

# Evaluation of the 2021 European Society of Cardiology guidelines in pre-existing right bundle branch block patients undergoing transcatheter aortic valve implantation with a balloon-expandable valve

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## Aims

The 2021 European Society of Cardiology guidelines recommend early pacemaker implantation in pre-existing right bundle branch block (RBBB) patients who develop PR prolongation or QRS axis change after transcatheter aortic valve implantation (TAVI). We aimed to evaluate this recommendation in TAVI recipients with a balloon-expandable valve (BEV).

## Methods and results

We retrospectively reviewed 188 pre-existing RBBB patients without pre-existing permanent pacemaker (PPM) who underwent TAVI with a BEV at our institution in 2015–19. Patients who developed high-degree atrioventricular block (HAVB) during TAVI or within 24 h post-TAVI were excluded. Eligible patients were divided according to the guideline-directed criteria ( $\Delta$ PR interval  $\geq 20$  ms and/or QRS axis change). Patients who met the criteria ( $n = 102$ , 54.3%), compared with those who did not ( $n = 86$ ), had a higher prevalence of baseline right axis deviation and were more likely to have received a larger valve with greater oversizing. The 30-day delayed HAVB rate did not differ significantly between the groups (3.9% vs. 4.7%,  $P = 1.00$ ; odds ratio = 0.84, 95% confidence interval = 0.20–3.45). There was also no significant difference in terms of death (5.0% vs. 8.4% at 1 year; overall log-rank  $P = 0.94$ ) or a composite of death or PPM implantation (14.8% vs. 16.6% at 1 year; overall log-rank  $P = 0.94$ ) during follow-up post-TAVI. The majority of PR prolongations (79.4%) and QRS axis changes (52.0%) regressed within the following 24 h.

## Conclusion

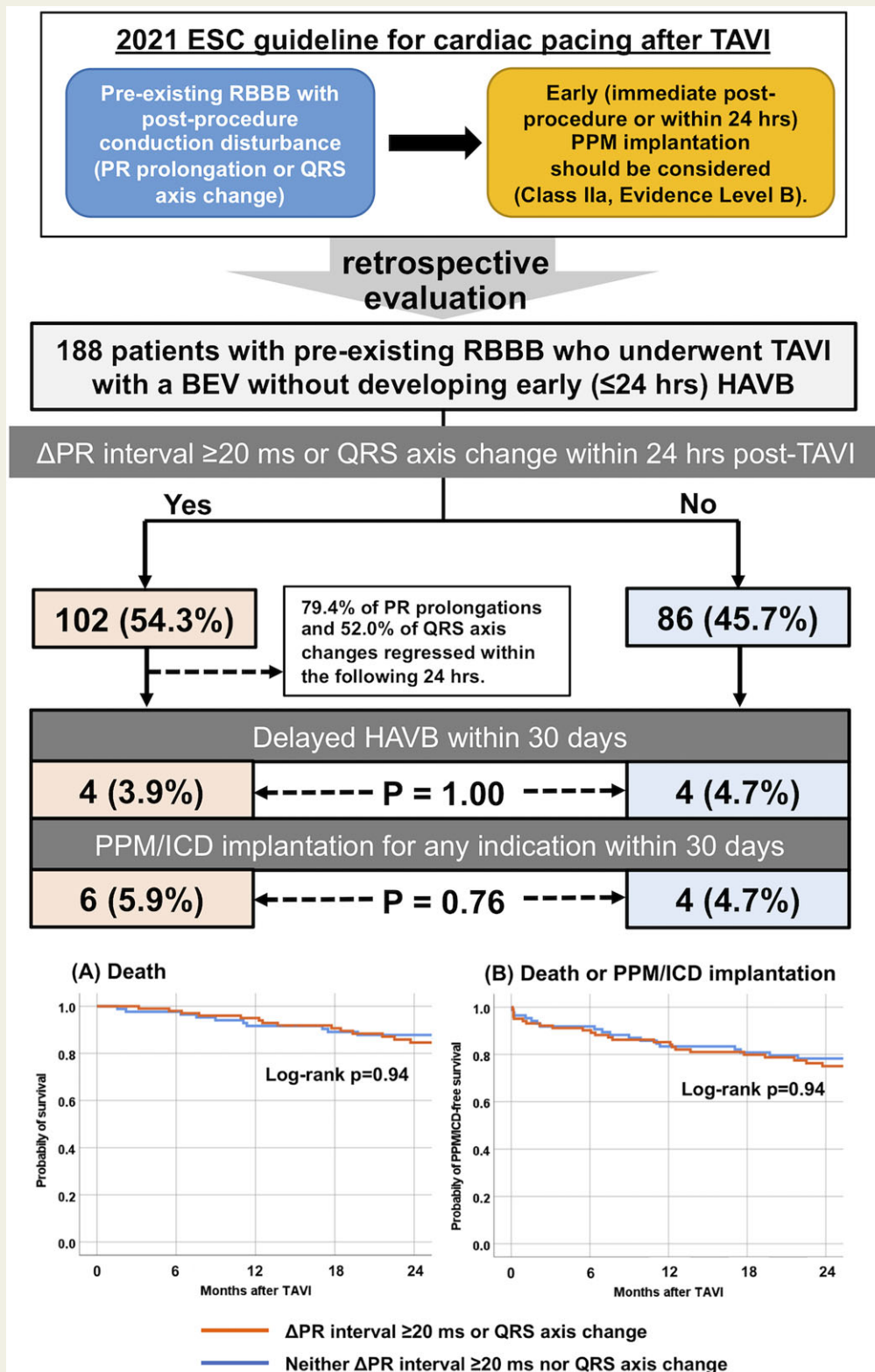
The present data did not demonstrate an association of significant changes in PR interval or QRS axis with heightened delayed HAVB risk in BEV recipients with pre-existing RBBB. Prospective studies are warranted to confirm these findings.

