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Clinical Research

Impact of New-Onset Persistent Left Bundle Branch Block on Late Clinical Outcomes in Patients Undergoing Transcatheter Aortic Valve Implantation With a Balloon-Expandable Valve

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Objectives The aim of this study was to determine the impact of new-onset persistent left bundle branch block (NOP-LBBB) on late outcomes after transcatheter aortic valve implantation (TAVI).

Background The impact of NOP-LBBB after TAVI remains controversial.

Methods A total of 668 consecutive patients who underwent TAVI with a balloon-expandable valve without pre-existing LBBB or permanent pacemaker implantation (PPI) were included. Electrocardiograms were obtained at baseline, immediately after the procedure, and daily until hospital discharge. Patients were followed at 1, 6, and 12 months and yearly thereafter.

Results New-onset LBBB occurred in 128 patients (19.2%) immediately after TAVI and persisted at hospital discharge in 79 patients (11.8%). At a median follow-up of 13 months (range 3 to 27 months), there were no differences in mortality rate between the NOP-LBBB and no NOP-LBBB groups (27.8% vs. 28.4%; adjusted-hazard ratio: 0.87 [95% confidence interval (CI): 0.55 to 1.37]; $p = 0.54$). There were no differences between groups regarding cardiovascular mortality ($p = 0.82$), sudden death ($p = 0.87$), rehospitalizations for all causes ($p = 0.11$), or heart failure ($p = 0.55$). NOP-LBBB was the only factor associated with an increased rate of PPI during the follow-up period (13.9% vs. 3.0%; hazard ratio: 4.29 [95% CI: 2.03 to 9.07], $p < 0.001$. NOP-LBBB was also associated with a lack of left ventricular ejection fraction improvement and poorer New York Heart Association functional class at follow-up ($p < 0.02$ for both).

Conclusions NOP-LBBB occurred in ~1 of 10 patients who had undergone TAVI with a balloon-expandable valve. NOP-LBBB was associated with a higher rate of PPI, a lack of improvement in left ventricular ejection fraction, and a poorer functional status, but did not increase the risk of global or cardiovascular mortality or rehospitalizations at 1-year follow-up. (J Am Coll Cardiol Intv 2014;7:128–36) © 2014 by the American College of Cardiology Foundation

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The dismal prognosis associated with symptomatic severe aortic stenosis when left untreated is dramatically improved by standard aortic valve replacement (SAVR). However, despite its ability to relieve valvular obstruction, some studies have shown that patients undergoing SAVR have a poorer survival than that expected for the general population due partially to an excess of cardiovascular mortality and, specifically, sudden death (1). Among the factors associated with increased late mortality after SAVR, the occurrence of new-onset left bundle branch block (LBBB) has been associated with a higher risk of sudden death (2,3).

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Transcatheter aortic valve implantation (TAVI) has been established as a therapeutic option for patients with aortic stenosis considered to be at high or prohibitive surgical risk (4). The occurrence of new-onset LBBB is one of the most frequent complications after TAVI (5). Although the incidence and predictive factors of new conduction disturbances after TAVI have been well studied, data on the potential prognostic value of this conduction abnormality are scarce and controversial. Recently, 2 studies using mainly or exclusively the self-expandable CoreValve system (Medtronic, Minneapolis, Minnesota) reported opposite results; whereas Houthuizen et al. (6) showed a higher mortality rate at 1-year follow-up in patients who had a new-onset LBBB after TAVI, Testa et al. (7) failed to show any impact of new-onset LBBB after TAVI on mortality or on the rate of rehospitalizations for heart failure, unlike other previous studies showing that the appearance of new LBBB may trigger heart failure even in patients without overt cardiac disease (8,9). It is known that major differences exist between the self- and balloon-expandable valves regarding the incidence and evolution of conduction disturbances over time (5,10,11), and little evidence exists regarding balloon-expandable valves (11). The aim of this study was, therefore, to determine the impact of new-onset persistent (NOP) LBBB on late clinical outcomes in a large cohort of patients who had undergone TAVI with a balloon-expandable valve.

Methods

Study population. A total of 985 consecutive patients with symptomatic aortic stenosis considered not suitable for or at very high risk of SAVR underwent TAVI with a balloon-expandable valve at 4 centers. Of them, a total of 317 patients were excluded for the following reasons: aborted procedure without valve implantation (n = 20), procedural death (n = 7), previous permanent pacemaker implantation (PPI) (n = 152), pre-existing LBBB (n = 83), and PPI during hospitalization (n = 55). The final study population consisted of 668 patients (St. Paul's Hospital [Vancouver, British Columbia, Canada]: n = 303; Quebec Heart and Lung Institute [Quebec City, Quebec, Canada]: n = 220; St. Michael's Hospital [Toronto, Ontario, Canada]: n = 86; Hospital Universitari Vall d'Hebron [Barcelona, Spain]: n = 59). Of these, 168 patients from both the Quebec Heart and Lung Institute and Hospital Universitari Vall d'Hebron had already been included in a previous study (11). Details on the TAVI procedure are provided elsewhere (4). Data were prospectively collected in a dedicated database at each center. The study protocol was in accordance with the institutional ethics committee of each participating center, and all patients gave informed written consent for the procedures. The need for consent to participate in this research study was waived in view of its observational and anonymous nature. Periprocedural events were defined according to the Valve Academic Research Consensus (VARC) 2 criteria (12).

