Effects of Left Bundle Branch Block and Pacemaker Implantation on Left Ventricular Systolic Function After Transcatheter Aortic Valve Implantation

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Permanent pacemaker implantation (PPI) and left bundle branch block (LBBB) frequency after transcatheter aortic valve implantation (TAVI) and their effect on left ventricular ejection fraction (LVEF) remain controversial. We evaluated the incidence of PPI and new-onset LBBB after TAVI and their impact on LVEF at 6-month follow-up. Moreover, the impact of right ventricular (RV) pacing burden on changes in LVEF after TAVI was analyzed. The electrocardiograms of 377 patients (age 80 ± 7 years, 52% male) treated with TAVI were collected at baseline, after the procedure, at discharge, and at each outpatient follow-up. LVEF was measured at baseline before TAVI and 6 months after the procedure. Patients were divided into 3 groups according to the occurrence of LBBB, the need for PPI, or the absence of new conduction abnormalities. In patients with PPI, the influence of RV pacing burden on LVEF was analyzed. New-onset LBBB after TAVI occurred in 92 patients (24%), and PPI was required in 55 patients (15%). In patients without new conduction abnormalities, LVEF significantly increased during follow-up (56 ± 14% to 61 ± 12%, p <0.001). Patients with a baseline LVEF ≤50% presented with a significant recovery in LVEF, although the recovery was less pronounced in patients with new-onset LBBB. Moreover, patients with a baseline LVEF ≤50% who received PPI showed an improvement in LVEF at 6 months regardless of the RV pacing burden. New-onset LBBB hampers the recovery of LVEF after TAVI. Among patients with an LVEF ≤50%, pressure overload relief counteracts the effects of new-onset LBBB or RV pacing. **(Am J Cardiol 2022;00:1−6)**

Transcatheter aortic valve implantation (TAVI) has been established as a therapeutic option for patients with symptomatic severe aortic stenosis who cannot undergo surgery or who have a high surgical risk.[1,2] Subsequently, TAVI has been shown to have similar or superior outcomes to surgical aortic valve replacement in patients at intermediate and low surgical risk.[3] New generations of transcatheter valve prostheses have been designed to simplify the TAVI procedure and to reduce TAVI-related complications such as the incidence of stroke and of paravalvular leaks. However, the rate of permanent pacemaker implantation (PPI) after TAVI remains of concern (10.8% in the Society of Thoracic Surgeons-American College of Cardiology Transcatheter Valve Therapy Registry, including 276,316 patients treated with TAVI from 2011 to 2019), and its consequences for prognosis and left ventricular (LV) systolic function are still controversial and not well clarified.[4] In particular, the pacing burden may negatively affect LV systolic function. Currently, data on pacing burden are limited to short-term follow-up. The aim of this study was to investigate the incidence of new-onset left bundle branch block (LBBB) and of new PPI and their impact on LV systolic function measured by left ventricular ejection fraction (LVEF) in a large cohort of consecutive patients who underwent TAVI.

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Methods

A total of 804 consecutive patients with symptomatic severe aortic stenosis who underwent TAVI at the Leiden University Medical Centre (The Netherlands) between November 2007 and November 2017, and in whom a comprehensive 2-dimensional echocardiography at 6-month follow-up was performed, were evaluated. Patients with prior PPI before TAVI and patients who underwent a valve-in-valve procedure were excluded. A comprehensive clinical evaluation before TAVI was performed, and data were collected in the departmental Cardiology Information System (EPD-Vision; Leiden University Medical Center, Leiden, The Netherlands) and analyzed retrospectively. TAVI was performed after discussion in a dedicated heart team. The

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need for patient written informed consent was waived by the institutional review board of the Leiden University Medical Center owing to the study design, which concerns retrospective analysis of clinically acquired data. The data underlying this article will be shared on reasonable request to the corresponding author.

