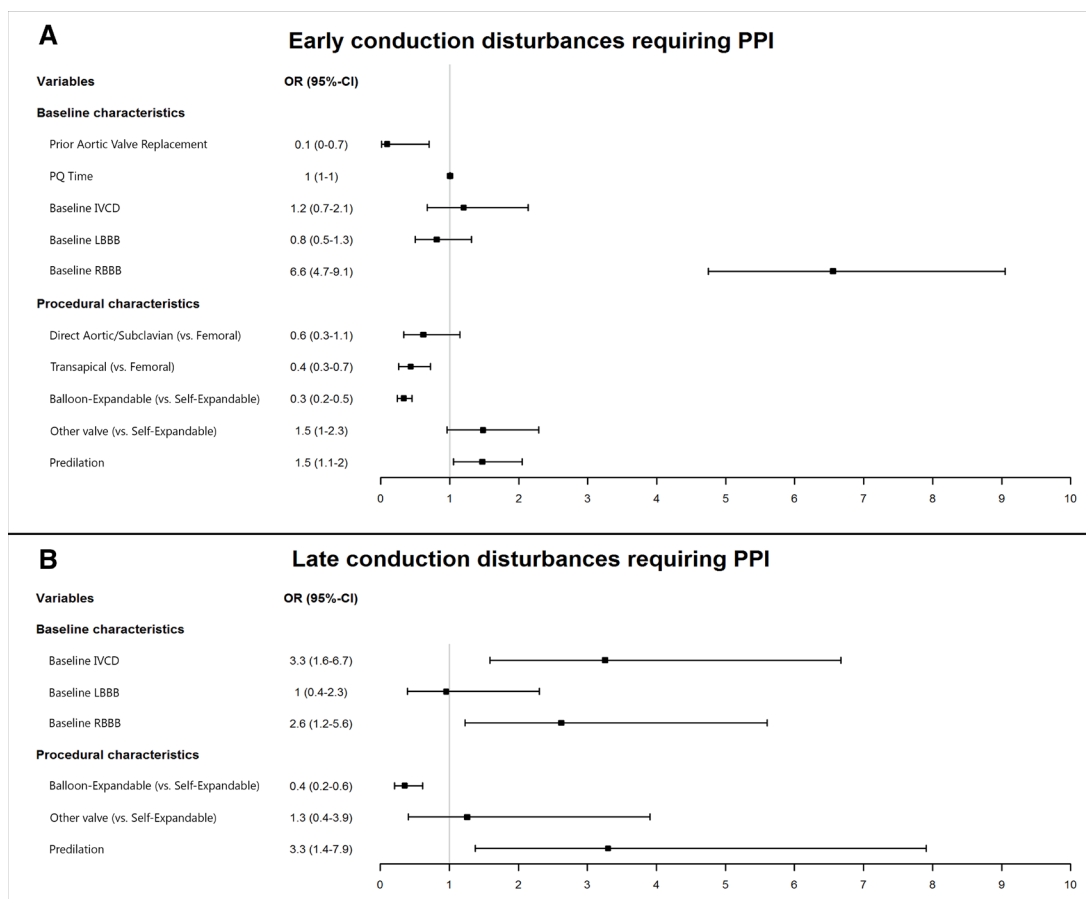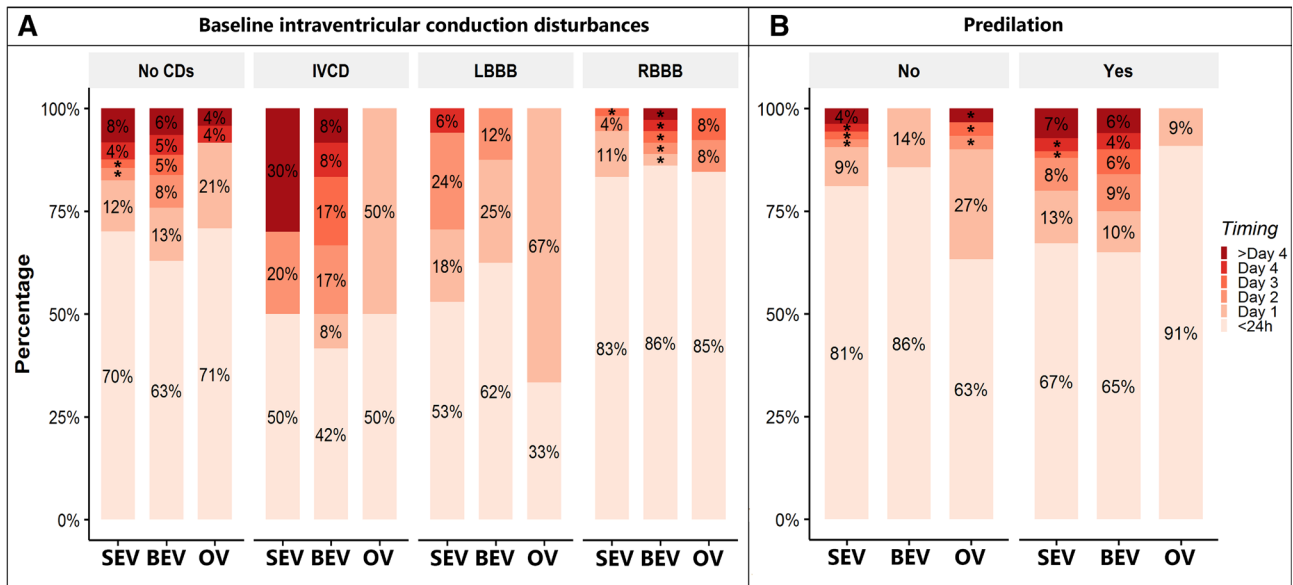

Figure 3 Multivariable predictors of (A) early onset of CDs (<48 hours) versus no CDs and (B) late onset of CDs (>48 hours) versus no CDs requiring PPI. CDs, conduction disturbances; PPI, permanent pacemaker implantation.

Figure 4 Subanalysis of patients requiring PPI, regarding the timing of onset of independent predictors for late CDs, per valve type. (A) Subanalysis of baseline intraventricular CDs and (B) subanalysis of periprocedural predilation. *2%–3%. CDs, conduction