Electrocardiographic data. Electrocardiographic (ECG) records were obtained from all patients at baseline, immediately after the procedure, and daily until hospital discharge. ECG tracings were analyzed by a cardiologist at each center. The diagnosis of intraventricular conduction abnormalities was based on American Heart Association/American College of Cardiology Foundation/Heart Rhythm Society recommendations for the standardization and interpretation of the electrocardiogram (13). PPI was indicated if third-degree or advanced second-degree atrioventricular block (AVB) was found at any anatomic level that was not expected to resolve after the intervention and for sinus node dysfunction with documented symptomatic bradycardia, in agreement with the American Heart Association/American College of Cardiology Foundation/Heart Rhythm Society guidelines for device-based therapy of cardiac rhythm abnormalities (14).

Abbreviations and Acronyms

AVB = atrioventricular block
CI = confidence interval
ECG = electrocardiographic
IQR = interquartile range
LBBB = left bundle branch block
LVEF = left ventricular ejection fraction
NOP-LBBB = new-onset persistent left bundle branch block
NYHA = New York Heart Association
PPI = permanent pacemaker implantation
SAVR = surgical aortic valve replacement
TAVI = transcatheter aortic valve implantation
VARC = Valve Academic Research Consensus

NOP-LBBB was defined as any new LBBB occurring during the hospitalization period after the TAVI procedure that persisted at hospital discharge, including patients who died during the hospitalization period without proven resolution of the LBBB.

Follow-up. Follow-up was carried out by clinical outpatient visits or telephone interviews at 30 days, 6 months, and 1 year, and yearly thereafter. The median follow-up was 13 months (interquartile range [IQR]: 3 to 27 months), and no patient was lost to follow-up. All clinical events were defined according to the VARC 2 criteria, and any death was

recorded and further classified as of cardiovascular or noncardiovascular cause (12). Any death of unknown cause was considered cardiovascular mortality as recommended by the VARC 2 criteria. Sudden cardiac death was defined as any unexpected death due to cardiac disease that occurred within 1 h after of the onset of symptoms (15). Rehospitalizations for all causes and heart failure were recorded during the follow-up period. Physicians responsible for the patients were contacted and/or medical charts were reviewed to determine the causes of rehospitalization and/or death when necessary.

Transthoracic echocardiography examinations were performed at baseline, at hospital discharge, and at 6- and 12-month follow-up. Echocardiographic data at follow-up were available for 341 patients (83% of the patients who reached the 6- and 12-month follow-up).

Statistical analysis. Qualitative variables are expressed as percentages and compared using the chi-square or Fisher exact test as appropriate. Continuous variables are given as mean ± SD or median (IQR) and compared using a 2-sided *t* test or Wilcoxon rank sum test depending on the variable distribution. Comparisons of clinical outcomes between NOP-LBBB and no NOP-LBBB patients were adjusted for baseline differences between groups using a logistic regression analysis (30-day mortality) or proportional hazards model (late mortality) that included variables with a p value <0.10 on univariate analysis. The following variables were included in the model: age, hypertension, diabetes mellitus, approach, and prosthesis size. A landmark analysis with a landmark cutoff at 30 days was used to further investigate the impact of NOP-LBBB on late mortality. To analyze factors associated with late PPI, a Fine-Gray Cox model was constructed to account for death as a competing risk event for the need of PPI. Survival curves were constructed using Kaplan-Meier estimates, and the log-rank test was used for between-group comparisons. Changes in left ventricular ejection fraction (LVEF) over time between groups were compared using a repeated-measures model with interactions. Further comparisons were performed using the Tukey technique. The predictors of significant LVEF changes over time were determined using a multivariate regression linear model including variables with a p value <0.10 on univariate analysis. Variables included in the model were hypertension, LVEF at baseline, transapical/transaortic approach, and NOP-LBBB. A p value <0.05 was considered statistically significant. Analyses were conducted using the statistical package SAS, version 9.2 (SAS Institute Inc., Cary, North Carolina).

Results

New-onset LBBB occurred in 128 patients (19.2%) immediately after the procedure. Of these, LBBB persisted at hospital discharge in 79 patients (11.8%; 56.4% of patients with new-onset LBBB). Baseline clinical characteristics, ECG and echocardiographic findings, procedural variables, and in-hospital outcomes according to the occurrence of NOP-LBBB are shown in Table 1. Patients who had NOP-LBBB were younger (p = 0.006), had a higher prevalence of hypertension (p = 0.040) and diabetes mellitus (p = 0.005), and more frequently underwent the TAVI procedure through transapical approach (p = 0.005) and received a 29-mm valve (p = 0.041). Transapical approach (odds ratio: 1.90 [95% confidence interval (CI): 1.15 to 3.16]; p = 0.013) and a larger valve size (29-mm valve) (odds ratio: 3.12 [95% CI: 1.22 to 7.97]; p = 0.017) remained as independent predictors of NOP-LBBB in the multivariate analysis.