Patients were implanted with balloon-expandable prosthesis (SAPIEN Edwards, SAPIEN XT, SAPIEN 3) or with self-expandable devices (Medtronic CoreValve or CoreValve Evolut R). Selection of the device size was based on measurements of the aortic root anatomy and of the aortic annulus on preprocedural dynamic multidetector row computed tomography (MDCT). TAVI was performed via transfemoral access, if adequate ilio-femoral arterial anatomy was present as assessed with multidetector row computed tomography, or through transsubclavian or transapical access otherwise. Positioning and deployment of the device was performed under fluoroscopic guidance, or by using combined fluoroscopic and transesophageal or transthoracic echocardiography guidance under conscious sedation, or general anesthesia. A temporary pacemaker lead was used for rapid right ventricular (RV) pacing during balloon predilation and during implantation of the prosthesis.

Electrocardiograms (ECG) were performed at hospital admission before TAVI, immediately after the procedure, at hospital discharge, and at each outpatient clinical follow-up. Calibration of the ECG was set at 0.1 mV/mm, and the paper speed was 25 mm/s. Heart rhythm, PR interval duration, QRS width, and the presence of atrio-ventricular block (AVB) and/or BBB were assessed. A first-grade AVB was defined as a PR interval ≥200 ms. Right BBB (RBBB) was defined as a QRS width ≥120 ms in the presence of typical RBBB morphology (rR' in V1). LBBB was defined as QRS duration ≥120 ms and QRS complex negative in V1 with small R or no R. QRS duration <120 ms was classified as no BBB.

Preoperative transthoracic echocardiography was performed using commercially available ultrasound systems (Vivid 7, Vivid E9 and E95; General Electric Healthcare, Horten, Norway) equipped with 3.5 MHz or M5S-D transducers. Parasternal, apical, subcostal, and suprasternal views were obtained according to current recommendations.[2] The echocardiographic data were digitally stored in cine-loop format, and data were retrospectively analyzed using commercially available software (EchoPac112.0.1; GE Medical Systems, Horten, Norway). LV dimensions and LVEF were assessed. Preoperative aortic valve function was evaluated using color and continuous and pulsed wave Doppler according to current recommendations.[2] Aortic valve area was calculated by the continuity equation and indexed for body surface area. Severe AS was defined according to current recommendations as an aortic valve area <1.0 cm^2, indexed aortic valve area <0.6 cm^2/m^2, or mean transvalvular pressure gradient ≥40 mmHg.[2]

At each ECG performed at follow-up, the presence of a new LBBB was documented, and any admission for new PPI was recorded. The PPI decision relied on criteria according to current guidelines[5] and was reported in every case. Patients were divided into 3 groups based on the presence of new-onset LBBB, PPI due to total AV block within 45 days from the procedure, or the absence of new conduction abnormalities. A comprehensive echocardiographic evaluation before TAVI and 6 months after the procedure was available in all subjects included. In addition, all patients were followed up for the occurrence of all-cause mortality.

Continuous variables are presented as mean±standard deviation or as the median (interquartile range) and categorical variables as frequencies (%), as appropriate. Comparisons of continuous variables across groups were assessed using the 1-way analysis of variance, and the chi-square or Fisher's exact test was used for comparison of categorical variables. For the comparison between 2 time points, a paired Sample *t* test for 2 related samples was used for normally distributed data. In addition, to investigate the influence of RV pacing burden on changes in LVEF over time, general linear models were used, introducing as main factors the categories of RV pacing burden. All analysis were performed with SPSS for Windows, version 23.0 (SPSS, Armonk, New York). All statistical tests were 2 sided. A p value <0.05 was considered statistically significant.

Results

A total of 377 patients formed the study group (mean age 80 ± 7, 52% male). Baseline clinical, echocardiographic, and procedural characteristics are summarized in Table 1.

Before TAVI, 75 patients (20%) were in atrial fibrillation, and 82 patients (22%) presented with sinus rhythm together with AVB (80 patients with first degree, 2 patients with second degree AVB). A total of 96 patients (25%) had baseline intraventricular conduction delay (50 patients RBBB and 46 patients LBBB). After TAVI, 92 patients (24%) developed a new LBBB, and 55 patients (15%) required PPI within 45 days from the day of the procedure. Of these 55 patients, 25 patients (41%) showed new LBBB after TAVI. Of note, 6 patients underwent PPI after the 6-month follow-up echocardiogram.

