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Clinical implications of new-onset left bundle branch block after transcatheter aortic valve replacement: analysis of the PARTNER experience

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Aims Cardiac conduction disturbances, including a left bundle branch block (LBBB), occur frequently following transcatheter aortic valve replacement (TAVR) and may be associated with adverse clinical events. This analysis examines the incidence and implications of new onset, persistent LBBB in patients undergoing TAVR with a balloon-expandable valve.

Methods and results Patients undergoing TAVR in the Placement of Aortic Transcatheter Valves (PARTNER) trial and continued access registries with baseline and discharge/7-day electrocardiograms were included. Prior permanent pacemaker implantation (PPI) and baseline intraventricular conduction abnormalities were exclusion criteria. Predictors of new LBBB were identified and outcomes compared between patients with and without new LBBB. New LBBB occurred in 121 of 1151 (10.5%) patients and persisted in more than half at 6 months to 1 year. The only predictor of new LBBB was prior coronary artery bypass grafting. New LBBB was not associated with significant differences in 1-year mortality, cardiovascular mortality, repeat hospitalization, stroke, or myocardial infarction. However, it was associated with increased PPI during hospitalization (8.3 vs 2.8%, $P = 0.005$) and from discharge to 1 year (4.7 vs. 1.5%, $P = 0.01$). The ejection fraction failed to improve after TAVR in patients with new LBBB and remained lower at 6 months to 1 year (52.8 vs. 58.1%, $P < 0.001$).

Conclusion Persistent, new-onset LBBB occurred in 10.5% of patients without intraventricular baseline conduction who underwent TAVR in the PARTNER experience. New LBBB was not associated with death, repeat hospitalization, stroke, or myocardial infarction at 1 year, but was associated with a higher rate of PPI and failure of left ventricular ejection fraction to improve.

Keywords Left bundle branch block • LBBB • Transcatheter aortic valve • PARTNER

Introduction

The Placement of Aortic Transcatheter Valves (PARTNER) trial established transcatheter aortic valve replacement (TAVR) as an alternative to surgical aortic valve replacement (SAVR) in high-risk surgical candidates and as the standard of care in inoperable patients with symptomatic, severe aortic stenosis.[1,2] With increasing adoption of this new technology, significant research efforts have focused on complications of TAVR, including cardiac conduction system disturbances. New-onset left bundle branch block (LBBB) is the most frequent conduction disturbance after TAVR with an exact frequency that varies based on the valve system used and the time after TAVR. The incidence of new LBBB after TAVR has been reported to range from 35 to 65% with the self-expanding Medtronic CoreValve system (MCV)(Medtronic, Minneapolis, MN, USA)[3–10] and from 3 to 30% with the balloon-expandable, Edwards SAPIEN or SAPIEN XT systems (ESV) (Edwards Lifesciences, Irvine, CA, USA).[4,6,11–15] Limited data exist regarding the persistence of LBBB after TAVR,

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although recent studies suggest that it may frequently be transient, resolving in more than a third of all cases prior to discharge.[3,11]

The clinical implications of persistent, new-onset LBBB after TAVR remain unclear, but several studies have now demonstrated an association with various adverse clinical outcomes. One recent study suggested an association of new LBBB after TAVR with 1-year mortality, but subsequent studies have failed to confirm this finding.[3–5,11,16] Several series have also demonstrated an association with permanent pacemaker implantation (PPI), failure of left ventricular ejection fraction (LVEF) to improve, and worse NYHA functional class.[3,8,11,17] However, the available literature is limited by lack of core lab adjudication, small sample size (particularly with respect to the Edwards SAPIEN valve system), and heterogeneity of patient populations.

The current study sought to define the incidence and predictors of persistent, new-onset LBBB in a much larger cohort of patients who underwent TAVR with the balloon-expandable SAPIEN valve within the PARTNER trial experience. We also investigated the impact of persistent new-onset LBBB after TAVR on subsequent clinical and echocardiographic outcomes.

Methods

Study population and design

The design and results of the PARTNER trial have been previously described.[1,2] Briefly, the trial enrolled patients with symptomatic, severe aortic stenosis who were considered to be inoperable (cohort B) or high-risk (cohort A) candidates for SAVR. High-risk surgical candidates, defined as those with an expected risk of mortality within 30 days of the procedure >15%, were randomized to undergo either SAVR or TAVR. In this group, the TAVR procedure was performed by either the transfemoral (TF) or transapical (TA) approach depending on the suitability of the iliofemoral arterial access. Inoperable patients, defined as those with an expected risk of mortality within 30 days or significant irreversible morbidity of 50%, were randomized to undergo TF TAVR or standard medical therapy. In all cases TAVR was performed with the Edwards SAPIEN transcatheter heart valve (Edwards Lifesciences, Irvine, CA, USA), a trileaflet bovine pericardial valve mounted within a balloon-expandable, stainless steel frame. Following completion of enrolment in the randomized trial, additional patients underwent TAVR by either the TF or TA approach in a continued access registry. The inclusion and exclusion criteria for the registry were the same as the randomized trial. The study was approved by the institutional review board at each participating site and all patients provided written informed consent.

The current analysis included patients who underwent TAVR in the PARTNER trial (randomized trial and continued access registry) and had both baseline and hospital discharge or 7-day EKGs analysed in the electrocardiographic core laboratory. Exclusion criteria included a history of PPI, paced rhythm on the discharge or 7-day EKG, and baseline intraventricular conduction disturbances, including LBBB, right bundle branch block (RBBB), intraventricular conduction delay (IVCD), left anterior fascicular block, left posterior fascicular block, and incomplete RBBB. Predictors of new-onset LBBB were identified and clinical and echocardiographic outcomes were compared between patients with and without new LBBB.