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## Graphical Abstract



## Keywords

Transcatheter aortic valve implantation • Right bundle branch block • High-degree atrioventricular block

## Introduction

Owing to encouraging results from pivotal randomized studies during the last decade, transcatheter aortic valve implantation (TAVI) is a minimally invasive standard treatment for symptomatic severe aortic stenosis.<sup>1</sup> Despite the enhanced safety of TAVI, there has been a relatively stable incidence (~10%) of post-TAVI permanent pacemaker (PPM) requirements in recent years.<sup>2</sup> Amongst several patient factors associated with post-TAVI PPM risk, pre-existing right bundle branch block (RBBB) is the most consistent and powerful predictor.<sup>3</sup> Therefore, a specific post-TAVI management algorithm is generally recommended for pre-existing RBBB TAVI recipients due to the heightened risk of high-degree atrioventricular block (HAVB) post-TAVI.<sup>4</sup>

The 2021 European Society of Cardiology (ESC) cardiac pacing guidelines for the first time offered recommendations post-TAVI, whereby early (immediate post-procedure or within 24 h) PPM implantation should be considered for patients with pre-existing RBBB who develop any further conduction disturbance (defined as transient HAVB, PR prolongation, or QRS axis change) during or after TAVI (Class IIa, Evidence Level B).<sup>5</sup> Such recommendations seem entirely reasonable in patients with pre-existing RBBB who develop peri-procedural HAVB, given the elevated risk of sudden cardiac death due to recurrent events after discharge.<sup>6,7</sup> However, the recommendation has yet to be validated in patients with pre-existing RBBB who developed PR prolongation or QRS axis change (in the absence of peri-procedural HAVB) due to a lack of supporting data. Balloon-expandable valves (BEVs) are associated with lower PPM risk compared with self-expanding valves (SEVs).<sup>8</sup> Therefore, this study sought to evaluate the ESC guideline recommendation for BEV recipients.

## Methods

### Study design

This was a retrospective study conducted at the Cleveland Clinic between January 2015 and December 2019. Data on patient characteristics, electrocardiogram (ECG), imaging data, procedural characteristics, and outcomes were collected from our prospective institutional registries or were manually collected from electronic medical records. Post-discharge outcomes were collected through our institutional electronic medical records in Epic (Epic Systems Corporation, Verona, WI, USA) as well as outside hospital records using 'Care Everywhere' function in Epic. The study was approved by the institutional review board of the Cleveland Clinic with a waiver of informed consent owing to the retrospective nature of the study.

### Patient selection

This study included consecutive adult patients aged  $\geq 18$  years who underwent TAVI at the Cleveland Clinic between January 2015 and December 2019. At our institution, no patient received a 'prophylactic' PPM during pre-TAVI assessment. The exclusion criteria were (i) patients with a pre-existing cardiac implantable electronic device, (ii) those without pre-existing RBBB (QRS duration  $\geq 120$  ms), (iii) those who received a SEV, and (iv) those who already developed HAVB during TAVI or within 24 h post-TAVI. HAVB includes persistent complete heart block (CHB), transient CHB, and advanced atrioventricular block. Advanced

atrioventricular block was defined as (i) Mobitz type II 2nd-degree atrioventricular block or 2:1 or more atrioventricular block in the presence of a QRS duration  $\geq 120$  ms, or (ii) a prolonged pause ( $>3$  s) or a fixed slow ( $<50$  b.p.m.) ventricular response rate in the setting of atrial fibrillation. Eligible patients in the present study were those with pre-existing RBBB who underwent TAVI with a BEV without developing an early ( $\leq 24$  h) HAVB. In this study, automated measurements of PR interval, QRS duration, and QRS axis based on an algorithm devised by GE Healthcare (Chicago, IL, USA) were used. All ECG measurements and tracings were reviewed, verified, and interpreted by two experienced cardiologists according to the standard definitions and guidelines by the American College of Cardiology (ACC)/American Heart Association (AHA)/Heart Rhythm Society (HRS) recommendations.<sup>9,10</sup> Since the ESC guidelines do not stipulate a minimum increase in PR interval for the criterion of PR prolongation, this study defined PR prolongation as  $\geq 20$  ms increase (i.e.  $\Delta$ PR interval  $\geq 20$  ms) from baseline to within 24 h post-TAVI in reference to a recent expert consensus document.<sup>4</sup> The standard definitions by the ACC/AHA/HRA recommendations were used to define three QRS axis categories<sup>9</sup>: normal axis (QRS axis:  $-30^\circ$  to  $90^\circ$ ), left-axis deviation ( $<-30^\circ$ ), and right-axis deviation ( $>90^\circ$ ). Since the ESC guidelines also do not define QRS axis change, this study defined QRS axis change as the change from one baseline axis category to another axis category within 24 h post-TAVI for the main analysis. The eligible patients were divided into two groups according to the presence or absence of the ESC guideline-directed ECG change (PR prolongation and/or QRS axis change).

### Baseline and procedural characteristics

Patient demographics, prior history and comorbidity, echocardiographic parameters, aortic valve data, ECG findings (baseline and post-TAVI), and procedural details were collected for the present analyses. Aortic valve annular parameters were measured using ECG-gated computed tomography (CT) images with contrast pre-TAVI (or cardiac magnetic resonance imaging in patients without pre-TAVI contrast CT due to poor renal function). Calcium score of aortic valve leaflets was quantified using ECG-gated contrast CT images pre-TAVI, where a pre-specified threshold was established to account for the hyperdensity of the applied contrast medium according to a prior study.<sup>11</sup> Calcification at the left ventricular outflow tract was also assessed using pre-TAVI CT images. These imaging data were collected using Aquarius iNtuition (TeraRecon Inc., Foster City, CA, USA). Oversizing was calculated based upon the methods described in a prior study.<sup>12</sup> Implantation depth of the BEV relative to the base of non-coronary cusp (NCC) was defined as the distance between the bottoms of the NCC and the valve stent frame in the final right anterior oblique caudal aortic root angiogram and was measured using SyngoDynamics (Siemens Healthcare, Malvern, PA, USA).

