Outcomes after pacemaker implantation in patients with new-onset left bundle-branch block after transcatheter aortic valve replacement

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New-onset left bundle branch block (N-LBBB) after transcatheter aortic valve replacement (TAVR) is a challenging clinical dilemma. In our single-center study, 60 out of 172 patients who underwent permanent pacemaker implantation (PPM) after TAVR had N-LBBB (34.9%). At a median follow-up duration of 357 days (IQR, 178; 560 days), two patients (3.5%) were completely pacemaker-dependent, and four others (7%) were partially dependent. Twelve patients (24%) recovered conduction in their left bundle at a median follow-up duration of 5 weeks (IQR, 4; 14 weeks). Due to the lack of clinical predictors of pacemaker dependency, active surveillance is warranted and may be an alternative to permanent pacemaker implantation. (Am Heart J 2019;218:128-32.)

Manuscript

Conduction disorders remain a challenging complication after transcatheter aortic valve replacement (TAVR) with high rates of permanent pacemaker (PPM) implantation.[1] The presence of advanced atrioventricular conduction disorders is a clear indication for permanent pacing. However, there is much less certainty regarding the indication for permanent pacing when an intraventricular conduction delay, such as new-onset left bundle branch block (N-LBBB), develops. There is wide variation in the management of these patients, ranging from routine permanent pacemaker placement to surveillance with wearable or implantable cardiac monitoring devices to routine clinical follow-up. Pacemaker implant as reported in many studies is based on clinical judgment and limited data exist on true pacing requirements with N-LBBB. We aimed to assess the pacemaker utilization and dependency rate and natural course of conduction abnormalities in patients who received pacemakers for N-LBBB after TAVR.

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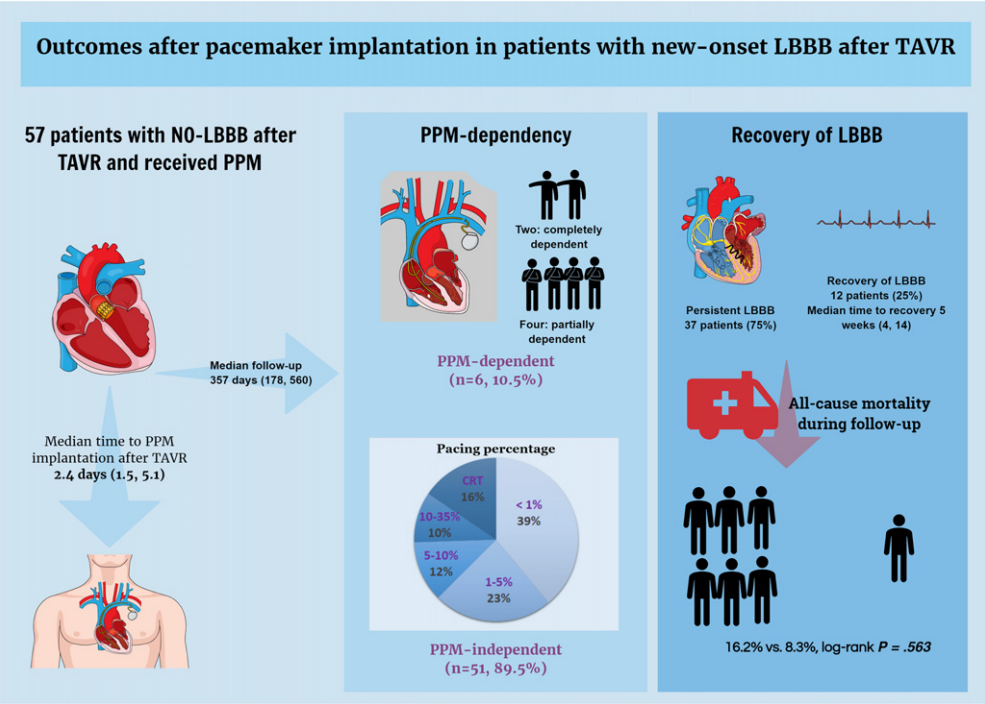
We identified patients at Minneapolis Heart Institute/Abbott Northwestern Hospital, Minneapolis, MN who received a PPM within 1 month after TAVR between January 2010 and May 2017. The following variables were collected for all patients: baseline demographics, peri-procedural TAVR data, electrocardiographic (EKG) findings, the indication of the pacemaker implant, the type of device, follow-up pacemaker data, computed tomography (CT) features, and all-cause mortality. Patients were classified into three categories of pacemaker dependency[1]: not dependent, patients who had less than 40% ventricular pacing and had underlying 1:1 atrioventricular (AV) conduction[2]; partially dependent, patients had more than 40% ventricular pacing despite pacemaker programming to avoid right ventricular (RV) pacing, or we could not exclude the possibility of intermittent high-grade AVB in the presence of significant ventricular pacing; and[3] dependent, complete heart block requiring ventricular pacing. Patients with completed follow-up who did not have biventricular pacing (CRT) were further assessed for resolution of LBBB. The time to recovery was documented based on reviewing subsequent EKGs and thus dependent on the clinical time point of the follow-up EKG rather than a real assessment of time to recovery. All statistical calculations and plots were performed with IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp, Armonk, NY, 2017).