Endpoint definitions

EKGs and transthoracic echocardiograms were obtained at baseline, hospital discharge or 7 days, 30 days, 6 months, and 1 year. Independent core laboratories analysed all EKGs and echocardiograms. A left bundle branch block was defined based on the standard definition as a QRS duration >0.12 s, delayed onset of intrinsicoid deflection in leads V5 and V6, broad monophasic R waves that are usually notched in leads I, V5, and V6, and secondary ST- and T-wave changes opposite in direction to the major QRS deflection.[18] For the purposes of this study, new LBBB was defined as LBBB that was present on the discharge or 7-day EKG but not on the baseline ECG. Clinical outcomes included 30-day and 1-year rates of all-cause mortality, cardiovascular mortality, stroke, myocardial infarction, repeat hospitalization, and PPI for bradycardia. EKG and echocardiographic outcomes were compared between baseline and a late timepoint, defined as 6 months to 1 year with preferential use of the 1 year data if available. Left ventricular systolic function was assessed by LVEF, as calculated by Simpson's biplane method, and the functional status was assessed based on the New York Heart Association class and 6-min walk test. A blinded clinical events committee (CEC) adjudicated all adverse clinical outcomes.

Statistical analysis

All analyses utilized the as-treated population. All results are presented as means ± standard deviation or counts and percentages as appropriate. Continuous variables were compared with the Wilcoxon rank-sum test and categorical variables were compared with the χ^2 test or Fisher's exact test. Outcomes at 30 days and 1 year were analysed with Kaplan–Meier estimates and compared between groups with the log-rank test. The change in LVEF within groups was assessed by the use of the Wilcoxon signed-rank test. For all tests, a two-sided alpha value of <0.05 was required for statistical significance. All statistical analyses were performed using the SAS software, version 9.2 (SAS Institute, Inc., Cary, NC, USA). The date of data extraction was 22 February 2013.

Results

Patient population and baseline characteristics

Transcatheter aortic valve replacement with an Edwards SAPIEN valve was performed in 2548 patients within the PARTNER randomized trial ($n = 519$) and continued access registry ($n = 2029$). After the exclusion of 583 due to the presence of a permanent pacemaker and 658 due to baseline intraventricular conduction disturbance (LBBB = 168, RBBB = 300, IVCD = 109, LAFB = 51, LPFB = 1, incomplete RBBB = 29), 1307 patients remained. An additional 156 were excluded due to a missing baseline or missing or uninterpretable discharge/7-day EKG, including a fully paced rhythm in 35 patients. This resulted in a final study population of 1151 patients (*Figure 1*). New LBBB occurred in 121 of 1151 patients (10.5%) and persisted in this group in 62 of 107 (57.9%) at 30 days and in 52 of 90 (57.8%) at 6 months to 1 year. A detailed description of the EKG findings with respect to LBBB and other cardiac conduction disturbances at each timepoint are provided in *Table 1*. In the group of patients that did not have a new LBBB at discharge or 7-days, LBBB occurred in only 16 of 897 (1.8%) at 30 days and 23 of 793 (2.9%) at 6 months to 1 year, among those with an EKG available.

The baseline characteristics of the patients, stratified by the occurrence of new LBBB, are shown in *Table 2*. Overall, the patient population was elderly with a mean age of 84.1 ± 7.2 years and at very high surgical risk as reflected by a mean STS score of 11.1 ± 3.6 and