### Outcome measures

The primary outcomes of interest were delayed HAVB and PPM or implantable cardioverter-defibrillator (ICD) implantation within 30 days post-TAVI. Delayed HAVB was defined as any HAVB episode occurring after 24 h and within 30 days post-TAVI. At our institution, the electrophysiology team decided on the need for PPM or ICD implantation in compliance with the ACC/AHA/HRA guidelines.<sup>10</sup> The secondary outcomes were death and PPM/ICD implantation during follow-up. Each patient was followed up until death or the date of the latest visit (in-person or online) or hospitalization on their medical records. Two experienced cardiologists reviewed all death cases and determined whether each death was a sudden death or not. Then, the incidences of sudden death and a composite of sudden death or PPM/ICD implantation were assessed.

## Statistical analysis

Categorical variables were presented as numbers and percentages and were compared using the Fisher's exact test or  $\chi^2$  test. Continuous variables were presented as mean  $\pm$  standard deviation or median and interquartile range (IQR) and were compared using Student's *t*-test or Mann–Whitney *U* test as appropriate. We compared the patient characteristics and outcomes between patients with and without  $\Delta$ PR interval  $\geq 20$  ms and/or QRS axis change. We also examined the consistency of outcome results in the cohort excluding Sapien XT recipients. As a sensitivity analysis, we redefined QRS axis change as an absolute change of  $\geq 30^\circ$  in QRS axis degree (i.e. absolute  $\Delta$ QRS axis  $\geq 30^\circ$ ) and recategorized the patients to compare outcomes. The agreement between the two different definitions of QRS axis change was assessed with the kappa coefficient.

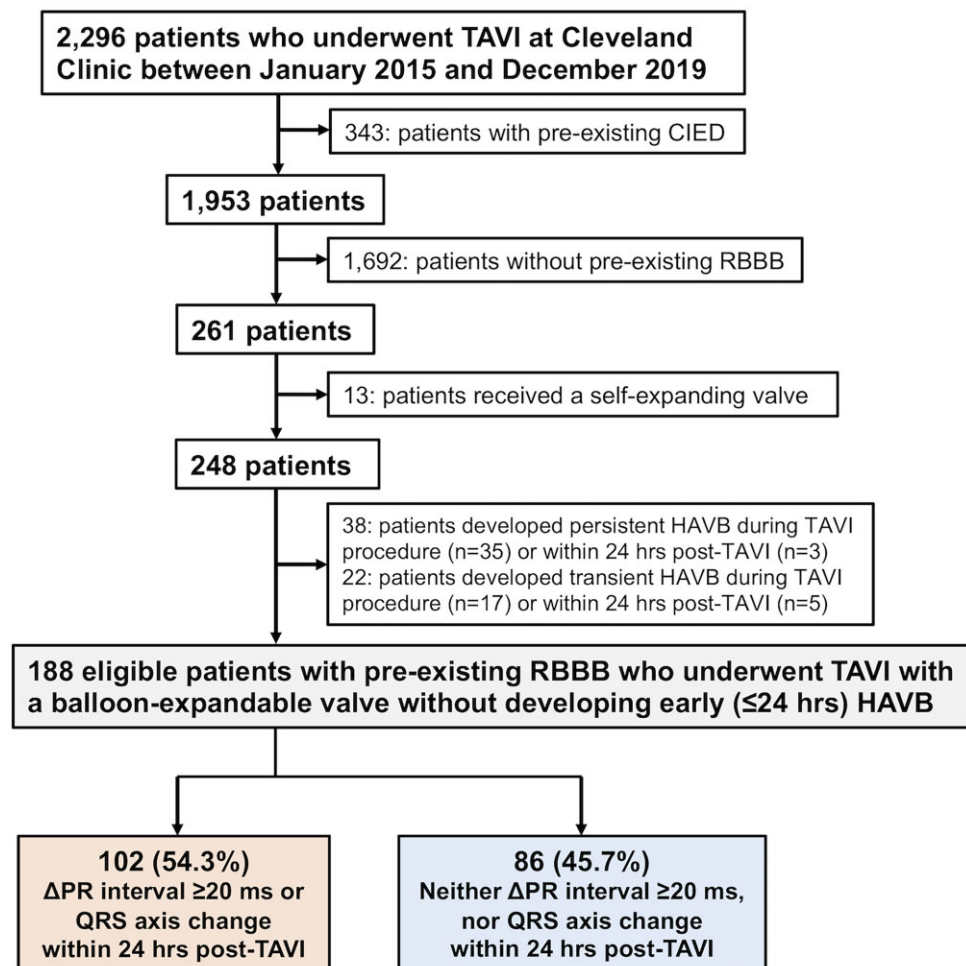
Univariable analysis was conducted to assess potential predictors of delayed HAVB. Predictive values for the guideline-directed ECG change and procedural factors in predicting delayed HAVB were also evaluated. Death and a composite of death or PPM/ICD implantation during follow-up were compared between patients with or without the ECG change using Kaplan–Meier curves with the log-rank test. A two-sided *P*-value of  $<0.05$  was considered significant in all hypothesis tests. All statistical

analyses were conducted using IBM SPSS Statistics, version 27 (IBM Corp., Armonk, NY, USA).