NOP-LBBB and mortality. At a median follow-up of 13 months (IQR: 3 to 27 months), a total of 189 patients (28.3%) had died; causes of death were classified as noncardiovascular in 75 patients (39.7%) and cardiovascular in 114 patients (60.3%). Sudden death occurred in 7 patients (1.0%, all during the follow-up period).

A total of 22 patients (27.8%) with NOP-LBBB died during the study period, 16 from cardiovascular causes (20.3%, sudden death: 1.3%). There were no differences between the NOP-LBBB and no NOP-LBBB groups regarding overall mortality (NOP-LBBB: 27.8%, no NOP-LBBB: 28.4%; hazard ratio [HR]: 0.83 [95% CI: 0.53 to 1.29]; p = 0.401 [p = 0.431 after adjusting for age differences, p = 0.538 after adjusting for baseline differences]), cardiovascular mortality (NOP-LBBB: 20.3%, no NOP-LBBB: 16.6%; HR: 1.03 [95% CI: 0.61 to 1.76]; p = 0.906 [p = 0.888 after adjusting for age differences, p = 0.820 after adjusting for baseline differences]), or sudden death (NOP-LBBB: 1.3%, no NOP-LBBB: 1.0%; HR: 0.91 [95% CI: 0.11 to 7.65]; p = 0.932 [p = 0.974 after adjusting for age differences, p = 0.872 after adjusting for baseline differences]) (Table 2). This lack of association between NOP-LBBB and mortality persisted when a landmark analysis with a cutoff at 30 days (before and after 30 days) was performed (Table 2). Survival curves for all-cause mortality, cardiovascular mortality, and sudden death are shown in Figure 1.

NOP-LBBB and PPI. Of the 668 patients discharged alive without PPI after TAVI, 29 patients (4.3%), 11 (13.4%) patients with NOP-LBBB and 18 (3.0%) of patients without NOP-LBBB required PPI after a median follow-up of 13 months (IQR: 3 to 27 months). The median time for PPI was 12 months (IQR: 5 to 38 months). PPI was needed due to a high degree of or complete AVB, sinus node dysfunction, symptomatic bradycardia, and slow atrial fibrillation in 16 (55.5%), 6 (20.7%), 4 (13.8%), and 3 (10.3%) patients, respectively. A high degree of or complete AVB was the reason for PPI at follow-up in 8 of the 9 patients with NOP-LBBB. Individual characteristics of patients requiring PPI during the follow-up period are shown in Online Table 1. NOP-LBBB was the only independent predictor of PPI during the follow-up period, even when considering death as a competing risk event (HR: 4.29 [95% CI: 2.03 to 9.07];

Table 1. Baseline and Procedural Variables According to the Occurrence of NOP-LBBB (n = 668)

	No NOP-LBBB (n = 589)	NOP-LBBB (n = 79)	p Value
Clinical characteristics			
Age, yrs	81 ± 8	78 ± 9	0.006
Male	286 (48.6)	39 (49.4)	0.905
Body mass index, kg/m^2	26 ± 6	27 ± 6	0.200
Hypertension	473 (80.3)	71 (89.9)	0.040
Diabetes mellitus	169 (28.7)	35 (44.3)	0.005
COPD	161 (27.3)	22 (27.8)	0.923
NYHA functional class >II	452 (76.7)	62 (78.5)	0.730
eGFR <60 ml/min	260 (44.1)	33 (41.8)	0.719
Coronary artery disease	401 (68.1)	58 (73.4)	0.261
Previous CABG	189 (32.1)	32 (40.5)	0.135
STS-PROM score, %	7.9 ± 4.9	7.6 ± 4.6	0.568
Log EuroSCORE, %	21.2 ± 14.1	20.8 ± 13.9	0.844
Echocardiography			
LVEF, %	56 ± 13	56 ± 11	0.841
Mean gradient, mm Hg	47 ± 17	45 ± 17	0.380
Aortic valve area, cm^2	0.60 (0.50–0.77)	0.62 (0.55–0.78)	0.504
PSAP >60 mm Hg	75 (12.7)	12 (15.2)	0.508
Procedural variables			
Procedural success	531 (90.2)	70 (88.6)	0.668
Valve in valve	25 (4.2)	3 (3.8)	0.999
Approach			
Transfemoral	333 (56.5)	30 (38.0)	0.001
Transapical	237 (40.2)	49 (62.0)	
Transaortic	19 (3.2)	0	
Prosthesis type			
Cribier-Edwards	37 (6.3)	2 (2.5)	0.440
Edwards Sapien	299 (50.8)	46 (58.2)	
Sapien XT	247 (41.9)	31 (39.2)	
Sapien 3	6 (1.0)	0	
Prosthesis size, mm			
20–23	274 (46.5)	35 (44.3)	0.041
26	294 (49.9)	36 (45.6)	
29	21 (3.6)	8 (10.1)	
In-hospital outcomes			
Moderate or more residual AR	74 (12.5)	9 (11.4)	0.763
Myocardial infarction	9 (1.5)	1 (1.3)	0.999
Major vascular complications	50 (8.4)	7 (8.9)	0.922
Major or life-threatening bleeding	124 (21.1)	13 (16.5)	0.342
Dialysis	5 (0.8)	1 (1.3)	0.532
Stroke	14 (2.4)	4 (5.1)	0.254
Death	29 (4.9)	5 (6.3)	0.594