Complete 6-month follow-up was available in the entire population (as per the inclusion criteria). Three subgroups of patients were identified according to the development of LBBB, the need for PPI within 45 days from the procedure, or the absence of new conduction abnormalities after TAVI. Comparisons of the baseline clinical and echocardiographic characteristics between these three subgroups are shown in Table 2. There were significant differences across groups for body surface area and for TAVI access, with transfemoral access more frequent in the group of patients requiring PPI. In contrast, patients who developed new-onset LBBB had peripheral artery disease more frequently than did the other groups, although this difference was not statistically significant.

Overall, LVEF improved at 6 months after TAVI from 55 ± 14% to 59 ± 12% (p <0.001). In the patients without new conduction abnormalities, LVEF significantly increased during follow-up (56 ± 14% to 61 ± 12%, p<0.001). In contrast, no changes in LVEF were observed in the group of patients requiring PPI and in the group of patients who developed new-onset LBBB (Figure 1).

Changes in LVEF were also analyzed according to baseline LVEF (≤50% vs >50%), as shown in Figure 2. All patients with a baseline LVEF ≤50% presented with a

Table 1
Baseline clinical and echocardiographic patient characteristics

Variable	Overall population (n=377)
Age (years)	80±7
Male	196 (52%)
Body surface area (m^2)	1.85±0.21
NYHA functional class III or IV	226 (60%)
Hypertension	285 (76%)
Dyslipidemia	236 (63%)
Diabetes mellitus	98 (26%)
Peripheral artery disease	122 (32%)
Smoker	93 (25%)
Prior myocardial infarction	74 (20%)
COPD	71 (19%)
Creatinine level (mmol/L)	89 [74-110]
Prior myocardial revascularization (PCI or CABG)	202 (54%)
Logistic EuroScore (%)	17.7±11.1
Medications Use	
Beta-blockers	223 (59%)
Calcium antagonists	89 (24%)
ACEi or ARB	190 (50%)
Baseline echocardiographic parameters	
LVEF (%)	55±14
AVA (cm2)	0.7±0.2
Mean gradient (mmHg)	44±17
Peak gradient (mmHg)	70±26
Procedural variables	
Approach	
Transfemoral	269 (71%)
Transapical	108 (29%)
TAVI type	
Sapien	67 (18%)
Sapien XT	87 (23%)
Sapien 3	163 (43%)
Corevalve	24 (6%)
Corevalve Evolut R	36 (10%)

ACE = angiotensinogen converting enzyme; ARBs=angiotensin II Receptor Blockers; AVA=aortic valve area; CABG=coronary. artery bypass grafting; COPD=chronic obstructive pulmonary disease; LVEF=left ventricular ejection fraction; NYHA=New York Heart Association; PCI=percutaneous coronary intervention.

Data are presented as mean value ± SD or as frequencies and percentages.

significant recovery of LV systolic function at 6-month follow-up; the improvement in LVEF was less pronounced among the patients who developed new-onset LBBB. Among patients with an LVEF ≤50% at baseline, those who developed new-onset LBBB showed worse LVEF at 6-month follow-up than did the other patient groups (47% vs 53% for the no conduction abnormalities group and vs 54% for the PPI group; p = 0.054 and p = 0.004, respectively) (Table 3). Patients with a baseline LVEF >50% who did not develop a new conduction abnormality after TAVI showed an improvement in LVEF. In contrast, the patients who developed LBBB or who underwent PPI showed a significant decrease in LVEF at 6-month follow-up (Table 3).