## Results

### Study patients

Figure 1 shows the patient selection for the present study. A total of 188 eligible patients with pre-existing RBBB who underwent TAVI with a BEV without developing early ( $\leq 24$ h) HAVB were identified. Overall, the mean age was  $79.6 \pm 9.2$  years; 24.5% were women; the median Society of Thoracic Surgeons–Predicted Risk of Mortality was 4.59% (IQR 3.26–7.87%); transfemoral approach was used in 93.6%. In total, 102 (54.3%) patients had the guideline-directed ECG change of PR prolongation and/or QRS axis change (52 developed  $\Delta$ PR interval  $\geq 20$  ms alone, 34 had developed QRS axis change alone, and 16 developed both changes) (Supplementary material online, Table S1). Patients with the ECG change, as compared to those without, had a higher prevalence of baseline right axis deviation, were more likely to have received a larger (29 mm) valve with a greater degree



**Figure 1** Patient selection. CIED, cardiac implantable electronic device; HAVB, high-degree atrioventricular block; RBBB, right bundle branch block; TAVI, transcatheter aortic valve implantation.

of valve oversizing (Table 1). Other characteristics did not differ significantly between the two groups. No patient died within 30 days after TAVI.

### Delayed high-degree atrioventricular block and permanent pacemaker implantation

The overall delayed HAVB rate was 4.3% ( $n = 8$ ). There was no significant difference in the delayed HAVB rate (3.9% vs. 4.7%,  $P = 1.00$ ) between patients with or without the guideline-directed ECG change (Table 2). All patients who developed delayed HAVB

received PPM implantation. In addition, two (2.0%) of the patients with the ECG change received PPM/ICD implantation for indications other than HAVB. There was no significant difference in the 30-day PPM/ICD rate (5.9% vs. 4.7%,  $P = 0.76$ ) between the groups. No other patients experienced bradyarrhythmia-related outpatient visits or readmission within 30 days post-TAVI. In the cohort excluding Sapien XT recipients, there was also no significant difference between patients with ( $n = 97$ ) or without ( $n = 82$ ) the ECG change in terms of delayed HAVB (3.1% vs. 4.9%,  $P = 0.70$ ) and 30-day PPM/ICD implantation (5.2% vs. 4.9%,  $P = 1.00$ ), consistent with the main analysis above.

**Table 1** Baseline and procedural characteristics of pre-existing RBBB patients with or without  $\Delta$ PR interval  $\geq 20$  ms or QRS axis change following TAVI

	$\Delta$ PR interval $\geq 20$ ms or QRS axis change ( $n = 102$ )	Neither $\Delta$ PR interval $\geq 20$ ms nor QRS axis change ( $n = 86$ )	P-value
Baseline characteristics			
Age (years)	79.9 $\pm$ 9.0	79.3 $\pm$ 9.4	0.67
Female	28 (27.5)	18 (20.9)	0.31
STS-PROM (%)	4.75 (3.25–7.32)	4.56 (3.32–8.02)	0.85
ESRD on dialysis	2 (2.0)	4 (4.7)	0.41
Left ventricular ejection fraction (%)	57.3 $\pm$ 10.5	56.7 $\pm$ 10.7	0.71
AV mean gradient (mmHg)	42.3 $\pm$ 15.0	43.5 $\pm$ 14.3	0.59
Bicuspid AV	7 (6.9)	3 (3.5)	0.35
Degenerated bioprosthetic valve	5 (4.9)	10 (11.6)	0.11
Calcium score of AV leaflets (HU) <sup>a</sup>	2117 (1138–3340) [ $n = 77$ ]	2308 (1428–2989) [ $n = 62$ ]	0.69
LVOT calcification <sup>b</sup>	50/96 (52.1)	38/76 (50.0)	0.88
Pre-TAVI baseline ECG findings			
Atrial fibrillation rhythm	11 (10.8)	12 (14.0)	0.51
First-degree AVB	38 (37.3)	26 (30.2)	0.36
Bifascicular block	30 (29.4)	22 (25.6)	0.62
QRS axis category			0.030
Normal axis	47 (46.1)	42 (48.8)	
Left-axis deviation	42 (41.2)	42 (48.8)	
Right-axis deviation	13 (12.7)	2 (2.3)	
PR interval (ms)	192 (173–224) [ $n = 91$ ]	188 (163–215) [ $n = 72$ ]	0.30
QRS duration (ms)	147 (138–156)	145 (136–160)	0.87
Procedural details			
Valve generation			1.00
Sapien XT	5 (4.9)	4 (4.7)	
Sapien 3	97 (95.1)	82 (95.3)	
Valve size			0.047
$\leq 23$ mm	32 (31.4)	20 (23.3)	
26 mm	34 (33.3)	44 (51.2)	
29 mm	36 (35.3)	22 (25.6)	
Pre-dilation	17 (16.7)	18 (20.9)	0.46
Post-dilation	48 (47.1)	32 (37.2)	0.19
Oversizing (%) <sup>c</sup>	5.2 (1.0–8.6) [ $n = 99$ ]	3.1 (0.4–6.9) [ $n = 81$ ]	0.025
Implantation depth relative to NCC (mm)	1.7 (0.9–3.2)	2.6 (0.8–3.7)	0.060

Values are  $n$  (%),  $n$ /total  $n$  (%), mean  $\pm$  standard deviation, or median (interquartile range). P-values are not corrected for multiplicity.

AV, aortic valve; AVB, atrioventricular block; CT, computed tomography; ECG, electrocardiogram; HU, Hounsfield unit; ESRD, end-stage renal disease; LVOT, left ventricular outflow tract; NCC, non-coronary cusp; STS-PROM, Society of Thoracic Surgeons-Predicted Risk of Mortality; TAVI, transcatheter aortic valve implantation.