The study flow diagram is illustrated in Figure S1. Of the 720 patients without prior pacemaker who underwent TAVR during the study period, 172 (23.9%) patients underwent pacemaker implantation within 1 month of the

Figure 1



Summary of the study findings (visual abstract).

procedure and typically before discharge. The most common indication was AVB (50.6%, n = 87) followed by N-LBBB (34.9%, n = 60). The N-LBBB was identified either intra-operatively or within 24–48 hours in all patients. Per institutional protocol, all patients who had relatively wide N-LBBB post TAVR underwent prophylactic permanent pacemaker implant. Characteristics of the included patients and procedural characteristics are demonstrated in Table 1.

Median follow-up time was 357 days (IQR, 178; 560 days). Follow-up data were available in 57 patients. Two patients were completely pacemaker dependent, and four others partially dependent. There were no statistically significant differences in baseline patient or procedural characteristics between the two groups (Table 1). The details of the six patients who were pacemaker dependent or partially dependent are illustrated in Table S1. Five patients were deemed pacemaker dependent during their first pacemaker check, and one patient was dependent 9 months after the pacemaker implant. Ventricular pacing rates are illustrated in Figure 1 (visual abstract).

After exclusion of 11 patients who had biventricular pacing or did not have an adequate follow-up with an EKG, 12 patients (24.5%) had recovery of the LBBB during follow-up. The median time to recovery was 5 weeks (IQR 4, 14 weeks). Six patients (50%) recovered from LBBB within 4 weeks of PPM implantation. There was no statistically significant difference in the baseline and procedural characteristics of patients who had LBBB recovery versus those who did not are shown in Table 2. At a median follow up of 357 days (IQR, 178; 560 days), eleven patients died (18.3%). One patient died in the pacemaker-dependent group (16.7%), and nine patients died in the pacemaker-independent group (17.6%). There was no significant difference in all-cause mortality between the LBBB recovery group compared with the non-recovery group (8.3% vs 16.2%, log-rank P = .563) (Figure S2).

In our single-center study, N-LBBB after TAVR was the second most common indication for PPM implantation in our cohort but the vast majority of patients who undergo PPM implantation (~90%) for N-LBBB are not pacemaker dependent in follow-up and 24% of these patients had recovery of their LBBB at a median follow-up duration of 5 weeks. (See Table 3.)