Among patients who received PPI after TAVI, data on the percentage of RV pacing at the latest available follow-up were analyzed to evaluate the effects on LVEF over time. The median time from PPI to the last interrogation of the pacemaker was 14 months (interquartile range 7 to 30 months). In 25% of the patients, the RV pacing burden was lower than 5%, whereas in 50% of the patients, the pacing burden was 73% or more. Of note, 16% of the PPI patients presented with a ventricular pacing burden of 100%. The association between RV pacing burden and changes in LVEF was not statistically significant (p = 0.072). However, patients with reduced LVEF at baseline (≤50%) showed an improvement in LVEF at 6 months, regardless of the RV pacing burden (Figure 3). In contrast, patients with preserved LVEF at baseline showed a significant impairment in LVEF at 6-month follow-up, even with a low RV pacing burden (Figure 3). These findings suggest that in patients with reduced LVEF, the afterload relief may be the main cause of LVEF improvement, and it is not influenced by RV pacing. In patients with preserved LVEF at baseline, the beneficial effects of afterload relief are counterbalanced by any RV pacing burden.

Discussion

The main findings of the present study can be summarized as (1) the occurrence of new LBBB and of the need for PPI after TAVI remains significant; (2) in the overall population, LVEF improved after TAVI, particularly in patients without new-onset LBBB or PPI requirement; (3) however, LVEF recovery was less pronounced in the subgroup of patients with baseline LVEF ≤50% with a new-onset LBBB than in the group without new conduction abnormalities; and (4) interestingly, LVEF decreased among patients with baseline LVEF >50% who developed a new LBBB or PPI requirement.

Despite growing operator experience and technical improvements in recent years, PPI after TAVI still remains a relatively frequent procedural complication. In the current series, 15% of patients required a PPI after the procedure, without any difference according to the type of valve implanted. In the literature, the incidence of PPI after TAVI showed a high variability, ranging from 4% to 36% according to the type of valve implanted, procedural maneuvers, and patient characteristics.[6]

The incidence of new-onset LBBB after TAVI ranges from 4% to 60%.[7] In the current study, the incidence of LBBB after TAVI was 24%. New-onset LBBB, similarly to PPI requirement, has been more frequently associated with the use of the self-expandable Corevalve prosthesis than with the balloon-expandable SAPIEN valve.[8] However, there are other factors that can increase the risk of new-onset LBBB after TAVI, such as anatomical factors, underlying conduction abnormalities such as atrial fibrillation, and procedural factors such as wire manipulation and balloon valvuloplasty.[9] Nevertheless, it has been suggested that new-onset LBBB may be transient, although other series have not confirmed this hypothesis.[10]

The implications of new-onset LBBB or PPI after TAVI for LV systolic function over time have been less investigated. In the present study, LVEF improved after TAVI in the overall population. In particular, LVEF significantly improved in patients without new conduction abnormalities after the procedure because of the well-known positive effect of afterload relief on LV function. In both the subgroups of patients who developed new LBBB or the

Table 2
Comparison of baseline characteristics between patients who did and did not develop new conduction abnormalities

Variable	No LBBB (n=253)	LBBB (n=92)	PPI (n=55)	p value
Age (years)	80±7	80±6	82±7	0.205
Male	127 (50%)	38 (55%)	31 (56%)	0.604
Body surface area (m^2)	1.83±0.21	1.92±0.21	1.87±0.21	0.004
NYHA functional class III or IV	145 (57%)	49 (71%)	32 (58%)	0.188
Hypertension	185 (73%)	56 (81%)	44 (80%)	0.302
Hyperlipidemia	163 (64%)	37 (54%)	36 (65%)	0.219
Diabetes mellitus	59 (23%)	25 (36%)	14 (25%)	0.099
Peripheral artery diseases	89 (35%)	25 (36%)	8 (15%)	0.009
Smoker	68 (27%)	16 (23%)	9 (16%)	0.241
Prior myocardial infarction	50 (20%)	9 (13%)	15 (27%)	0.140
COPD	54 (27%)	11 (18%)	6 (13%)	0.095
Prior myocardial revascularization (PCI or CABG)	132 (52%)	36 (52%)	34 (62%)	0.440
Logistic EuroScore (%)	18±11	18±11	16±12	0.503
Echocardiographic parameters				
LVEF (%)	56±14	53±15	57±13	0.276
AVA (cm^2)	0.74±0.20	0.76±0.21	0.74±0.22	0.792
Mean gradient (mmHg)	44±16	45±21	45±16	0.779
Peak gradient (mmHg)	70±25	71±32	70±24	0.915
Procedural variables				
Approach				
Transfemoral	169 (67%)	53 (77%)	47 (85%)	0.012