<sup>a</sup>Incalculable in 49 patients due to the lack of contrast CT images pre-TAVI or prior bioprosthetic valve.

<sup>b</sup>Unavailable in 16 patients due to the lack of appropriate CT images pre-TAVI or prior bioprosthetic valve.

<sup>c</sup>Unavailable in eight patients because AV annular data were unavailable due to neither contrast CT images nor cardiac magnetic resonance images.

**Table 2** Delayed HAVB and PPM/ICD implantation within 30 days post-TAVI

	$\Delta$ PR interval $\geq 20$ ms or QRS axis change (n = 102)	Neither $\Delta$ PR interval $\geq 20$ ms nor QRS axis change (n = 86)	P-value
Delayed HAVB	4 (3.9)	4 (4.7)	1.00
Persistent CHB	3 (2.9)	2 (2.3)	1.00
Transient CHB	1 (1.0)	1 (1.2)	1.00
Advanced AVB	0 (0.0)	1 (1.2)	0.46
PPM/ICD implantation for any indication	6 (5.9)	4 (4.7)	0.76
PPM/ICD implantation for delayed HAVB	4 <sup>a</sup> (3.9)	4 <sup>a</sup> (4.7)	1.00
PPM/ICD implantation for other indications	2 <sup>b</sup> (2.0)	0 (0.0)	0.50

CHB, complete heart block; HAVB, high-degree atrioventricular block; ICD, implantable cardioverter-defibrillator; PPM, permanent pacemaker.

<sup>a</sup>All patients receive dual-chamber PPMs.

<sup>b</sup>One patient received leadless PPM on Day 5 for bifascicular block and atrial fibrillation with slow rate response complicated by syncope with no other identifiable cause, while the other received cardiac resynchronization therapy with defibrillator on Day 27 for new-onset worsening left bundle branch block and low left ventricular ejection fraction.

## Sensitivity analysis using another definition of QRS axis change

In the sensitivity analysis using another definition of QRS axis change (i.e. an absolute change of  $\geq 30^\circ$ ), 104 (55.3%) patients had the guideline-directed ECG change of  $\Delta$ PR interval  $\geq 20$  ms and/or absolute  $\Delta$ QRS axis  $\geq 30^\circ$  (53 had  $\Delta$ PR interval  $\geq 20$  ms alone, 36 had absolute  $\Delta$ QRS axis  $\geq 30^\circ$  alone, and 15 had both changes). The agreement between the two different definitions of QRS axis change was moderate (agreement 83.5%; kappa coefficient = 0.58), whereas the agreement between the two overall ECG criteria using  $\Delta$ PR interval  $\geq 20$  ms and different QRS axis change definitions were substantial (agreement 90.4%; kappa coefficient = 0.81). There was no significant difference in delayed HAVB and 30-day PPM/ICD implantation between patients with or without the ECG changes of  $\Delta$ PR interval  $\geq 20$  ms and/or absolute  $\Delta$ QRS axis  $\geq 30^\circ$  (Supplementary material online, Table S2), consistent with the main analysis above.

## Potential predictors for delayed high-degree atrioventricular block

Univariable logistic regression analyses found no significant association between the presence of the guideline-directed ECG change and delayed HAVB risk (odds ratio = 0.84, 95% confidence interval = 0.20–3.45;  $P = 0.81$ ). In contrast, pre-dilation (4.81, 1.14–20.26;  $P = 0.032$ ) and implantation depth relative to the NCC (per 1 mm increase, 1.63, 1.08–2.46;  $P = 0.020$ ) were significantly associated with an increased risk of delayed HAVB (Table 3). Details of the eight patients who developed delayed HAVB are summarized in Table 4. Seven out of eight HAVB events occurred within 7 days after TAVI. Patients who developed delayed HAVB, as compared with those who did not, were more likely to have undergone pre-dilation (50.0% vs. 17.2%,  $P = 0.014$ ) and had a greater implantation depth [2.7 (3.9–4.2) mm vs. 1.9 (0.8–3.4) mm,  $P = 0.009$ ]. All patients who developed delayed HAVB had an implantation depth of  $> 2.0$  mm.

## Regression of electrocardiogram changes

Of the 68 patients who developed  $\Delta$ PR interval  $\geq 20$  ms within 24 h post-TAVI, 54 (79.4%) showed  $\geq 20$  ms decrease in their PR interval within the following 24 h, of whom 1 patient, who had pre-existing tri-

fascicular block, developed delayed HAVB on post-TAVI Day 2 (Case No. 5 in Table 4). Of the 50 patients who developed QRS axis change within 24 h post-TAVI, 26 (52.0%) demonstrated recovery to baseline QRS axis within the following 24 h, none of whom developed delayed HAVB. When we further divided the patients with ECG changes within 24 h post-TAVI according to persistent ECG change (i.e. changes without  $\geq 20$  ms decrease in PR interval or recovery to baseline QRS axis between 24 and 48 h post-TAVI) or not, patients with persistent ECG change ( $n = 36$ ) had numerically higher rates of delayed HAVB (8.3% vs. 1.5%,  $P = 0.12$ ) and 30-day PPM/ICD (11.1% vs. 3.0%,  $P = 0.18$ ) than those without persistent ECG change ( $n = 66$ ).

## Predictive values of electrocardiogram and procedural parameters for delayed high-degree atrioventricular block

$\Delta$ PR interval  $\geq 20$  ms and QRS axis change within 24 h each showed a low positive predictive value (1.5% and 6.0%, respectively) in predicting delayed HAVB (Table 5). Persistent change of the QRS axis between 24 and 48 h post-TAVI showed a higher positive predictive value (12.5%, 3/24) than that (6.0%) of QRS axis change within 24 h. The combination of pre-dilation and implantation depth also showed a relatively high positive predictive value.