The occurrence of a N-LBBB after TAVR is common with the incidence ranging from 2% to 61%.[2] Although many studies have provided insights on the predictors of post-TAVR N-LBBB,[2] less is known about the implications of LBBB as it relates to pacing requirements. Pacemaker implant as a study end-point is not necessarily a surrogate for pacemaker utilization. In our analysis, we have witnessed a small percentage of N-LBBB patients who would progress to high grade or complete heart block requiring ventricular pacing (3.5%). In the patients who

Table 1. Baseline characteristics of the included patients

	n = 60	Pacemaker-dependent (n = 6)	Pacemaker-independent (n = 51)	*P*
Clinical characteristics, n (%)				
Age (mean± SD)	79.8±8.6	80.7±6.2	79.9±8.7	.85
Male gender	34 (56.7)	5 (83.3)	27 (53)	.33
Diabetes mellitus	30 (50)	4 (66.7)	24 (47)	.63
Hypertension	58 (96.7)	6 (100)	49 (96)	.5
Dyslipidemia	47 (78.3)	5 (83.3)	40 (78.4)	.8
History of atrial fibrillation	22 (36.7)	3 (50)	18 (35.3)	.8
Tobacco use	35 (55)	5 (83.3)	29 (56.9)	.42
Chronic kidney disease (GFR <60)	32 (53.3)	5 (83.3)	24 (47)	.21
Left ventricular ejection fraction				
[<30%], n (%)	6 (10)	0 (0)	5 (9.8)	.97
[30-50%], n (%)	7 (11.7)	0 (0)	7 (13.7)	.76
[>50%], n (%)	47 (78.3)	6 (100)	39 (76.5)	.42
History of CAD	35 (58.3)	3 (50)	31 (60.8)	.94
History of stroke	9 (15)	1 (1.7)	7 (13.7)	.67
History of CABG surgery	15 (25)	1 (16.7)	13 (25.5)	.67
Patient on β-blockers	45 (75)	4 (66.7)	38 (74.5)	.94
STS Score (mean± SD)	5.4±4.4	4.7±1.6	5±2.8	.87
CT features				
Porcelain aorta, (n) %	2 (3.3)	0 (0)	2 (3.9)	.5
Membranous septum length (mm) (mean ± SD)	6.5±1.4 [58] *	6.5±0.9	6.6±1.4 [50] *	.92
Calcification in the non-coronary cusp, n (%)	59 (98.3)	6 (100)	50 (98)	.2
Calcification in basal septum, n (%)	9 (15)	0 (0)	9 (17.7)	.6
Calcification of the left coronary cusp, n (%)	56 (93.3)	5 (83.3)	48 (94.1)	.9

GFR, Glomerular filtration rate; *CAD*, coronary artery disease; *CABG*, coronary artery bypass graft surgery; *STS* score, Society of Thoracic Surgeons surgical risk score.

Table 2. Procedural characteristics

Procedural characteristics n (%)	n = 60	Pacemaker-dependent (n = 6)	Pacemaker-independent (n = 51)	*P*
Pre-TAVR first degree AV block	11 (18.3)	2 (33.3)	8 (15.7)	.61
Pre-TAVR RBBB	2 (3.3)	1 (16.7)	1 (2)	.5
QRS duration after TAVR (ms) (mean ± SD)	152.7±16.8 [56] *	154.3± 16.8	152.5±16.6	.8
Post-TAVR QRS duration ≥150 (ms)	32 (57) [56] *	3 (50)	12 (23.5)	.36
Valve system used [57] *				
Self-expanding valve, n (%)	26	3 (50)	23 (45)	.83
Balloon-expandable valve, n (%)	28	3 (50)	25 (49)	.69
Other valves, n (%)	3	0	3 (5)	.72
Time from TAVR to PPM implantation (days) median (IQR)	2.4 (1.5, 5.1)	1.5 (1.4, 5.3)	2.3 (1.4, 4.6)	.92
Implantation depth (mm) (mean± SD)	5.6±2 [34] *	5±1.5 [3] *	5.4±2 [29] *	.97
Under/over sizing (%) (mean ± SD)	13.3±7.9 [59] *	14.6±11.2	13.2±7.6 [50] *	.7
Transfemoral access, n (%)	53 (88.3)	5 (83.3)	46 (90.2)	.85
Post-dilation, n (%)	8 (13.3)	0 (0)	8 (15.7)	.67
Type of pacemaker				
Dual chamber	42 (70)	4 (66.7)	36 (70.6)	.78
Single chamber	10 (16.7)	2 (33.3)	8 (15.7)	.61
Biventricular AICD	8 (13.3)	0 (0)	7 (13.7)	.75