disturbances; BEV, balloon-expandable valve; PPI, permanent pacemaker implantation; SEV, self-expandable valve; OV, other valve.

with PPI (2% of study population),[2] independent predictors for LCP appeared to be self-expandable valves, predilation, pre-existing IVCD and pre-existing RBBB,[3] patients with a

balloon-expandable valve without predilation did not develop LCP, and[4] mortality rate did not differ between patients without PPI, ECP and/or LCP.
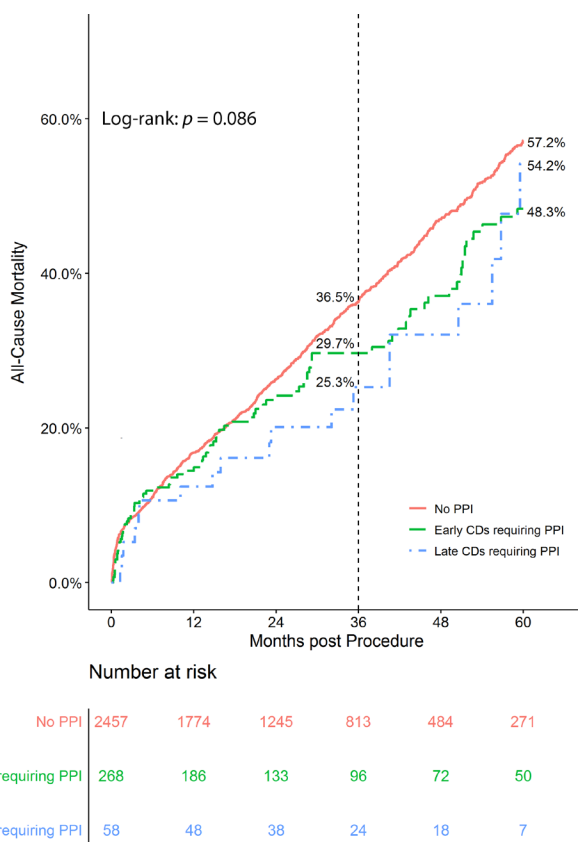
Late onset CDs requiring a PPI after TAVI