## Follow-up outcomes

The median follow-up period after TAVI was 29.4 months (IQR 19.9–41.9 months). Overall, 49 (26.1%) patients died and 22 (11.7%) received PPM/ICD implantation. There was no significant difference between patients with or without the guideline-directed ECG change in terms of death (5.0% vs. 8.4% at 1 year; overall log-rank  $P = 0.94$ ) or a composite of death or PPM/ICD implantation (14.8% vs. 16.6% at 1 year; overall log-rank  $P = 0.94$ ) during follow-up (Figure 2). Sudden death occurred in 6 patients during follow-up (3 with the guideline-directed ECG change died on post-TAVI Day 373, 1025, and 1029; 3 without the ECG change died on post-TAVI Day 67, 898, and 1504). There were no significant differences between the groups in terms of sudden death (0.0% vs. 1.3% at 1 year; overall log-rank  $P = 0.94$ ) and a composite of sudden death or PPM/ICD implantation (9.9% vs. 9.5% at 1 year; overall log-rank  $P = 0.97$ ).

**Table 3** Univariable analyses for delayed HAVB post-TAVI

	Odds ratio	95% CI	P-value
Guideline criteria			
ΔPR interval ≥20 ms or QRS axis change	0.84	0.20–3.45	0.81
ΔPR interval ≥20 ms (N = 157)	0.32	0.03–2.90	0.31
QRS axis change	1.70	0.39–7.38	0.48
Baseline characteristics			
Age, per 1-year increase	1.00	0.93–1.08	0.99
Female	(–)	(–)	(–)
STS-PROM, per 1% increase	0.85	0.64–1.13	0.27
Left ventricular ejection fraction, per 1% increase	0.99	0.93–1.05	0.66
AV mean gradient, per 1 mmHg increase	0.95	0.89–1.00	0.060
Calcium score of AV leaflets, per 100 HU increase (N = 139)	0.95	0.88–1.02	0.18
LVOT calcification (N = 172)	0.56	0.13–2.41	0.43
Pre-TAVI baseline ECG findings			
Atrial fibrillation rhythm	2.52	0.48–13.32	0.28
First-degree AVB	2.00	0.48–8.28	0.34
Bifascicular block	0.36	0.04–3.01	0.35
Procedural details			
Sapien 3 (vs. Sapien XT)	0.33	0.04–2.97	0.32
Valve size			
≤23 mm	(–)	(–)	(–)
26 mm	1.26	0.29–5.48	0.76
29 mm	Reference		
Pre-dilation	4.81	1.14–20.26	0.032
Post-dilation	0.18	0.02–1.52	0.12
Oversizing, per 1% increase (N = 180)	1.06	0.96–1.19	0.26
Implantation depth relative to NCC, per 1-mm increase	1.63	1.08–2.46	0.020

AV, aortic valve; AVB, atrioventricular block; CI, confidence interval; ECG, electrocardiogram; HU, Hounsfield unit; LVOT, left ventricular outflow tract; NCC, non-coronary cusp; STS-PROM, Society of Thoracic Surgeons-Predicted Risk of Mortality; TAVI, transcatheter aortic valve implantation. P-values are not corrected for multiplicity.

## Discussion

This study evaluated the 2021 ESC guideline recommendations for PPM in BEV-TAVI recipients with pre-existing RBBB. The present analysis failed to show an association of the guideline-directed ECG change (PR segment prolongation or QRS axis change post-TAVI) with delayed HAVB risk in pre-existing RBBB patients. The HAVB and PPM requirements appeared to occur at a similar rate regardless of the presence or absence of the guideline-directed ECG change.

### Electrocardiogram changes and delayed high-degree atrioventricular block risk in transcatheter aortic valve implantation recipients with pre-existing right bundle branch block

A recent meta-analysis reported that patients with pre-existing RBBB had a >3-fold higher PPM risk at 30 days post-TAVI than those without pre-existing RBBB (38.1% vs. 11.4%; risk ratio 3.56).<sup>13</sup> Importantly, however, the majority of HAVB events leading to PPM implantation occurred at an early phase (during the TAVI procedure or very shortly thereafter). A Canadian study reported that 88.1%

(52/59) of 30-day HAVB events occurred during the TAVI procedure or very shortly thereafter in pre-existing RBBB patients,<sup>6</sup> which was comparable to that (88.2%, 60/68) in the present study. The risk stratification and workflow of pre-existing RBBB patients without developing early HAVB remain key issues, whereby one has to balance prolonged ECG monitoring post-TAVI (and increasing hospital length of stay) with the risk of being discharged home with a subsequent risk of HAVB. The new ESC guidelines incorporated PR prolongation and QRS axis change in the recommendation in light of current knowledge on the post-TAVI HAVB risk.<sup>5</sup> However, the present analysis failed to unravel an association of the guideline ECG change criteria with delayed HAVB risk. One possible reason for this result is that all patients in the present analysis received a BEV. Nonetheless, the delayed HAVB rate in the present analysis was similar to that (4.5%) of the above-mentioned Canadian analysis that had a ~20% SEV rate.<sup>6</sup> Implantation depth—an important factor determining the propensity for early and delayed HAVB and PPM rates—was not reported in the Canadian analysis.