Values are mean ± SD, n (%), or median (interquartile range).

AR = aortic regurgitation; CABG = coronary artery bypass graft; COPD = chronic obstructive pulmonary disease; eGFR = estimated glomerular filtration rate; Log EuroSCORE: Logistic EuroSCORE (European System for Cardiac Operative Risk Evaluation)-predicted risk of mortality; LVEF = left ventricular ejection fraction; NOP-LBBB = new-onset persistent left bundle branch block; NYHA = New York Heart Association; PASP = pulmonary artery systolic pressure; STS-PROM = Society of Thoracic Surgeons predicted risk of mortality.

p < 0.001). Survival curves showing freedom from PPI over time are shown in Figure 2.

NOP-LBBB, rehospitalizations, and functional status. A total of 281 patients (42.1%) needed rehospitalization at a median follow-up of 13 months (IQR: 3 to 27 months), 85 of them (12.7%, 30.2% of total hospitalizations) due to heart failure. There was no association between NOP-LBBB and hospitalizations for all causes (55.7% vs. 40.2%; HR: 1.27 [95% CI: 0.91 to 1.77]; p = 0.154 [p = 0.138 after adjusting for age differences, p = 0.112 after adjusting for baseline differences]) or heart failure (16.5% vs. 12.2%; HR: 1.30 [95% CI: 0.72 to 2.35]; p = 0.390 [p = 0.409 after adjusting for age differences, p = 0.546 after adjusting for baseline differences]) (Table 3).

Differences in New York Heart Association (NYHA) functional class at baseline and follow-up period across the study groups are shown in Figure 3. NOP-LBBB was associated with a poorer NYHA functional class at the 6- and 12-month follow-up (p = 0.015).

NOP-LBBB, valve hemodynamics, and LVEF. Changes in LVEF between baseline and follow-up are shown in Figure 4. The presence of hypertension (estimated coefficient: −3.37 [95% CI: −6.66 to −0.76]; p = 0.045), a higher LVEF at baseline (estimated coefficient: −7.69 [95% CI: −8.72 to −6.66]; p < 0.001), the use of transapical approach (estimated coefficient: −2.89 [95% CI: −5.45 to −0.31]; p = 0.028), and the occurrence of NOP-LBBB (estimated coefficient: −4.70 [95% CI: −8.41 to −0.99]; p = 0.006) were associated with a lower improvement in LVEF over time. In the multivariate analysis, a higher LVEF at baseline and the occurrence of NOP-LBBB were the only independent predictors of the lack of improvement in LVEF at follow-up (estimated coefficients: −7.58 [95% CI: 8.60 to −6.55] and −4.00 [95% CI: −6.91 to −1.10]; p = 0.007, R^2 = 0.422, respectively).

Discussion

The rate of new-onset LBBB of ~20% observed in the present study is similar to that reported in previous studies of TAVI using balloon-expandable valves (5,11,16). Also in accordance with previous studies, about one-half of the conduction disturbances occurring after balloon-expandable valve implantation resolved within the few days after the procedure, leading to a rate of NOP-LBBB of ~10% (11). Previous studies have shown that, unlike transient conduction disturbances, NOP-LBBB is partially determined by factors such as a lower (more ventricular) implantation of the stent valve frame, which is probably associated with more permanent mechanical damage of the left conduction system (11,17,18). Also, the use of both the transapical approach and 29-mm valves was associated with a higher incidence of NOP-LBBB, may be due to a greater damage of the ventricular septum in these cases. However, these observations