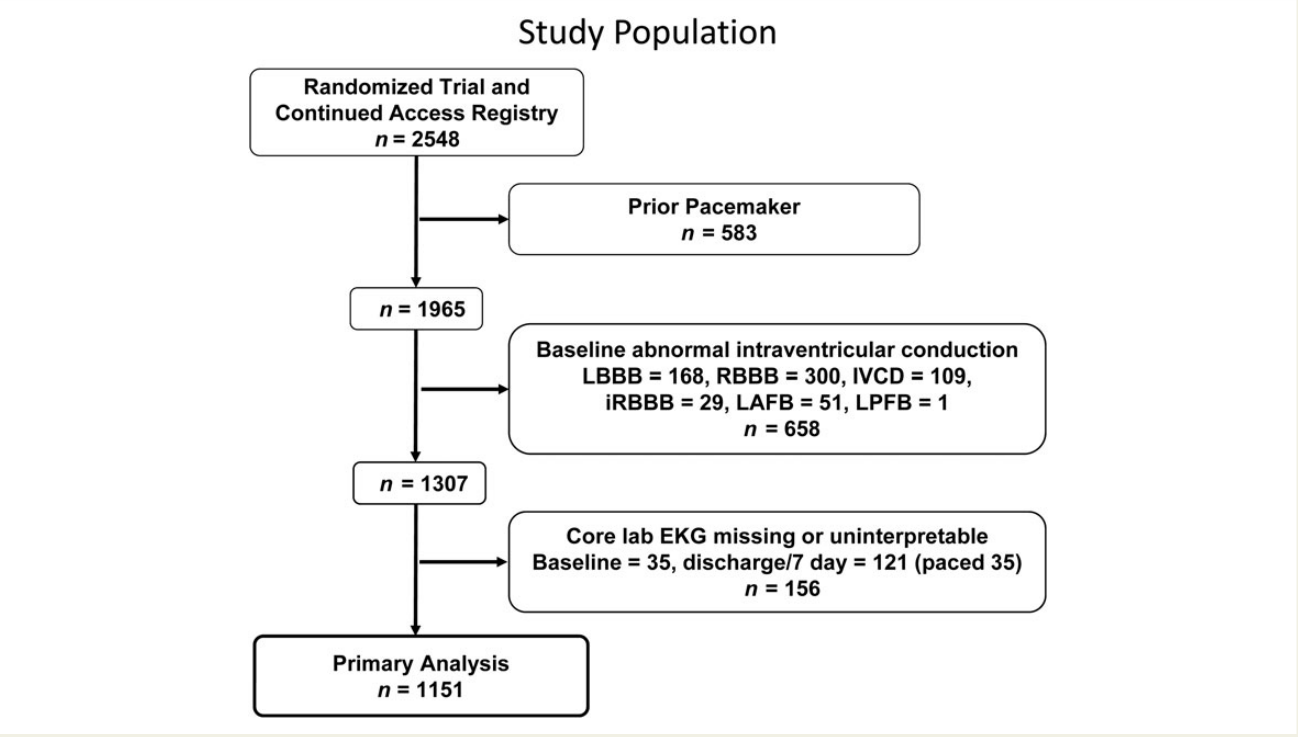

Figure 1 Study population. This flowchart illustrates the derivation of the final study population.

Table 1 Evolution of cardiac conduction disturbances after transcatheter aortic valve replacement

Outcome (%)	Baseline	Discharge	30 days	6 month–1 year
LBBB	0	10.5	7.8	8.5
LAFB	0	2.6	3.7	7.3
LPFB	0	0.2	0	0.1
RBBB	0	1.7	1	1.9
iRBBB	0	0.9	0.9	1.7
IVCD	0	5.5	4.9	6.3
First Deg AVB	12.7	13.3	12.2	17.4
Second Deg AVB	0.1	0.1	0	0.1

Values are %. LBBB, left bundle branch block; LAFB, left anterior fascicular block; LPFB, left posterior fascicular block; RBBB, right bundle branch block; iRBBB, incomplete right bundle branch block; IVCD, intraventricular conduction disturbance; first Deg AVB, first degree AV block; second Deg AVB, second degree AV block.

logistic Euroscore of 24.7 ± 15.7, without significant differences between groups. There was also a high burden of cardiovascular and medical comorbidities, including hypertension (92.6%), diabetes (37.5%), coronary artery disease (CAD) (75.6%), prior coronary artery bypass surgery (CABG) (37.7%), peripheral vascular disease (43.0%), cerebrovascular disease (25.3%), major arrhythmia (44.1%), and chronic obstructive pulmonary disease (44.7%). These baseline characteristics were similar between groups with the exception of a numerically higher rate of diabetes (45.5 vs. 36.6%, $P = 0.057$) and a significantly higher rate of prior CABG (48.8 vs. 36.4%, $P < 0.008$) in the new LBBB group.

Electrocardiographic and echocardiographic characteristics

Baseline electrocardiographic and echocardiographic characteristics are displayed in *Table 3*. As required by the study design, baseline EKGs were available for all patients. There were no significant differences between patients with and without LBBB with respect to cardiac rhythm disturbances (including atrial fibrillation), bradycardia, and measures of supraventricular conduction, including PR interval, first degree AV block, and second degree AV block type 1.

Baseline echocardiographic data were available for 1092 patients (94.9%). The baseline LVEF was similar between patients with and without new LBBB. There were no significant differences between the groups with respect to other echocardiographic variables including indices of hypertrophy, annulus diameter, and left ventricular outflow tract diameter.

Procedural outcomes

The procedural outcomes are compared between patients with and without new LBBB in *Table 4*. Among those with new LBBB, there was a non-significantly higher rate of access by the TA route (50.4 vs. 42.2%, $P = 0.09$). There were no significant differences between the groups in terms of the rate of successful valve implantation, implanted valve size, post-dilatation, post-dilatation balloon size,

Table 2 Baseline patient characteristics

Characteristic	New LBBB ($n = 121$)	No LBBB ($n = 1030$)	*P*-value
Age (years)	83.7 ± 7.3	84.2 ± 7.2	0.44
Male sex (%)	43.0	43.8	0.86
STS score	11.3 ± 3.5	11.1 ± 3.6	0.45
Logistic EuroSCORE	25.8 ± 14.9	24.6 ± 15.7	0.22
Frailty (%)	7.8	12.6	0.13
NYHA (%)			
Class III	45.5	47.5	0.67
Class IV	47.1	48.5	0.76
CAD (%)	80.2	75.0	0.22
Prior MI	25.6	25.2	0.93
Prior PCI	36.4	38.3	0.68
Prior CABG	48.8	36.4	0.008
Prior BAV (%)	19.0	21.1	0.59
Arrhythmia (%)	34.7	41.8	0.13
PVD (%)	47.5	42.5	0.29
Porcelain aorta (%)	0.8	4.2	0.08
CVD (%)	27.5	24.9	0.56
Hypertension (%)	94.2	92.4	0.48
Dyslipidaemia (%)	83.5	83.2	0.94
Diabetes mellitus (%)	45.5	36.6	0.057
Renal disease (CR ≥ 2) (%)	17.4	15.6	0.62
Liver disease (%)	3.3	2.7	0.57
Chronic obstructive pulmonary disease (%)	42.1	45.0	0.56
Oxygen dependent (%)	13.2	12.4	0.80
Pulmonary hypertension (%)	33.0	38.6	0.20

Values are % or mean ± SD.

ratio of the prosthesis diameter to annulus diameter, or ratio of the prosthesis diameter to LVOT diameter. The occurrence of a new LBBB was associated with a longer hospitalization post-TAVR procedure (6.80 days vs. 6.15 days, $P = 0.007$).