AVA = aortic valve area; CABG=coronary artery bypass grafting; COPD=chronic obstructive pulmonary. disease; LBBB=left bundle branch block; LVE-F=left ventricular ejection fraction; NYHA=New York Heart Association; PCI=percutaneous coronary intervention; PPI=permanent pacemaker implantation.
Data are presented as mean value ± SD or as frequencies and percentages.

requirement of PPI, no changes in LVEF were observed. Interestingly, in patients with preserved LVEF (>50%) at baseline, the occurrence of both new LBBB and PPI showed a negative impact on LVEF after the procedure, in line with the results of previous studies.[10,11] In the study by Eschalier et al,[12] patients who developed LBBB after TAVI showed a decrease in LVEF compared with patients who did not develop LBBB. LBBB is known as a predictor of worse outcomes in patients with cardiovascular disease.[13] This observation is explained by many factors, including ventricular dyssynchrony and adverse cardiac remodeling with a negative impact on LVEF, that eventually lead to heart failure (HF) and an increased risk of complete AVB and arrhythmias. In a meta-analysis involving 17 studies, Regueiro et al[14] showed that new-onset LBBB after TAVI was associated with an increased risk of cardiac mortality and PPI at 1-year follow-up. Of note, in our population, 41% of the patients who needed a PPI showed a new-onset LBBB immediately after TAVI. Interestingly, Klaeboe et al[15] raised some concerns about LBBB after TAVI, suggesting that new-onset LBBB after TAVI did not show the classical ventricular dyssynchrony as observed in HF patients who benefit from cardiac resynchronization therapy.

The systematic follow-up of the patients in the current analysis allowed us to measure the RV pacing burden and correlate it with the changes in LVEF over time. Interestingly, when considering the effect of the percentage of RV pacing on LVEF at follow-up, the deleterious effect on LVEF was more pronounced in patients with preserved LVEF at baseline than in patients with impaired LVEF at baseline. An explanation for these results may rely on the type of LV remodeling that occurs in patients with severe

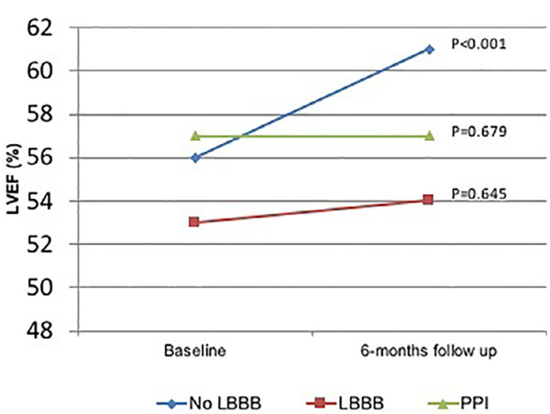

Figure 1. Comparison of LVEF at baseline and at 6-mo follow-up between the three subgroups.

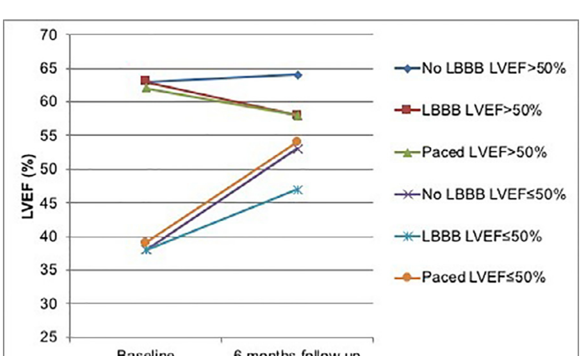

Figure 2. LVEF over time according to baseline LVEF ≤50% and LVEF>50%, the development of new conduction abnormalities, and the need for PPI.