Table 2. NOP-LBBB and Mortality After Transcatheter Aortic Valve Implantation

Cause of Death	No NOP-LBBB (n = 589)	NOP-LBBB (n = 79)	p Value
All cause			
Univariate HR/OR			
Cumulative	1.00	0.83 (0.53–1.29)	0.401
≤30 days	1.00	1.26 (0.51–3.01)	0.611
>30 days to maximum	1.00	0.73 (0.44–1.23)	0.240
Age-adjusted HR/OR			
Cumulative	1.00	0.84 (0.53–1.31)	0.431
≤30 days	1.00	1.32 (0.53–3.25)	0.552
>30 days to maximum	1.00	0.73 (0.43–1.24)	0.244
Multivariate-adjusted HR/OR			
Cumulative	1.00	0.87 (0.55–1.37)	0.538
≤30 days	1.00	1.47 (0.57–3.75)	0.423
>30 days to maximum	1.00	0.75 (0.44–1.29)	0.300
Cardiovascular			
Univariate HR/OR			
Cumulative	1.00	1.03 (0.61–1.76)	0.906
≤30 days	1.00	1.26 (0.47–3.35)	0.644
>30 days to maximum	1.00	0.88 (0.45–1.71)	0.702
Age-adjusted HR/OR			
Cumulative	1.00	1.04 (0.61–1.78)	0.888
≤30 days	1.00	1.26 (0.47–3.37)	0.643
>30 days to maximum	1.00	0.88 (0.45–1.73)	0.718
Multivariate-adjusted HR/OR			
Cumulative	1.00	1.07 (0.62–1.85)	0.820
≤30 days	1.00	1.46 (0.53–4.04)	0.468
>30 days to maximum	1.00	0.90 (0.44–1.75)	0.704
Sudden death			
Univariate HR/OR			
Cumulative	1.00	0.91 (0.11–7.65)	0.932
≤30 days	—	—	—
>30 days to maximum	—	—	—
Age-adjusted HR/OR			
Cumulative	1.00	0.97 (0.11–8.20)	0.974
≤30 days	—	—	—
>30 days to maximum	—	—	—
Multivariate-adjusted HR/OR			
Cumulative	1.00	0.84 (0.10–7.39)	0.872
≤30 days	—	—	—
>30 days to maximum	—	—	—

Values are hazard ratio (HR)/odds ratio (OR) (95% confidence interval).
NOP-LBBB = new-onset persistent left bundle branch block.

must be interpreted with caution because this study was not designed to evaluate the predictors of NOP-LBBB.

NOP-LBBB and mortality. The presence of LBBB has been classically considered a marker of poorer long-term survival in patients with pre-existing cardiac disease (8,9) and in apparently healthy individuals without overt disease (8,19). It has been shown that LBBB can affect the hemodynamic and electrical performance of the heart, leading to mechanical

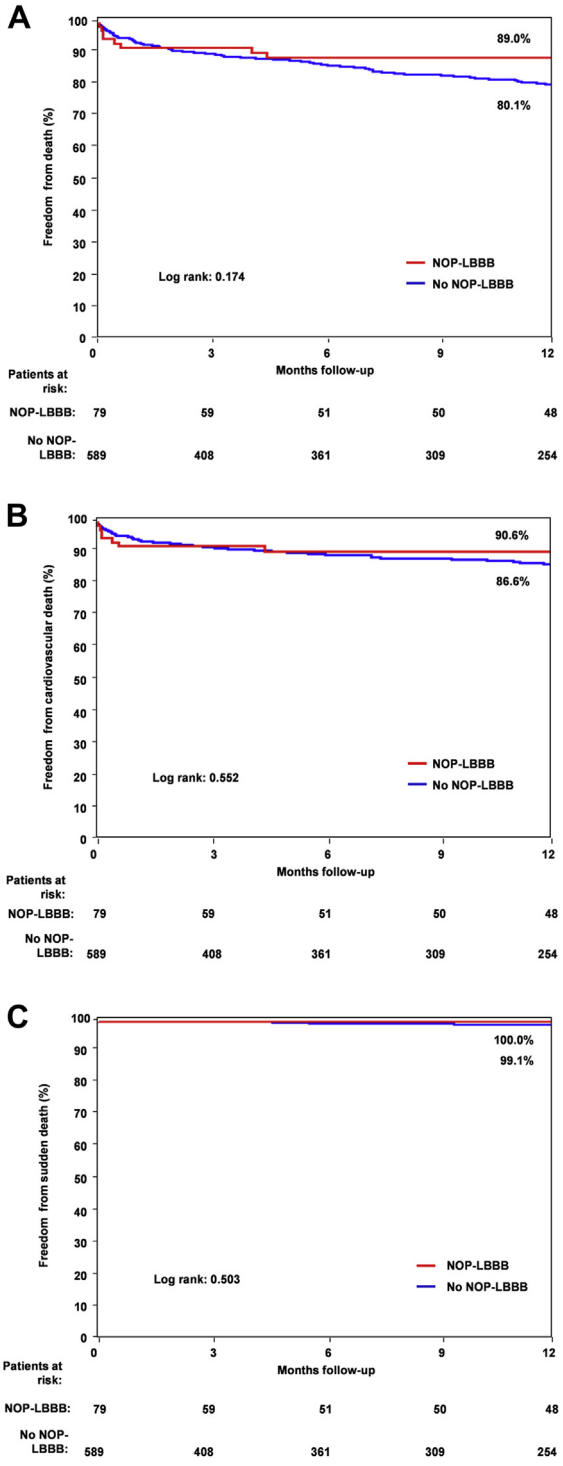

Figure 1. Survival Curves at 1-Year Follow-Up

Kaplan-Meier survival curves at 1-year follow-up for overall mortality **(A)**, cardiac mortality **(B)**, and sudden cardiac death **(C)**, according to the occurrence of new-onset persistent left bundle branch block (NOP-LBBB).

