Predictive Factors and Long-Term Clinical Consequences of Persistent Left Bundle Branch Block Following Transcatheter Aortic Valve Implantation With a Balloon-Expandable Valve

Marina Urena, MD,* Michael Mok, MD,* Vicenç Serra, MD,† Eric Dumont, MD,*
Luis Nombela-Franco, MD,* Robert DeLarochellière, MD,* Daniel Doyle, MD,* Albert Igual, MD,†
Eric Larose, MD,* Ignacio Amat-Santos, MD,* Mélanie Côté, MSc,* Hug Cuéllar, MD,†
Philippe Pibarot, PhD,* Peter de Jaegere, MD, PhD,‡ François Philippon, MD,*
Bruno Garcia del Blanco, MD,† Josep Rodés-Cabau, MD*

Quebec City, Quebec, Canada; Barcelona, Spain; and Rotterdam, the Netherlands

Objectives   This study evaluated the predictive factors and prognostic value of new-onset persistent left bundle branch block (LBBB) in patients undergoing transcatheter aortic valve implantation (TAVI) with a balloon-expandable valve.

Background   The predictors of persistent (vs. transient or absent) LBBB after TAVI with a balloon-expandable valve and its clinical consequences are unknown.

Methods   A total of 202 consecutive patients with no baseline ventricular conduction disturbances or previous permanent pacemaker implantation (PPI) who underwent TAVI with a balloon-expandable valve were included. Patients were on continuous electrocardiographic (ECG) monitoring during hospitalization and 12-lead ECG was performed daily until hospital discharge. No patient was lost at a median follow-up of 12 (range: 6 to 24) months, and ECG tracing was available in 97% of patients. The criteria for PPI were limited to the occurrence of high-degree atrioventricular block (AVB) or severe symptomatic bradycardia.

Results   New-onset LBBB was observed in 61 patients (30.2%) after TAVI, and had resolved in 37.7% and 57.3% at hospital discharge and 6- to 12-month follow-up, respectively. Baseline QRS duration (p = 0.037) and ventricular depth of the prosthesis (p = 0.017) were independent predictors of persistent LBBB. Persistent LBBB at hospital discharge was associated with a decrease in left ventricular ejection fraction (p = 0.001) and poorer functional status (p = 0.034) at 1-year follow-up. Patients with persistent LBBB and no PPI at hospital discharge had a higher incidence of syncope (16.0% vs. 0.7%; p = 0.001) and complete AVB requiring PPI (20.0% vs. 0.7%; p < 0.001), but not of global mortality or cardiac mortality during the follow-up period (all, p > 0.20). New-onset LBBB was the only factor associated with PPI following TAVI (p < 0.001).

Conclusions   Up to 30% of patients with no prior conduction disturbances developed new LBBB following TAVI with a balloon-expandable valve, although it was transient in more than one third. Longer baseline QRS duration and a more ventricular positioning of the prosthesis were associated with a higher rate of persistent LBBB, which in turn determined higher risks for complete AVB and PPI, but not mortality, at 1-year follow-up.   (J Am Coll Cardiol 2012;60:1743–52) © 2012 by the American College of Cardiology Foundation

New-onset left bundle branch block (LBBB) is the most frequent conduction alteration associated with transcatheter aortic valve implantation (TAVI) (1–10). Several studies have evaluated the predictive factors of new-onset LBBB following TAVI, but most of them have focused on patients undergoing TAVI with the self-expandable system (Cor-

eValve, Medtronic Inc, Minneapolis, Minnesota) (1,2,4–6,8). Furthermore, all studies to date have included patients with conduction disturbances prior to TAVI (including patients with prior pacemaker in some), which may indeed lead to a more difficult interpretation of the exact role of TAVI on the development of new conduction disturbances and its predictors.