Post-TAVI PR interval prolongation and QRS axis change are relatively common regardless of subsequent occurrence of delayed HAVB or not because it can be caused by not only a permanent injury of the conduction system but also transient oedema caused by the TAVI

**Table 4** Details of patients who developed delayed HAVB post-TAVI

Case No.	Guideline criteria: $\Delta$ PR interval $\geq 20$ ms/QRS axis change within 24 h	Age/sex	STS-PROM (%)	Pre-TAVI PR/QRS duration (ms)	$\Delta$ PR/ $\Delta$ QRS duration within 24 h post-TAVI (ms)	QRS axis degree ( $^{\circ}$ ), baseline/post-TAVI	Approach, diseased valve, and implanted prosthesis	Pre-/post-dilation to NCC (mm)	Implantation depth relative to NCC (mm)	Type and timing of delayed HAVB	Type of implanted device
1	No/Yes	66 M	2.25	198/166	-6/-6	-36/101	Transaortic, native bicuspid valve, Sapien XT 29 mm	Yes/No	6.1	Persistent CHB, Day 3	Dual-chamber PPM
2	No/Yes	87 M	7.32	218/126	+4/-2	-21/-42	TF, native tricuspid, S3 26 mm	Yes/No	4.1	Persistent CHB, Day 5	Dual-chamber PPM
3	No/Yes	78 M	6.00	AF/144	NA/+16	61/-74	TF, native tricuspid, S3 29 mm	Yes/No	4.2	Persistent CHB, Day 6	Dual-chamber PPM
4	No/No	79 M	5.38	216/152	+4/-8	-55/-37	TF, native tricuspid, S3 26 mm	Yes/No	4.2	Persistent CHB, Day 1 (after 24 h post-TAVI)	Dual-chamber PPM
5	Yes/No	79 M	4.35	344/166 (tri-fascicular block)	+52/+6	-48/-44	TF, native tricuspid, S3 26 mm	No/No	2.2	Transient CHB, Day 2	Dual-chamber PPM
6	No/No	77 M	3.32	AF/156	NA/-6	-68/-66	TF, native tricuspid, S3 26 mm	No/Yes	2.6	AF with advanced AVB, Day 13	Dual-chamber PPM
7	No/No	82 M	2.54	164/152	NA/+8	80/90	TF, native tricuspid, S3 29 mm	No/No	2.7	Persistent CHB, Day 4	Dual-chamber PPM
8	No/No	89 M	4.18	234/126	-30/-6	85/51	TF, native tricuspid, S3 26 mm	No/No	3.7	Transient CHB, Day 2	Dual-chamber PPM

AF, atrial fibrillation; CHB, complete heart block; HAVB, high-degree atrioventricular block. NA, not available; NCC, non-coronary cusp; PPM, permanent pacemaker; S3, Sapien 3; STS-PROM, Society of Thoracic Surgeons-Predicted Risk of Mortality; TAVI, transcatheter aortic valve implantation; TF, transfemoral.



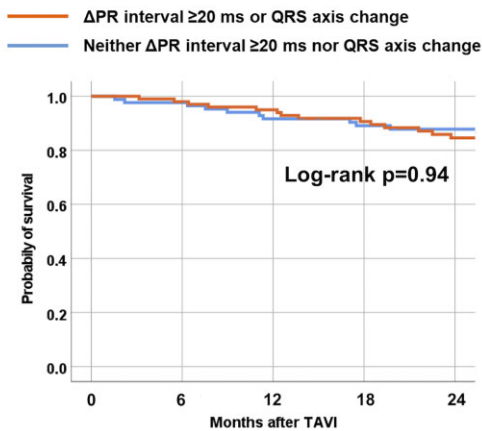
**Table 5** Predictive values for delayed HAVB among patients with pre-existing RBBB who did not developed HAVB within 24 h post-TAVI

	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
ECG changes within 24 h post-TAVI				
ΔPR interval ≥20 ms or QRS axis change	50.0	45.6	3.9	95.3
ΔPR interval ≥20 ms (N = 157)	20.0	55.9	1.5	95.5
QRS axis change	37.5	73.9	6.0	96.4
ECG changes between 24 and 48 h post-TAVI				
Persistent change of PR interval or QRS axis <sup>a</sup>	37.5	81.7	8.3	96.7
Persistent change of PR interval <sup>a</sup> (N = 157)	0.0	90.8	0.0	96.5
Persistent change of QRS axis <sup>a</sup>	37.5	88.3	12.5	97.0
Procedural factors				
Pre-dilation	50.0	82.8	11.4	97.4
Implantation depth >1 mm	100.0	30.6	6.0	100.0
Implantation depth >2 mm	100.0	55.6	9.1	100.0
Implantation depth >3 mm	62.5	70.6	8.6	97.7
Pre-dilation and implantation depth >1 mm	50.0	85.6	13.3	97.5
Pre-dilation and implantation depth >2 mm	50.0	88.3	16.0	97.5
Pre-dilation and implantation depth >3 mm	50.0	90.6	19.0	97.6

ECG, electrocardiogram; HAVB, high-degree atrioventricular block; TAVI, transcatheter aortic valve implantation.

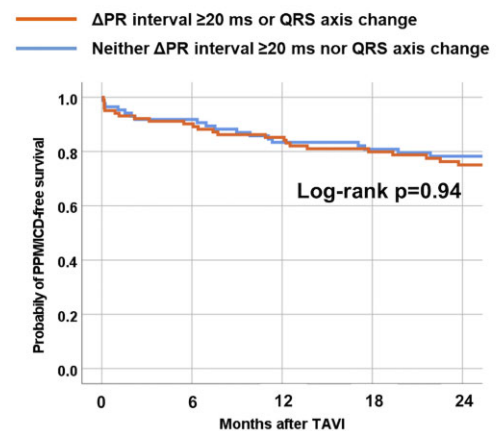
<sup>a</sup>Persistent change of PR interval or QRS axis was defined as ΔPR interval ≥20 ms or QRS axis change that occurred within 24 h post-TAVI and did not show ≥20 ms decrease of PR interval or recovery to baseline QRS axis within the next 24 h, respectively.