Clinical outcomes

Clinical follow-up was complete in >94% of patients at 1 year (365 ± 30 days). There were no significant differences between patients with and without new LBBB with respect to 30-day or 1-year all-cause mortality, cardiovascular mortality, stroke, or myocardial infarction (*Tables 5* and *6*, *Figure 2*). New LBBB was, however, associated with numerically higher rates of repeat hospitalization at 30 days and 1 year and significantly higher PPI rates both during the index hospitalization (8.3 vs. 2.8%, $P = 0.005$) and from discharge to 1-year (4.7 vs. 1.5%, $P = 0.01$). The most frequent indications for pacemaker implantation in the new LBBB group included high-degree atrioventricular block (47%) and tachycardia-bradycardia syndrome (47%), as delineated in *Figure 3*.

To evaluate the possibility that the clinical impact of new LBBB after TAVR was blunted by the implantation of permanent pacemakers in a subset of patients during the index hospitalization, an additional analysis was performed in which these patients were excluded (Supplementary material online, *Table S1*). The results of this analysis were similar to those of the primary analysis with respect to major clinical outcomes. Specifically, there was no difference in 1-year mortality (16.9 vs. 17.7%, $P = 0.73$) between patients with and without new LBBB after excluding patients in either group who underwent PPI during the index hospitalization. There remained, however, a numerically higher rate of repeat hospitalization (23.5 vs. 16.3%, $P = 0.08$) and a significantly higher rate of pacemaker implantation (5.1 vs. 1.5%, $P = 0.01$) in the group with new LBBB.

The clinical outcomes of the subgroup of patients who developed new LBBB after hospital discharge ($n = 33$) were also analysed. The 1-year clinical outcomes, including mortality and pacemaker implantation, of these patients did not differ statistically from those of patients without new-LBBB after TAVR.

Left ventricular function

Echocardiograms that were interpreted by the core laboratory were available at hospital discharge or 7 days in 1087 of 1120 (97.1%) surviving patients, at 30 days in 1012 of 1109 (91.3%), and at 6 months to 1 year in 718 of 1010 (71.1%). Although LVEF was similar at baseline (54.4 vs. 55.4%, $P = 0.24$), it was significantly lower at discharge (52.2 vs. 55.8%, $P < 0.001$), 30-days (53.0 vs. 56.0%, $P = 0.003$), and 1-year (53.4 vs. 57.4%, $P = 0.02$) in the group with new LBBB (*Figure 4*). Within the groups, the LVEF declined significantly among those with new LBBB (−1.8%, $P = 0.027$), but improved in the group without new LBBB (2.9%, $P < 0.001$), between baseline and 6 months or 1 year. The evolution of LVEF was also stratified by baseline LVEF (<35, 35–50, and >50%), as shown in *Figure 4*. The difference in recovery of LVEF between those with and without new LBBB was the greatest in the group with severe left ventricular dysfunction (LVEF <35%) at baseline. In this group, the LVEF in those with and without new LBBB was similar at baseline (29.1 vs. 27.8%, $P = 0.34$), but was markedly lower at 1 year in those with a new LBBB (38.3 vs. 48.3, $P = 0.02$). In the overall population, the differences in LVEF did not correlate with significant differences in heart failure symptoms (NYHA class) or 6-min walk test at 1 year.

Discussion

The current report represents the largest published analysis of the occurrence and implications of new-onset persistent LBBB after TAVR and the only one with CEC adjudication of important clinical endpoints and core laboratory analysis of EKGs and echocardiograms. The principal findings of this study can be summarized as follows: (i) following TAVR with the balloon-expandable ESV, new-onset LBBB that persisted at discharge or 7 days occurred in 10.5% of patients with normal baseline intraventricular conduction and remained present in nearly 60% of this group at 30 days and at 6 months to 1 year; (ii) a history of CABG was the only significant predictor of new LBBB in this analysis; (iii) new LBBB was not associated with any difference in 1-year rates of all-cause mortality, cardiovascular mortality, stroke, or myocardial infarction; (iv) new LBBB was associated with numerically higher rates of repeat hospitalization at

Table 3 Baseline EKG and echocardiographic characteristics

Characteristic	New LBBB ($n = 121$)	No LBBB ($n = 1030$)	*P*-value
Electrocardiogram (%)			
Sinus rhythm	78.5	74.2	0.30
Atrial tachyarrhythmia[a]	18.2	23.7	0.17
Bradycardia[b]	2.5	1.1	0.18
First degree AVB	16.5	12.2	0.18
Second degree AVB, type 1	0.8	0	0.11
Echocardiogram			
AV peak velocity (m/s)	4.3 ± 0.7	4.3 ± 0.6	0.57
AV mean gradient (mmHg)	47.6 ± 15.7	46.2 ± 14.5	0.36
Aortic valve area (cm^2)	0.65 ± 0.18	0.65 ± 0.20	0.73
AV annulus dimension (cm)	1.94 ± 0.26	1.95 ± 0.25	0.69
LVOT dimension (cm)	1.98 ± 0.17	2.00 ± 0.18	0.31
LVOT/annulus	1.04 ± 0.13	1.04 ± 0.113	0.68
LV mass (g)	239.6 ± 66.2	239.2 ± 73.4	0.79
IVSD dimension (cm)	1.61 ± 0.32	1.59 ± 0.32	0.59
LVOT/IVSD	1.28 ± 0.30	1.31 ± 0.30	0.34
LVED dimension (cm)	4.38 ± 0.70	4.40 ± 0.73	0.85
LVEF (%)	54.4 ± 11.0	55.4 ± 11.8	0.24

Values are % or mean ± SD.
[a]Atrial fibrillation, atrial flutter, or atrial tachycardia.
[b]Sinus bradycardia, sinus pauses, or junctional bradycardia.