The most important finding of our study is that LCP occurred only in 2% of all TAVIs (representing 18% of all patients that required a PPI). Previous studies have reported rates ranging from 4% to 9% in all TAVIs.[7 12] These reported higher rates might be explained by their more strict definition of late onset CDs, that is, the actual presence of advanced CDs with or without PPI indication instead of the onset of CDs requiring PPI. Only one recent study of De-Torres-Alba *et al* studied this actual onset of LCP and found a similar rate of 22%.[13]

Risk factors for late onset CDs requiring a PPI after TAVI

A total of 2% of all patients with TAVI of our cohort developed LCP, and are therefore not considered to be suitable for early discharge. Independent risk factors for LCP appeared to be pre-existing IVCD, pre-existing RBBB, self-expandable valves and predilation. From table 1, it seems as if postdilation would be a greater risk factor then predilation in the LCP group. Indeed, postdilation was a significant risk factor in the univariate analysis. However, in multivariable analyses, the presence of valve type and predilation cancelled out the independent effect of postdilation on LCP. In addition, predilation appeared to be a confounder of valve type and an independent risk factor. No interaction between valve type and predilation was found. The observed independent risk factors in our study are consistent with previous studies regarding baseline RBBB as predictor for late onset CDs.[7 14] We provided three additional independent risk factors, that is, baseline IVCD, valve type and predilation. These independent risk factors were present in 98% of the patients with LCP. Thus, these risk factors could reduce the risks of unrecognised LCP and help to identify patients not suitable for safe early discharge. Another important finding is that the factors prior aortic valve replacement, PQ time, transapical approach and baseline IVCD are different predictors for LCP

Figure 5 Relation of timing of onset of conduction disturbances requiring PPI to all-cause mortality. Kaplan–Meier graph of cumulative incidence of all-cause death up to 5 years according to no PPI, early onset CDs requiring PPI and late onset CDs requiring PPI. CDs, conduction disturbances; PPI, permanent pacemaker implantation.

compared with ECP. Prior aortic valve replacement, PQ time and transapical approach are only associated with ECP. Importantly, baseline IVCD was not associated with ECP but did show a three times greater risk for LCP. Remarkably, none of the 158 patients with both a balloon-expandable valve and without predilation developed LCP. A recent meta-analysis of the impact of balloon predilation found lower PPI rates in patients without predilation.[15] This supports the theory that predilation could result in direct trauma and ischaemia to the conduction system causing early CDs.[16] Additionally, predilation could result in indirect trauma through ongoing tissue inflammation, oedema and haemorrhage, thereby contributing to late CDs after TAVI.[8 17] Our results of the independent risk factors for LCP indicate that possible candidates for safe early discharge are (1) patients without CDs in the first 48 hours after TAVI if no risk factors for LCP are present or (2) if a balloon-expandable valve without predilation was implanted. The nomogram (online supplementary figure 1) helps the clinician to estimate the individual risk for LCP. Nevertheless, to prove the true predictive value and generalisability of this risk model, next step would be external validation. This would be a substantial contribution for clinical practice and would improve the cost-effectiveness of the procedure and patient comfort.