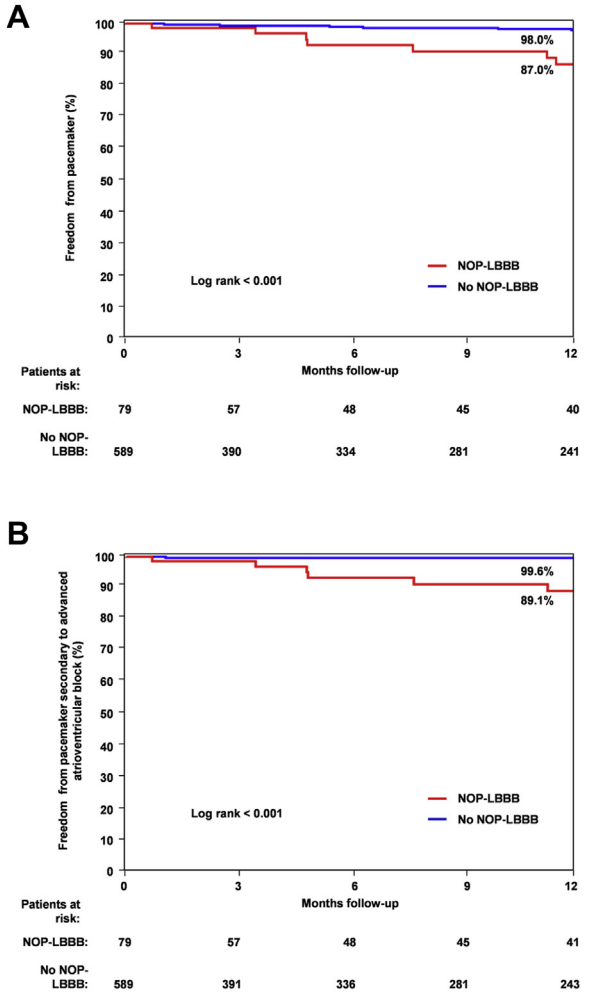

Figure 2. Permanent Pacemaker Implantation at 1-Year Follow-Up

Kaplan-Meier curves at 1-year follow-up showing freedom from permanent pacemaker implantation **(A)** and freedom from pacemaker implantation due to advanced or complete atrioventricular block **(B)**, according to the occurrence of new-onset persistent left bundle branch block (NOP-LBBB).

ventricular asynchrony, which in turn can result in increased end-systolic volumes, septal hypertrophy, abnormal perfusion, and an impairment of systolic and diastolic ventricular performance (20). It is not known, however, whether the presence of LBBB is directly associated with higher mortality or is merely an indicator of the severity of underlying cardiac disorders. Importantly, in most of the studies showing a relationship between LBBB and mortality, the follow-up was very long, ranging from 3 to 30 years (2,3,19,21).

The occurrence of new-onset LBBB after SAVR has been a matter of concern, and studies on the impact of new LBBB on late mortality after SAVR have provided different results (2,3,21–24). The relatively limited sample size of all of these studies, differences between studies regarding inclusion

Table 3. NOP-LBBB and the Risk of Rehospitalization

	No NOP-LBBB (n = 589)	NOP-LBBB (n = 79)	p Value
Rehospitalizations for all causes			
Univariate HR/OR	1.00	1.27 (0.91–1.77)	0.154
Age-adjusted HR/OR	1.00	1.29 (0.92–1.79)	0.138
Multivariate-adjusted HR/OR	1.00	1.32 (0.94–1.86)	0.112
Rehospitalizations for heart failure			
Univariate HR/OR	1.00	1.30 (0.72–2.35)	0.390
Age-adjusted HR/OR	1.00	1.29 (0.71–2.34)	0.409
Multivariate-adjusted HR/OR	1.00	1.21 (0.66–2.22)	0.546

Values are HR/OR (95% confidence interval).
Abbreviations as Table 2.

criteria (any new LBBB vs. only NOP-LBBB), and considerable variability in the length of follow-up may partially explain these differences.