Table 4 Procedural characteristics

Characteristic	New LBBB ($n = 121$)	No LBBB ($n = 1030$)	*P*-value
Successful valve implantation (%)	97.5	98.1	0.50
Access route (%)			
Transfemoral	49.6	57.5	0.09
Transapical	50.4	42.2	
Valve size (%)			
23 mm	57.6	59.3	0.72
26 mm	42.4	40.7	
Prosthesis diameter/annulus diameter	1.27 ± 0.16	1.26 ± 0.16	0.59
Prosthesis diameter/LVOT diameter	1.23 ± 0.09	1.22 ± 0.11	0.25
Post-dilatation (%)	9.3	9.2	0.98
Time to discharge post-procedure (days)	6.8 ± 2.3	6.2 ± 2.4	0.007

Values are % or mean ± SD.

Table 5 30-day outcomes

Outcome	New LBBB ($n = 121$)	No LBBB ($n = 1030$)	*P*-value
Mortality (%)			
From any cause	4.1	3.6	0.77
From cardiovascular cause	2.5	2.1	0.75
Repeat hospitalization (%)	10.1	5.7	0.06
Stroke (%)	5.0	3.7	0.50
Myocardial infarction (%)	1.7	0.4	0.07
New permanent pacemaker (%)	9.9	2.9	<0.0001

Values are % or mean ± SD.

30 days and 1 year that did not reach statistical significance; (v) new LBBB was associated with significantly higher rates of PPI, both before hospital discharge and from discharge to 1 year; (vi) patients with new LBBB, compared with those without new LBBB, failed to show improvement in LVEF, and this difference was most pronounced in those with severely depressed LVEF at baseline.

Cardiac conduction disturbances, including LBBB, are a frequent complication of both SAVR and TAVR. This is most likely due to the high prevalence of underlying conduction system abnormalities in patients with aortic valve disease and the close proximity of the aortic valvular complex to the cardiac conduction system, including the AV node, the bundle of HIS, and the left bundle branch.[19] The exact mechanisms of conduction system disturbances and new-onset LBBB may differ between SAVR and TAVR with either the self-expanding or balloon-expandable system. Mechanisms during SAVR may include injury to the conduction system from direct surgical

Table 6 One-year outcomes

Outcome	New LBBB ($n = 121$)	No LBBB ($n = 1030$)	*P*-value
Mortality (%)			
From any cause	17.1	18.4	0.67
From cardiovascular cause	10.3	6.1	0.14
Repeat hospitalization (%)	23.6	16.6	0.08
Stroke (%)	7.2	5.9	0.62
Myocardial infarction[a] (%)	1.2	0.9	0.95
New permanent pacemaker (%)			
Total	12.9	4.3	<0.001
Post discharge	4.7	1.5	0.01

[a]Excludes periprocedural myocardial infarction.

trauma, mechanical compression, haemorrhage, or ischaemia.[20–23] On the other hand, potential mechanisms during TAVR may include injury by wire manipulation or balloon aortic valvuloplasty, compression of the conduction system by the valve frame, haematoma, or ischaemia.[7,15,24,25]

The incidence of new LBBB after SAVR has been reported to range from 6 to 32%.[20–22,26] The exact incidence after TAVR has been shown to vary based on the valve system used and the elapsed time from the procedure. The rate of new LBBB after TAVR with the self-expanding MCV is higher, ranging from ~35 to 65% in various series.[3–10] The incidence of new LBBB following TAVR with the balloon-expandable ESV is substantially lower with various small series reporting rates from 3 to 30%.[4,6,11–15] The difference in rates between the two valve systems likely reflects design features, including stent geometry and properties (self-expanding vs. balloon expandable), that influence the position of the deployed valve with respect to the left ventricular outflow tract and septum and the radial force exerted in these areas.[27] Limited data exists