Table 3
Comparison between baseline and 6-month follow-up LVEF in patients with preserved /reduced LVEF (> versus ≤50%) at follow-up, and the development of new conduction defects/need for permanent pacemaker implantation at follow-up

	Baseline LVEF	6 months follow-up LVEF	p value
Follow-up: No LBBB and LVEF≤50% (n=76)	38±8%	53±13%	<0.001
Follow-up: LBBB and LVEF≤50% (n=28)	38±10%	47±15%	<0.001
Follow-up: PPI and LVEF≤50% (n=13)	39±8%	54±9%	<0.001
Follow-up: No LBBB and LVEF>50% (n=177)	63±7%	64±10%	0.192
Follow-up: LBBB and LVEF>50% (n=42)	63±7%	58±8%	0.006
Follow-up: PPI and LVEF>50% (n=41)	62±8%	58±8%	0.014

LBBB = left bundle branch block; LVEF=left ventricular ejection fraction; PPI=permanent pacemaker. implantation.

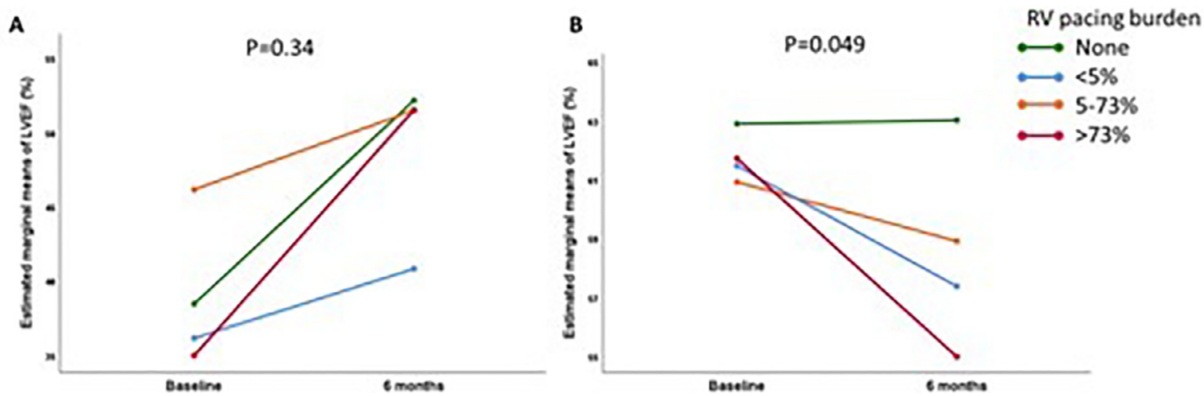

Figure 3. Changes in LVEF according to the percentage of right ventricular pacing. Panel A shows the changes in LVEF for patients with impaired LVEF (≤50%) at baseline whereas panel B shows the changes in LVEF for patients with preserved LVEF at baseline (>50%).

aortic stenosis. These patients develop LV concentric hypertrophy and increased stiffness with increased filling pressures, which eventually results in LV systolic dysfunction. The afterload relief after TAVI may be the main driver of LVEF recovery in patients with impaired baseline LVEF, even if mechanical dyssynchrony occurs because of RV pacing or development of LBBB. In contrast, the negative effect of ventricular dyssynchrony induced by chronic pacing in patients with preserved LVEF may be more deleterious. Nadeem et al[16] investigated the effect of RV pacing after TAVI and demonstrated that LVEF at 1-year follow-up showed a trend towards decline in patients with >40% of paced rhythm. Moreover, in the study by Monteiro et al,[17] the need for PPI within 30 days after TAVI was predictive of LVEF worsening at 1 year follow-up. However, the investigators did not stratify patients according to LVEF at baseline and did not consider the percentage of RV pacing. Chamandi et al[18] showed that PPI was associated with a high risk of HF hospitalization at follow-up that may be partly explained by the deleterious influence of RV pacing on the LV contraction pattern.

The present study has some limitations. This is a single-center, retrospective, observational analysis with its inherent limitations. In this study, we demonstrated that both acquired LBBB and PPI had a negative impact on LVEF after TAVI, but clinical data on patients' functional status at follow-up were not systematically collected. Finally, prospective studies are needed to investigate the role of cardiac resynchronization therapy in this field.

Disclosures

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