Very few data exist on the clinical impact of new-onset LBBB after TAVI. Three previous studies have shown a negative effect of new-onset LBBB on left ventricular function at 1-year follow-up, with either a lack of improvement or even reduction in LVEF in those patients with new LBBB (11,25,26), in accordance with the results of this study. However, the clinical relevance of these changes in ventricular function remains to be determined. More recently, Houthuizen et al. (6) reported a higher rate of all-cause mortality and cardiovascular mortality at 1-year follow-up in those patients in whom new LBBB after TAVI developed. These results differ from those reported in the present study, in which NOP-LBBB was not associated with any increase in overall or cardiovascular mortality. Although the sample size and length of follow-up were similar in the

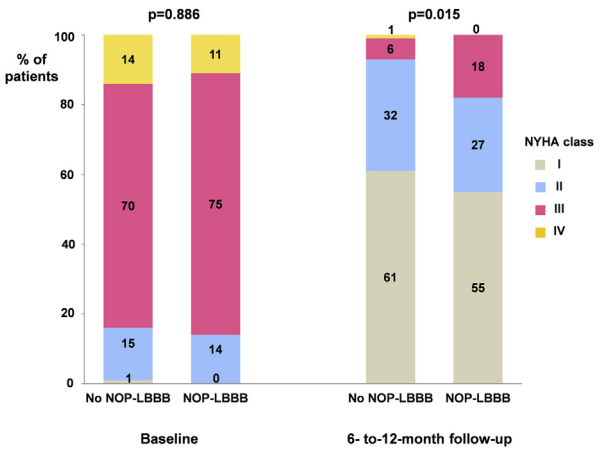

Figure 3. Functional Status and NOP-LBBB

Changes in New York Heart Association (NYHA) functional class over time according to the occurrence of new-onset persistent left bundle branch block (NOP-LBBB).

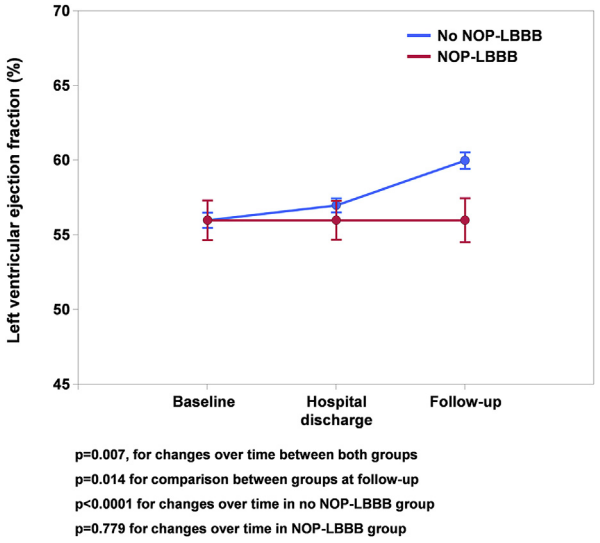

Figure 4. Left Ventricular Ejection Fraction and NOP-LBBB

Changes in left ventricular ejection fraction after transcatheter aortic valve implantation, according to the occurrence of new-onset persistent left bundle branch block (NOP-LBBB).

2 studies, some significant differences should be highlighted. First, the global risk of the patients included in this study was higher (logistic EuroSCORE [European System for Cardiac Operative Risk Evaluation] of ~21% vs. 16%), most likely related to a higher prevalence of cardiac and noncardiac comorbidities, and this also translated into a higher cumulative mortality rate (28.3% vs. 20.6%). The potential clinical impact of new conduction abnormalities after TAVI may differ between moderate- and high-risk patients, partially due to differences in the relative weight of comorbidities in clinical outcomes. Second, the present study included only patients with new LBBB that persisted at hospital discharge, whereas the Houthuizen et al. (6) study included patients with any new LBBB within 7 days after TAVI. This may be particularly relevant when using the balloon-expandable Edwards system (Edwards Lifesciences Corporation, Irvine, California), for which the occurrence of new LBBB is transient (recovery within a few hours or days) in about one-half of the cases (11). Finally, another important difference between the 2 studies is the use of different transcatheter valve systems. Although the present study evaluated only patients who underwent TAVI with a balloon-expandable transcatheter heart valve system, Houthuizen et al. (6) included a mix of self- and balloon-expandable valves, with the majority of patients receiving a self-expandable CoreValve system (Medtronic), and the incidence and evolution over time of conduction disturbances are different between the 2 balloon- and self-expandable valve systems (10,11). In accordance with the results of our study, Testa et al. (7) did not find any association between new LBBB and all-cause and cardiovascular mortality at 1-year follow-up in a large cohort of patients who underwent self-expandable transcatheter valve implantation. Two of the main differences with respect to the Houthuizen et al. (6) study were the inclusion of higher-risk patients (mean logistic EuroSCORE of ~23%) and the inclusion of persistent LBBB (vs. new-onset LBBB). These differences between studies may partially explain the controversial results regarding the clinical impact of new LBBB after TAVI, but this will need to be further evaluated in future studies.