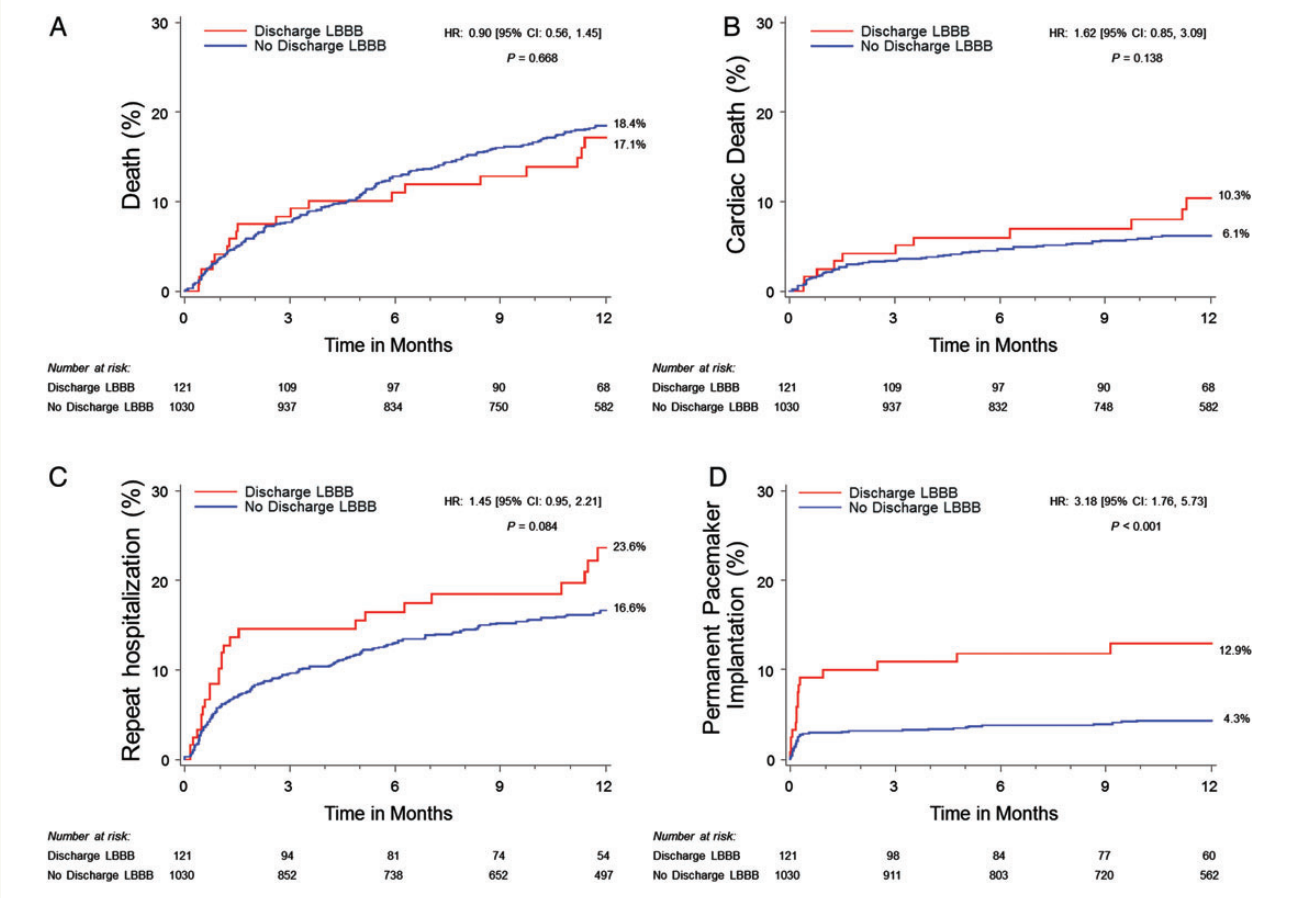

Figure 2 One-year clinical outcomes. Kaplan–Meier curves are displayed for 1-year clinical outcomes, including (*A*) mortality, (*B*) cardiovascular mortality, (*C*) repeat hospitalization, and (*D*) permanent pacemaker implantation.

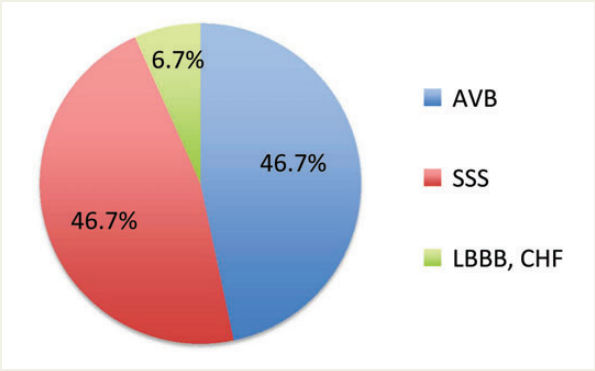

Figure 3 Pacemaker indications in patients with new left bundle branch block. The indications for pacemaker implantation among patients with new left bundle branch block after transcatheter aortic valve replacement are shown in this figure. AVB, advanced atrioventricular block, including high-degree atrioventricular block and complete heart block; SSS, sick sinus syndrome (including tachycardia-bradycardia syndrome); LBBB, CHF, left bundle branch block, refractory CHF, and chronotropic incompetence.

regarding the persistence of LBBB after TAVR but recent studies suggest that it is frequently transient, resolving in more than one-third of cases prior to hospital discharge.[3,11] Therefore, the rate of new LBBB at discharge or 7-days of 10.5% in the current analysis correlates well with the previously reported rates of new LBBB after TAVR with ESV.

Among patients with new LBBB after TAVR in the current study, the LBBB persisted in nearly 60% of cases at both 30 days and 6 months to 1 year. This is similar to the results of prior small series (<70 patients) that demonstrated resolution of new LBBB within 1 month of TAVR with ESV in 30–50% of patients.[6,12,14] It is also consistent with a recent, larger series of ~200 patients treated with ESV that reported resolution of new LBBB present at discharge in nearly 50% of cases by 6 months to 1 year.[11] Our finding that resolution of the new LBBB generally occurred within 30 days, without further change between 30 days and 6 months to 1 year represents a further advance in the understanding of the time course of new LBBB after TAVR with ESV. Notably, this may be distinct from the case with the self-expanding MCV for which studies have shown a lesser degree or no resolution of new LBBB between discharge and 30 days or 6 months.[3,5,10]