Importantly, while it has been shown that the vast majority of conduction disturbances occur during the TAVI procedure, a significant number resolve within the first days following the procedure, especially with the use of a balloon-expandable valve (9,10). However, no data exist on the factors associated with persistent (vs. transient) new-onset LBBB following TAVI and its clinical consequences. It is therefore unknown whether patients leaving the hospital with a new-onset LBBB following TAVI have a higher risk for clinical events, particularly new-onset complete atrioventricular block (AVB) and/or sudden death. The objectives of this study were therefore to: 1) determine the incidence and predictors of new-onset persistent LBBB in patients without baseline intraventricular conduction abnormalities undergoing TAVI with a balloon-expandable valve; and 2) evaluate the long-term prognostic significance of persistent LBBB in this population.

Methods

Study population. Of 348 consecutive patients (Quebec Heart & Lung Institute: n = 263; Vall d'Hebron hospital: n = 85), who underwent TAVI with a balloon-expandable valve (Sapien or Sapien XT, Edwards Lifesciences, Irvine LLC, California); 146 patients were excluded because of the following reasons: prior pacemaker (n = 57), prior intraventricular conduction abnormalities (complete or incomplete right or left bundle branch block, n = 83), death, or conversion to open heart surgery before the first ECG (4 and 2 patients, respectively). The final study population consisted of 202 patients. Details about the TAVI procedure have been previously reported (11). All baseline, procedural, and post-operative data were prospectively recorded. Periprocedural complications were defined according to the Valve Academic Research Consortium criteria (12). The degree of native aortic valve calcification was measured (in Agatston units) in all patients who had noncontrast ECG-gated computed tomography prior to the procedure (n = 131; 65%). Patients underwent transthoracic echocardiography at baseline, at hospital discharge, and at 6- to 12-month follow-up. The position of the

transcatheter valve after implantation was evaluated by transesophageal echocardiography (long-axis view) as previously described (9).

ECG data and criteria for pacemaker implantation. ECG tracings were recorded at baseline (within 24 h prior to the procedure), immediately after the procedure, and then every 24 h until hospital discharge. Furthermore, patients were on continuous ECG monitoring during the entire hospitalization period following the procedure. All ECG tracings were analyzed by a cardiologist blinded to the clinical data. The diagnosis of intraventricular conduction abnormalities was based on recommendations from the Amer-

Table 1	Baseline and Procedural Characteristics of the Study Population (n = 202)
Baseline characteristics	
Age (yrs)	80 ± 8
Female	121 (59.9)
Body mass index (kg/m²)	27 ± 5
Comorbidities	
Hypertension	178 (88.1)
Diabetes mellitus	67 (33.2)
COPD	50 (24.8)
CAD	118 (58.4)
eGFR (ml/min)	56.8 ± 23.0
Baseline treatment	
Beta-blockers	94 (46.5)
Calcium channel blockers	58 (28.7)
Amiodarone	13 (6.4)
STS-PROM score (%)	7.5 ± 3.7
ECG (ms)	
PR interval	174 ± 38
QRS duration	92 ± 10
Echocardiography	
LVEF (%)	57 ± 12
Mean gradient (mm Hg)	47 ± 18
Aortic valve area (cm²)	0.64 ± 0.22
Computed tomography	
Aortic valve calcification (Agatston units)	3227 ± 2121
Procedural variables	
Success	190 (94.1)
Approach, n (%)	
Transapical	117 (57.9)
Transfemoral	85 (42.1)
Ratio valve prosthesis size/aortic annulus	1.17 ± 0.07
Prosthesis ventricular depth* (mm)	1.87 ± 2.62
In-hospital outcomes	
Death	14 (6.9)
Stroke	4 (2.0)
Myocardial infarction	2 (1.0)
Major bleeding	23 (11.4)
Major vascular complications	7 (3.5)
Pacemaker implantation	14 (6.9)
Length of stay (days)	7 (5–10)

Values are mean ± SD, n (%), or median (interquartile range). *Distance between the hinge point of the mitral valve and the ventricular end of the valve prosthesis frame (transesophageal echocardiography [TEE], long-axis view).

CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; ECG = electrocardiography; eGFR = estimated glomerular filtration ratio; LVEF = left ventricular ejection fraction; STS-PROM = Society of Thoracic Surgeons predicted risk of mortality.

ican Heart Association/American College of Cardiology Foundation/Heart Rhythm Society (AHA/ACCF/HRS) for the standardization and interpretation of ECGs (13). The policies for permanent pacemaker implantation (PPI) were in accordance with the ACC/AHA/HRS guidelines for device-based therapy of cardiac rhythm abnormalities (14).

Transient LBBB was defined as the occurrence of new LBBB that resolved before hospital discharge. *Persistent LBBB* was defined as any new-onset LBBB that persisted at hospital discharge. Those patients who developed LBBB after the procedure and required a PPI or died before hospital discharge (without proven resolution of the LBBB) were also included in the group of patients with persistent LBBB.

Follow-up. Follow-up was carried out by clinical visits or phone contact at 30 days, 6 months, 1 year, and yearly thereafter. The minimum follow-up for the study population was 6 months (median [range]: 12 [6 to 24] months), and no patient was lost to follow-up. An ECG tracing was obtained at 6- to 12-month follow-up in 97% of survivors at that time point.

Statistical analysis. Categorical variables were compared using the chi-square or Fisher exact test as appropriate. Continuous variables were compared using the *t* or Wilcoxon rank sum test and 1-way analysis of variance if comparisons involved >2 groups. A repeated-measures model with interaction was used to compare the changes

in left ventricular ejection fraction (LVEF) at different time points between groups (persistent LBBB vs. absent or transient LBBB). Post-hoc comparisons were performed using the Tukey test. The predictors of new-onset, persistent LBBB (vs. absent or transient LBBB) were determined using a binary logistic regression model that included variables with a p value ≤0.10 on univariate analysis. Age, baseline QRS duration, and ventricular depth of the prosthesis were the variables included in the analysis. The predictors of significant LVEF changes over time were determined using a multivariate regression linear model that included variables with a p value <0.10 on univariate analysis. Hypertension, new-onset persistent LBBB and peak troponin T were the variables included in the analysis. Cumulative outcomes at 1-year follow-up were assessed by Kaplan-Meier estimates and compared using the log-rank test. A 30-day landmark analysis was also performed. The results were considered significant with p values <0.05. All analyses were conducted using the statistical package SAS version 9.2 (SAS Institute Inc., Cary, North Carolina).