TAVR, Transcatheter aortic valve replacement; *PPM*, permanent pacemaker; *IQR*, inter-quartile range; *AICD*, automated implantable cardioverter defibrillator; *RBBB*, right bundle-branch block; *ms*, millisecond.
*Numbers between square brackets represent the number of subjects with available data when different from the total number of patients.

were deemed partially dependent, it was challenging to determine the exact clinical relevance of the ventricular pacing percentage. In the two patients who had AF with a slow ventricular response, for example, the risk of life-threatening bradycardia in the absence of ventricular pacing is low; these patients were included in our partially-dependent group solely based on a pre-set definition of 40% ventricular pacing as being potentially clinically relevant.

Our results are in line with to the MARE study "The Ambulatory Electrocardiographic Monitoring for the

Table 3. Characteristics of the LBBB recovery versus non-recovery patients

	Recovery of the LBBB (n = 12)	No recovery of the LBBB (n = 37)	*P*
Clinical characteristics n (%)			
Age (mean ± SD)	80±11	80.7±6.8	.78
Male gender	6 (50)	22 (59.5)	.81
Diabetes mellitus	4 (33.3)	18 (48.7)	.70
Hypertension	12 (100)	35 (94.6)	.98
Dyslipidemia	9 (75)	30 (81)	.97
History of atrial fibrillation	4 (33.3)	14 (37.8)	.95
Chronic kidney disease (GFR <60)	5 (41.7)	18 (48.7)	.93
LVEF <30%	0 (0)	1 (2.7)	.55
LVEF 30%-50%	0 (0)	6 (16.2)	.33
LVEF >50%	12 (100)	30 (81)	.25
History of CAD	7 (58.3)	22 (59.5)	.79
History of CABG	3 (25)	8 (21.6)	.88
Peripheral arterial disease	3 (25)	8 (21.6)	.88
STS score	4.1±2	5.1±2.8	.32
Pre-TAVR first degree AVB, n (%)	2 (16.7)	7 (18.9)	.80
Pre-TAVR RBBB, n (%)	0 (0)	1 (2)	.54
CT features			
Porcelain aorta, n (%)	0 (0)	2 (5.4)	.99
Membranous septum length (mm) (mean ± SD)	6.1±1.3	6.7±1.4 [36]	.15
Calcification in the non-coronary cusp, n (%)	12 (100)	36 (97.3)	.55
Calcification in basal septum, n (%)	2 (16.7)	6 (16.2)	.68
Calcification in the left coronary cusp, n (%)	12 (100)	34 (91.2)	.75
Valve system used			
Self-expanding, n (%)	3 (25)	20 (54)	.16
Balloon expandable, n (%)	9 (75)	14 (38)	.06
Others, n (%)	0 (0)	3 (8)	.74
Implantation depth (mm) (mean ± SD)	4.6±1 [7] *	6.1±2 [20] *	.09
Under/over sizing (%) (mean ± SD)	12.2±8.3	13±8.4 [36] *	.77
Transfemoral access, n (%)	12 (100)	32 (86.5)	.43
Post dilation, n (%)	0 (0)	8 (21.6)	.19

SD, Standard deviation; *GFR*, glomerular filtration rate; *CAD*, coronary artery disease; *CABG*, coronary artery bypass graft surgery; *STS* score, Society of Thoracic Surgeons surgical risk score; *TAVR*, transcatheter aortic valve replacement; *PPM*, permanent pacemaker; *IQR*, inter-quartile range; *AICD*, automated implantable cardioverter defibrillator; *RBBB*, right bundle branch block; *LAFB*, left anterior fascicular block; *LPFB*, left posterior fascicular block.
*Numbers in square brackets indicate the number of patients with the reported variable when different from the total number of patients.