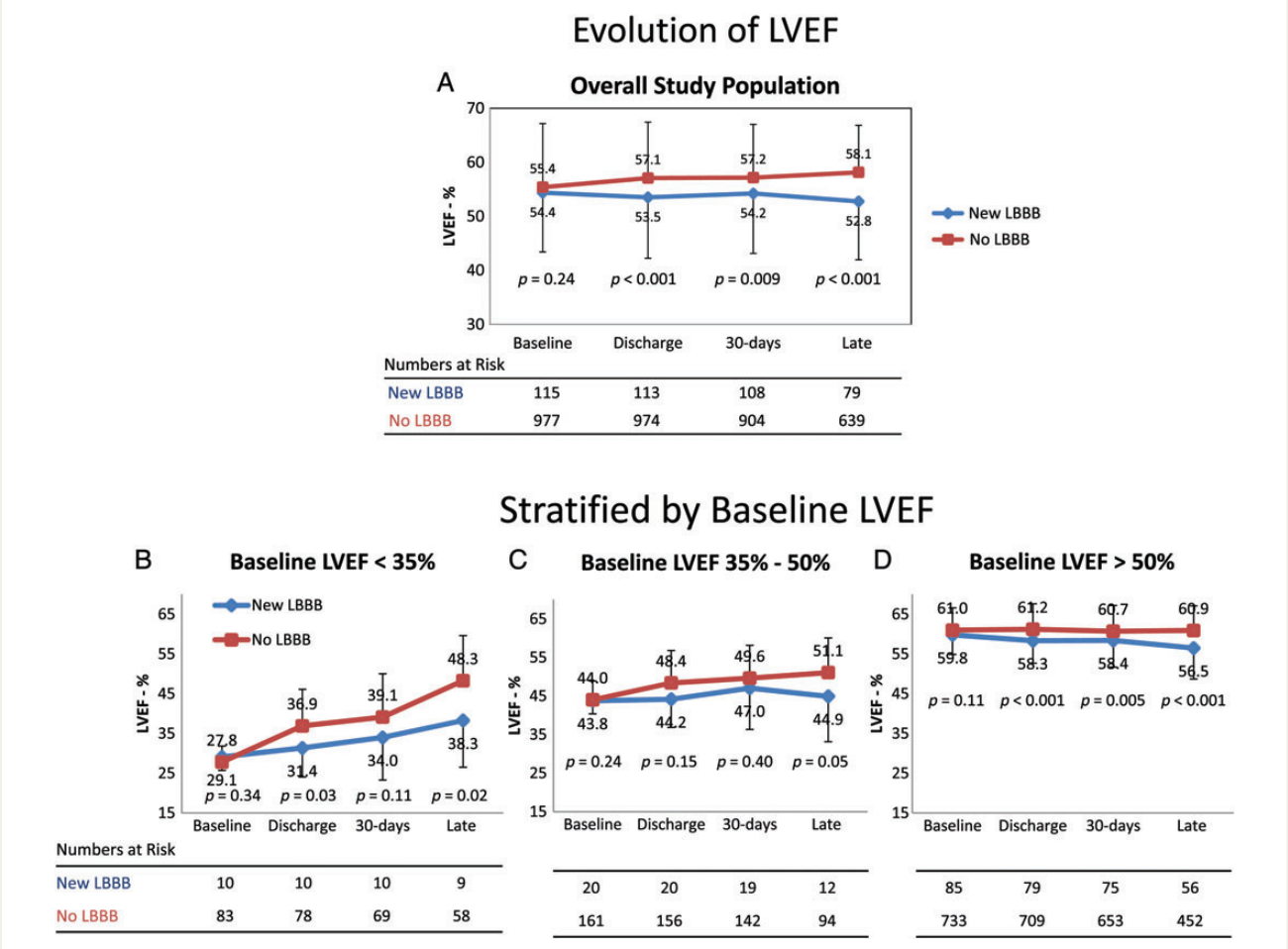

Figure 4 Evolution of left ventricular ejection fraction. The evolution of left ventricular ejection fraction over time is shown for (*A*) the overall population and stratified by baseline left ventricular function: (*B*) LVEF < 35%, (*C*) LVEF 35 to 50%, and (*D*) LVEF > 50%.

Predictors of new left bundle branch block after transcatheter aortic valve replacement

Prior studies have identified the use of MCV vs. ESV, depth of valve implantation (with both MCV and ESV), and baseline QRS width as risk factors for new LBBB after TAVR.[3,4,6,11] The current study identifies a history of CABG as a potential novel predictor of new LBBB after TAVR. Mechanisms by which prior CABG might increase the risk of conduction system disturbances could include prior surgery-related conduction system injury, greater predilection to ischaemic injury and differences in medication use (i.e. chronotropic agents). However, this should be viewed as hypothesis-generating rather than definitive given that several previously identified or potential predictors of new LBBB after TAVR, including depth of valve implantation and degree of annular calcification were not available in this analysis. Further study is therefore necessary to assess the contribution of prior CABG to the risk for new LBBB after TAVR.

Prognostic significance of new left bundle branch block after transcatheter aortic valve replacement

New LBBB after SAVR has been associated with adverse clinical events, including mortality, sudden death, syncope, complete atrioventricular block, and PPI at long-term follow-up.[21,22,26] Until recently, the clinical implications of persistent, new-onset LBBB after TAVR have been unclear, but several series have now suggested associations with subsequent adverse clinical outcomes, including mortality, syncope, complete atrioventricular block, and PPI.[3,4,11] The putative mechanisms for these associations include progression of the LBBB conduction disturbance to complete atrioventricular block or dysynchrony-induced left ventricular dysfunction.