Results

The baseline and procedural characteristics of the study population are shown in Table 1.
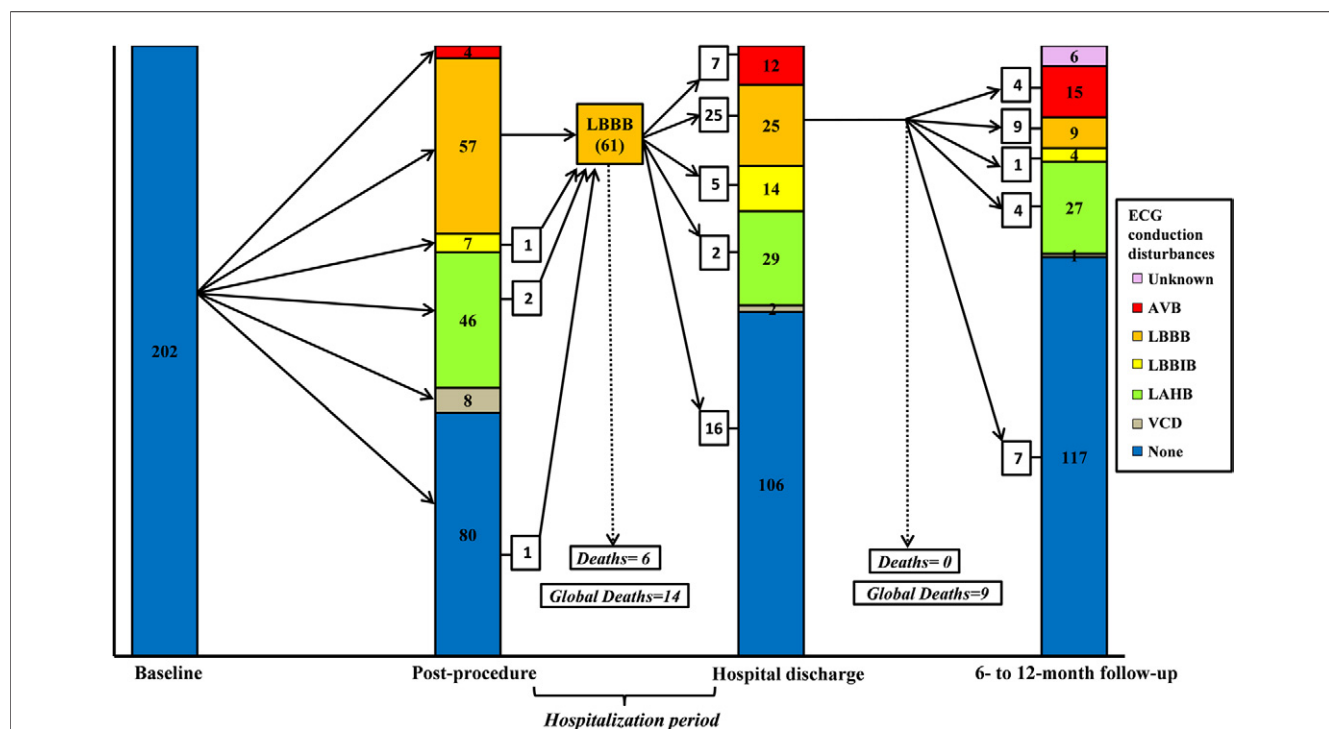
Figure 1   Conduction Abnormalities Following TAVI

Flowchart showing the occurrence of intraventricular conduction abnormalities immediately following transcatheter aortic valve implantation, during the hospitalization period and up to 6- to 12-month follow-up. CAVB = complete atrioventricular block; ILBBB = incomplete left bundle branch block; IVCD = nonspecific intraventricular conduction disturbances; LAHB = left anterior hemiblock; LBBB = left bundle branch block; TAVI = transcatheter aortic valve implantation.

New-onset conduction disturbances and LBBB following TAVI. New-onset LBBB and overall conduction disturbances following TAVI are shown in Figure 1. New-onset, complete LBBB was observed in 57 patients (28.2%) on the first ECG following the procedure, and an additional 4 patients developed new-onset LBBB at a mean of 24 ± 17 h (range: 12 to 48 h) following TAVI, leading to a global incidence of new-onset LBBB during the hospitalization period of 30.2%. The ECG performed at hospital discharge showed the persistence and resolution of LBBB in 25 and 23 patients, respectively.

At 6- to 12-month follow-up, no conduction disorders were observed in 65% of survivors at that time point. In patients with persistent LBBB at hospital discharge (n=25), LBBB had resolved in 12 patients (48%), 4 patients required PPI because of third-degree AVB (16%), and LBBB persisted in 9 patients (36%). No new-onset LBBB was documented in any patient after hospital discharge. The mean changes in QRS duration throughout the study period are shown in Figure 2.

Predictive factors of new-onset, persistent LBBB. Baseline and procedural characteristics of the patients, grouped according to the occurrence of persistent LBBB (vs. transient or no LBBB) following the TAVI procedure are shown in Table 2. Factors associated with persistent LBBB (vs. no or transient LBBB) in the univariate analysis were ventricular depth of the prosthesis (3.04 ± 1.72 mm vs. 1.56 ± 2.73 mm; $p = 0.009$), longer baseline QRS duration (96 ± 10 ms vs. 91 ± 11 ms; $p = 0.005$) and younger age (77 ± 9 years vs. 80 ± 7 years; $p = 0.010$). In the multivariate analysis, prosthesis ventricular depth (odds ratio [OR]: 1.37 for each increase of 1 mm; 95% confidence interval [CI]: 1.06 to 1.77; $p = 0.017$), and baseline QRS duration (OR: 1.24 for each increase of 4 ms; 95% CI: 1.01 to 1.51; $p = 0.037$) were independent predictors of persistent LBBB. No predictors of transient LBBB were identified.