NOP-LBBB and PPI at 1-year follow-up. A high risk of AVB has been observed in patients and individuals without overt cardiac disease in the presence of LBBB (27,28). Previous studies including a relatively small number of patients showed a higher rate of PPI at follow-up among those patients in whom a new LBBB developed after either SAVR or TAVI (2,11,29). The present study confirmed these results in a large cohort of patients who had received a balloon-expandable valve. Of note, patients with NOP-LBBB that progressed toward an advanced or complete AVB accounted for almost one-half (46%) of PPIs required during the first year after TAVI, and 53% of PPIs were due to complete AVB during the study period. After the immediate mechanical injury of the left bundle branch after valve implantation, a further late injury of the conduction system related to an inflammatory or cicatrization process may explain these late conduction disturbances Also, the occurrence of NOP-LBBB may identify a group of patients more prone to the development of conduction abnormalities, which would require PPI at midterm follow-up. Testa et al. (7) found a higher rate of PPI in the NOP-LBBB group at 1 month after TAVI, but this difference was no longer significant at 1-year follow-up. Interestingly, the rate of PPI among patients with new LBBB was 18%, slightly higher than the 13% observed in our study. However, the rate of PPI at 1-year follow-up among patients with no conduction disturbances at hospital discharge was as high as 17%, and this was much higher than the 3% observed in our study. Therefore, the differences between the 2 studies may be explained by the very high rate of PPI during the follow-up period in patients without conduction disturbances after self-expandable valve implantation, much higher than that expected according to the age of the study population. Future studies including a much larger number of patients will be needed to elucidate the factors associated with the progression of conduction disturbances and the need for PPI late after TAVI with balloon- and self-expandable transcatheter valves.

NOP-LBBB, LVEF, functional status, and rehospitalizations. Previous studies have shown the deleterious effect of NOP-LBBB on LVEF after TAVI, with either a lack of improvement or even a decrease in LVEF compared with patients with no new conduction abnormalities (11,25,26). In accordance with these studies, a lack of improvement in LVEF at 6 to 12 months after TAVI was also observed in

the present study in those patients with NOP-LBBB compared with an increase in LVEF in patients with no NOP-LBBB. Also, patients with NOP-LBBB exhibited an impaired functional status at follow-up, with 18% of the patients in NYHA functional class higher than II compared with only 7% of the patients with no new conduction abnormalities after TAVI. These results differ from those reported by Testa et al. (7), showing the lack of differences in LVEF changes and NYHA functional class at follow-up between patients with and without new LBBB after TAVI with a self-expandable valve. As mentioned previously, in the work of Testa et al. (7), there was a rate of PPI as high as 17% within the year after TAVI in patients with no new LBBB (similar to the 18% in patients with new LBBB), and this may have been associated with LV mechanical dyssynchrony similar to that of LBBB. In addition, a tendency toward a higher rate of moderate or severe paravalvular leaks was also observed in the new LBBB group, and this might also have mitigated the potential differences in LVEF and NYHA functional class between the NOP-LBBB and no NOP-LBBB groups.

The appearance of a new LBBB has been associated with a higher incidence of rehospitalizations secondary to decompensated heart failure in patients with a diagnosis of heart failure (8) and in those without overt cardiac disease (9). NOP-LBBB was not associated with a higher rate of rehospitalizations due to heart failure in the present study, and this was in accordance with previous studies in the TAVI field (7,11). Most patients had normal LVEF pre-TAVI, and longer-term follow-up may be necessary to detect an increase in rehospitalizations secondary to LV mechanical dyssynchrony in these patients. Also, the number of events was limited, and a larger sample size with a longer follow-up may be needed to detect differences between groups.

Study limitations. The study was not designed to confirm the null hypothesis. Although the electrocardiograms were evaluated by experienced cardiologists in each center, there was no centralized core laboratory for ECG analysis. There was no central committee to adjudicate clinical events, and although centers followed the VARC 2 definitions, this might be relevant for the classification of mortality events as cardiovascular versus noncardiovascular. However, this probably has only minor importance with respect to overall mortality or PPI (yes/no) events. Finally, the duration of the follow-up was relatively short, and this might have led to an underestimation of the impact of LBBB, especially in view of the fact that studies evaluating the relationship between LBBB and mortality in non-TAVI candidates had a follow-up ranging from 3 to 30 years (2,3,8,24).

Conclusions

The occurrence of conduction disturbances, and particularly of LBBB, remains an important issue in the TAVI field. Determining the prognostic value of these conduction disturbances is of major clinical relevance, especially considering that specific therapies (e.g., PPI, resynchronization) might be applied to potentially modify clinical outcomes. The present study showed that NOP-LBBB after TAVI with a balloon-expandable valve was not associated with any increased risk of mortality (overall and cardiovascular) or rehospitalization (any cause or heart failure) at 1-year follow-up. However, NOP-LBBB was associated with a higher rate of advanced or complete AVB requiring PPI and predicted a lack of LVEF improvement and poorer functional status after TAVI. Future studies will have to further evaluate both the clinical impact of left ventricular changes and the factors associated with the further progression of conduction disturbances in patients in whom LBBB develops after TAVI. Continuous follow-up of these patients over time is mandatory to determine the impact of NOP-LBBB at longer term follow-up.

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Key Words: aortic stenosis ■ heart failure ■ left bundle branch block ■ permanent pacemaker implantation ■ transcatheter aortic valve implantation ■ transcatheter aortic valve replacement.

APPENDIX

For a supplemental table, please see the online version of this article.