Predictors for timing of onset of CDs in patients requiring a PPI

In addition to these main results, the present study provides several important insights regarding factors influencing the timing of onset of CDs requiring PPI. First, we found that balloon-expandable valves have lower odds to develop both early and LCP compared with self-expanding valves. Unexpectedly, no significant difference regarding ECP vs LCP was observed between the different valve types. Although this difference in pacemaker rates and CDs after TAVI between valve types is well known and partly caused by the higher radial force on the conduction system generated with the deployment of self-expandable valves,[18] we expected the onset of LCP for the self-expandable valve to be more increased as well. Since the radial force on the conduction system of the self-expandable valve is increased due to continued expansion of the frame a few days post-deployment.[19 20] Possible explanations for the lack of differences in LCP between the valves are that the majority of CDs requiring PPI occurred within 48 hours, or that the mechanism for LCP is not driven by valve expansion. Second, our study showed that there was no significant difference in implantation depth between ECP and LCP. This implies that implantation depth does not influence the timing of onset of CDs as well.

Impact of PPI and timing of onset of CDs on survival

No difference in all-cause mortality between the three groups of no PPI, ECP and/or LCP was observed at 5-year follow-up. To date, the prognostic implications for a PPI after TAVI remains controversial.[5] To our knowledge, the long-term mortality rate with a follow-up time over 2 years were addressed only recently by Chamandi et al and Costa et al.[21 22] Chamandi et al reported no differences between patients with and without PPI in total mortality at median follow-up of 4 years. Although borderline statistically significant, the study of Costa and coworkers showed an higher all-cause death rate at 6 years of follow-up for patients with a PPI (KM estimate 41.7% vs 57%; plog-rank=0.034). Remarkably, this higher rate was observed even in patients with PPI that were not pacemaker dependent at 1 month after TAVI.

Key messages

What is already known about this subject?
► Conduction disturbances (CDs) leading to permanent pacemaker implantation (PPI) are common complications following transcatheter aortic valve implantation (TAVI), and usually lead to prolonged post-procedural monitoring, limiting early discharge possibilities.

What does this study add?
► Little is known about the onset and associated predictors of new CDs requiring PPI. However, this is essential for identifying patients for an early and safe discharge.
► Risk factors for late onset of CDs in patients requiring PPI (LCP) are pre-existing intraventricular conduction delay, pre-existing right bundle branch block, self-expandable valves and predilation. At least one of these risk factors was present in 98% of patients with LCP.
► Patients with a balloon-expandable valve without predilation did not develop LCP.

How might this impact on clinical practice?
► Safe early discharge might be feasible in patients without CDs in the first 48 hours after TAVI if no risk factors for LCP are present, or if a balloon-expandable valve without predilation was implanted.

Study limitations

This study consists of a retrospective analysis of prospectively collected data and has the limitations inherent to this study design. The electrocardiograms, implantation depth, indication for PPI and timing of onset of CDs requiring PPI were interpreted at each centre, without core laboratory evaluation. Therefore, the indication for PPI might have been different across centres. Data regarding the timing of decision for PPI and the use of post procedural atrioventricular node–blocking medications, which might have affected the onset of new CDs and need for PPI, were not available. Finally, only new CDs of patients with a PPI post-TAVI were evaluated. Temporary new CDs in the no PPI cohort were not assessed.

CONCLUSIONS

Safe early discharge might be feasible in patients without CDs in the first 48 hours after TAVI if no risk factors for LCP are present, or if a balloon-expandable valve without predilation was implanted. This would be a substantial contribution for clinical practice and would improve the cost-effectiveness of the procedure and patient comfort. Mortality rate was not different between patients with ECP, LCP or patients without PPI.

Conference presentations

Preliminary results were presented at Transcatheter Cardiovascular Therapeutics (TCT) and European Society of Cardiology (ESC) Congress in 2019.[23 24]

Competing interests PRS was a member of the Keystone Heart advisory board.

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Data availability statement No data are available for sharing. The data, analytic methods, and study materials will be made available to other researchers for approved funded reasonable requests to reproduce the results.

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