Detection of High-Degree Atrio-Ventricular Block in Patients with New-onset PeRsistent LEft Bundle Branch Block after Transcatheter Aortic Valve Implantation." The study reported the one-year results on 103 patients with new LBBB after TAVR.[3] Twenty-one percent of the patients had bradyarrhythmia events (16% had high-grade AVB), and only 10% of those patients required treatment with a pacemaker. Three patients in the MARE study had sudden cardiac deaths (3%) which is similar to the percentage of our patients who were deemed completely dependent on their pacemaker at follow-up.

In the 2018 ACC/AHA/HRS Guidelines, Surveillance for bradycardia in patients with N-LBBB after TAVR is a class IIa recommendation. However, the current goals of early ambulation and discharge create pressure to decide regarding pacemaker implant soon after TAVR. Implanting a PPM is a class IIb recommendation for those patients.[4] The use of electrophysiological studies (EPS) to identify patients at high risk of AVB after TAVR is emerging. However, there is still a need for an optimal definition of an abnormal EPS.[5,6] There is currently a need for more informed clinical decision-making regarding the optimal management of patients with new LBBB after TAVR. Given that only 10% of our cohort were pacemaker-dependent, only 3.5% required significant rescue ventricular pacing, the median duration to LBBB recovery was 5 weeks, and the fact that most patients who were pacemaker-dependent were deemed so during their first pacemaker check, continuous cardiac monitoring for several weeks might be an alternative to permanent pacing in these patients. Nevertheless, despite the small percentage of patients who required permanent pacing, the clinical consequences are significant and thus cardiac monitoring or pacemaker implantation is likely preferable to routine follow-up in the early period after TAVR.

The results of the ongoing "LBBB-TAVI" study (Assessment of the Prognosis of Persistent Left Bundle Branch Block (LBBB)After Transcatheter Aortic Valve Implantation (TAVI) by an Electrophysiological and Remote Monitoring Risk-adapted Algorithm) (NCT02482844) would help guide the clinical decision-making for these patients. Newer technologies are needed to help pace patients transiently in the early

period after TAVR to prevent adverse events until they declare whether they will develop high-grade AV block or recover conduction.

Our study has a few limitations. As a retrospective single-arm study, it carries the inherent limitations of selection bias and the presence of confounders. The main goal of our study was to identify and report the outcomes of the specific cohort of patients who had post-TAVR N-LBBB and received PPMs; our study was not designed to assess the outcomes of patients with N-LBBB with and without pacemaker implants. The low number of patients and events limited the ability to use more robust analysis like regression models to identify predictors of pacemaker dependency although we reviewed several variables including ECG findings and computed-tomography data. Finally, it remains challenging to definitively characterize the clinical need for pacing retrospectively in certain patients. A low pacing percentage identified when pacemaker programming is optimized to prevent ventricular pacing may still be clinically relevant for intermittent or high-grade AVB. Also, patients may also develop intermittent or late AV block that may not be directly related to TAVR but rather intrinsic conduction disease progression.

In our study, 10.5% of patients required significant ventricular pacing and only 3.5% were completely pacemaker-dependent after PPM implantation for N-LBBB after TAVR. One in four patients recovered conduction in their left bundle within the first few weeks. More studies are needed to identify predictors of pacer dependence and guide targeted implantation for N-LBBB given the expanding use of TAVR. Initial pacemaker programming to avoid RV pacing is reasonable given the vast majority do not ultimately require significant ventricular pacing. Active surveillance may be an alternative to PPM implantation in these patients and preferable to routine follow-up given the potential severe clinical consequences of developing sudden AV block.

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