With respect to mortality, one recent, mixed series of >600 patients who underwent TAVR with either the ESV ($n = 292$, 43%) or MCV ($n = 387$, 57%), suggested an association of new-onset LBBB with all-cause mortality beyond 1-year that was independent of the valve system.[4] However, other recent studies, including a series of 202 patients treated with ESV and series of 818 and 275 patients treated with MCV, failed to substantiate this association.[3,5,11] The current study, which represents the largest available experience, both overall and specifically with ESV, does not show any association of new LBBB after TAVR with 1-year overall or cardiovascular mortality.

This study does, however, demonstrate an association of new LBBB with PPI, both prior to hospital discharge and from discharge to 1 year. This is in agreement with the aforementioned studies, which also demonstrated higher rates of progression to complete atrioventricular block, syncope, and requirement for PPI among those with new LBBB after TAVR.[3,11] Although our analysis shows that the indication for pacemaker implantation was bradycardia, specifically advanced atrioventricular block or sick sinus syndrome, in all but a single case, it remains possible that the higher rate of PPI in part reflects a lower physician threshold for pacemaker implantation in patients with new LBBB after TAVR. Further research is required to determine whether additional testing, possibly including serial EKG, 24-h Holter monitoring, event monitoring, or invasive electrophysiology study, can identify the subgroup of patients with new LBBB that will progress to require PPI.

Impact of new left bundle branch block on evolution of left ventricular function

Prior studies have demonstrated preservation or potential improvement of left ventricular function after TAVR, particularly among patients with depressed ventricular function at baseline.[28–30] There is now mounting evidence that TAVR-related conduction disturbances may attenuate subsequent improvement in left ventricular function. A recent study of 90 patients who underwent TAVR with either the ESV or MCV, showed that new conduction disturbances, including LBBB and PPI, were associated with significant left ventricular dyssynchrony by speckle-tracking echocardiography and failure of LVEF to improve at 1 year.[17] Both the current, large study and the prior analysis of >200 patients treated with ESV showed failure of the LVEF to improve at 6 months to 1-year among patients with new LBBB.[11] The other large study of LBBB after TAVR in 818 MCV recipients failed to show any impact of new LBBB on the evolution of LVEF up to 1 year.[3] This may be due to fact that echocardiographic follow-up in this study was complete in <50% of the patients and echocardiograms were not interpreted in a core laboratory, although it remains possible that the impact of new LBBB on LVEF is different after TAVR with MCV than with ESV.

An important new finding in the current analysis is that the difference in LVEF at 6 months to 1 year between patients with and without new LBBB was most pronounced among those with severe left ventricular dysfunction (LVEF < 35%) at baseline. This finding should be viewed as being hypothesis-generating given the relatively limited number of patients, but is consistent with the known detrimental effect of ventricular conduction delays in heart failure patients that may be effectively treated with cardiac resynchronization therapy.[31,32] This raises several intriguing questions that warrant additional investigation. Further studies of TAVR in patients with poor baseline left ventricular function are necessary to determine whether the larger difference in LVEF between those with and without new LBBB in this group translates to differences in other outcomes, including symptomatic heart failure. There are now several case reports in the literature describing the potential utility of cardiac resynchronization therapy after TAVR in patients with new LBBB, depressed left ventricular function, and symptomatic heart failure.[33,34] Further research is required to determine whether prophylactic cardiac resynchronization might be warranted in patients with low baseline LVEF and new LBBB after TAVR. It is also possible that patients with poor baseline left ventricular function should be preferentially treated with ESV as opposed to MCV given the lower expected rate of conduction disturbances.

Limitations

This study consists of a retrospective analysis of existing data and is subject to all of the limitations inherent in this type of study design. Nevertheless, the use of the PARTNER data provides a large and robust data set that is particularly notable for CEC-adjudicated endpoints and the use of EKG and echocardiographic core laboratories. An important limitation of the study is that the first available post-procedure EKG was from discharge or 7-days, and prior studies

have demonstrated that >30% of new-onset LBBB after TAVR resolve prior to discharge. Nevertheless, it is likely, from a mechanistic standpoint, that persistent new-onset LBBB is more relevant to subsequent clinical outcomes. Another limitation is that although this analysis included a broad array of potential clinical, EKG, and echocardiographic predictors of new LBBB, certain previously identified or potential predictors, such as depth of valve implantation and degree of annular calcification, are not available in the data set. Data on the use of medications, including negative chronotropic agents, that may be relevant to the development or progression of conduction system disturbances are also not available. Finally, the analysis regarding the evolution of LVEF stratified by baseline ventricular function can only be viewed as being hypothesis generating given the limited number of patients with low baseline LVEF. Further studies of TAVR in patients with impaired left ventricular function are necessary to define the impact of cardiac conduction disturbances, including LBBB, in this population.

Conclusion

Among patients with normal baseline intraventricular conduction who underwent TAVR with a balloon-expandable valve in the PARTNER experience, new-onset LBBB that persisted at discharge or 7 days occurred in 10.5% of patients. The only significant predictor of new LBBB was a history of CABG surgery. New LBBB was not associated with 1-year mortality, cardiovascular mortality, stroke, or myocardial infarction. However, new LBBB was associated with a numerically higher rate of repeat hospitalization and significantly higher rate of PPI and a failure of LVEF to improve after TAVR. The difference in improvement of left ventricular function between those with and without new LBBB was most pronounced among patients with severely depressed left ventricular function at baseline.

Supplementary material

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

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