**A Death**



No. at risk	0	6	12	18	24
ΔPR ≥20 ms or QRS axis change	102	98	92	78	66
Neither ΔPR ≥20 ms nor QRS axis change	86	82	75	69	62

**B Death or PPM/ICD implantation**



No. at risk	0	6	12	18	24
ΔPR ≥20 ms or QRS axis change	102	90	82	70	59
Neither ΔPR ≥20 ms nor QRS axis change	86	77	68	63	56

**Figure 2** Kaplan–Meier estimates of follow-up outcomes of pre-existing right bundle branch block patients with or without the European Society of Cardiology guideline-directed electrocardiogram change after transcatheter aortic valve implantation with a balloon-expandable valve. ICD, implantable cardioverter-defibrillator; PPM, permanent pacemaker; TAVI, transcatheter aortic valve implantation.

procedure *per se*.<sup>14,15</sup> In our analysis, about one-third of patients developed ΔPR interval ≥20 ms within 24 h post-TAVI, nearly 80% of whom subsequently demonstrated a ≥20 ms decrease of their PR interval within the following 24 h. Similarly, one-quarter of patients developed

QRS axis change within 24 h post-TAVI, of whom about half showed QRS axis recovery towards their baseline axis within the subsequent 24 h. These findings appear consistent with prior serial ECG studies showing that the majority of BEV recipients harbour early (immediately

post-TAVI) ECG change and subsequent (within 24–48 h post-TAVI) recovery.<sup>14–16</sup> The reversibility of those ECG changes may also be related to conflicting results regarding the impact of PR prolongation in prior studies: one study identified  $\Delta$ PR interval as a predictor of delayed HAVB,<sup>17</sup> while another study did not.<sup>18</sup> More importantly, incremental impact of those ECG changes on the HAVB risk in the presence of pre-existing RBBB has yet to be investigated—representing a unique aspect of the present analysis. Although not statistically significant in the present analysis (due to low numbers), our data do suggest that persistent ECG change (particularly, persistent QRS axis change) after 24 h post-TAVI may be more predictive for delayed HAVB than ECG changes detected only within 24 h. Further studies are required to understand the role of PR prolongation and QRS axis change in the post-TAVI risk stratification of pre-existing RBBB patients.

## Relationship between procedural factors and electrocardiogram changes

Since the TAVI procedure can disturb the conduction system via balloon dilation or valve deployment, it appears theoretically reasonable that procedural factors (e.g. pre- or post-dilation and implantation depth of valve) would closely correlate with post-TAVI ECG changes (e.g.  $\Delta$ PR interval,  $\Delta$ QRS duration, QRS axis change). However, there is scarce data on these associations in prior studies. Interestingly, the univariable analysis in the present study found pre-dilation and valve implantation depth relative to the NCC as potential predictors for delayed HAVB. This finding should be cautiously interpreted as it could be affected by multiple testing and was limited by a lack of multivariable adjustment. Nonetheless, the finding may be reasonable from an anatomical perspective<sup>19</sup> because implantation depth is well established as a predictive factor,<sup>5</sup> and pre-dilation was reported to damage infranodal atrioventricular conduction in an electrophysiological study.<sup>20</sup>

## Study limitations

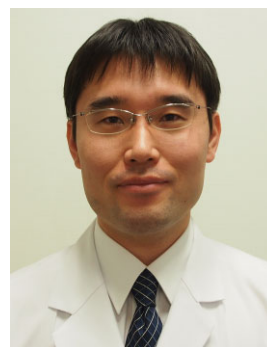
This is a retrospective analysis of a single, high-volume TAVI centre. Given the variability of post-TAVI PPM risk across different hospital settings, our data may not be generalizable to other institutions. This study only included BEV recipients, given the strong preponderance of BEV over SEV at our institution during the study period. Since SEVs are known to be associated with more frequent and delayed ECG changes post-TAVI<sup>15</sup> and subsequent higher PPM risk than BEVs,<sup>8</sup> our data should not be generalized directly to SEV recipients. Although the present study was one of the largest TAVI studies with detailed post-TAVI ECG changes in patients with pre-existing RBBB, the sample size of this study may be too small to evaluate the ESC guideline recommendations. Therefore, larger multicentre studies are warranted to confirm our findings. This study used automated measurements of the PR interval and QRS axis based on a computer-based algorithm, which may have been subject to slight measurement variability.<sup>21,22</sup> We should note that the possibility of asymptomatic transient HAVB following hospital discharge could not be ruled out in this study because ambulatory ECG monitoring was not used routinely for all patients.

## Conclusions

The present analysis evaluates the 2021 ESC guidelines for cardiac pacing in post-TAVI patients with pre-existing RBBB. While most of the HAVB

events typically cluster within the first 24 h post-TAVI, delayed HAVB occurred in 4.3% in our BEV recipients with pre-existing RBBB, supporting the recommendation that early consideration of PPM and more prolonged in-patient monitoring (out to 3–4 days post-TAVI) for those patients at higher risk of delayed HAVB. However, our data failed to demonstrate an association between the proposed ESC guideline criteria (PR prolongation or QRS axis change) and heightened delayed HAVB risk. Larger prospective studies are required to validate the ESC guideline recommendations among TAVI recipients with pre-existing RBBB in the context of ECG changes and procedural factors upon delayed HAVB risk.

## Lead author biography



Toshiaki Isogai, MD, MPH, had been working as a general and interventional cardiologist at Tokyo Metropolitan Tama Medical Center, Tokyo, Japan. He earned his MPH degree at The University of Tokyo in 2014. His research mainly used Japanese large-scale administrative claims and registry data. He commenced his structural heart disease research fellowship at the Cleveland Clinic, OH, USA in 2019.

## Supplementary material

Supplementary material is available at *European Heart Journal Open* online.

## Data availability statement

Data cannot be shared for ethical/privacy reasons.

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**Conflict of interest:** none declared.

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