Prognostic value of new-onset, persistent LBBB. Clinical outcomes during the hospitalization period according to the occurrence of new-onset LBBB are shown in Table 3. At a median (range) follow-up of 12 (6 to 24) months, a total of 32 patients had died, with no differences between patients with and without persistent LBBB. There was 1 case of sudden death during the follow-up period, which occurred 9 months after TAVI in a patient with no LBBB at hospital discharge. Survival curves at 1-year follow-up are shown in Figures 3A and 3B. The overall rate of PPI was higher in patients with persistent LBBB compared to the rest of the study population (34.2 vs. 4.3%; $p = 0.001$). Freedom from PPI curves up to 1-year follow-up are shown in Figure 3C. Thirty-day landmark analyses for cumulative outcomes are shown in Figures 3D to 3F. Baseline and procedural characteristics of the patients grouped according to the need for PPI are shown in Table 4. The occurrence of new-onset LBBB following the procedure (hazard ratio: 5.99; 95% CI: 2.93 to 15.61; $p < 0.001$) was the only factor associated with PPI during the entire study period.
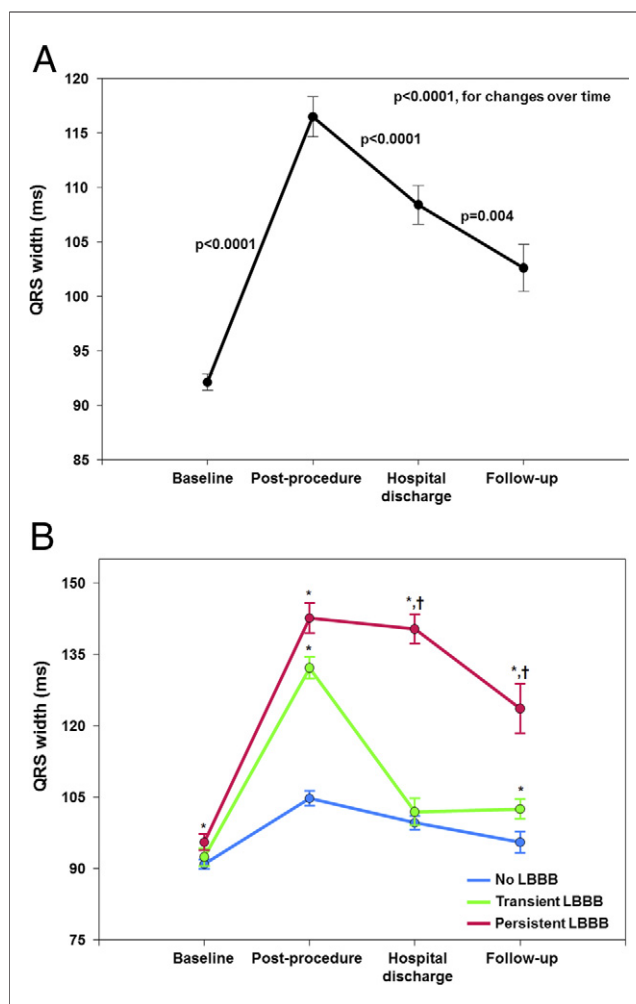

Figure 2   Changes in QRS Width Following TAVI

Changes in mean QRS duration following transcatheter aortic valve implantation and up to 6- to 12-month follow-up in overall population **(A)** and according to the occurrence of new-onset left bundle branch block **(B)**. Error bars indicate standard errors. *Different from the No LBBB group, $p < 0.05$; †different from the Transient LBBB group, $p < 0.0001$. Abbreviation as in Figure 1.

Late Clinical outcomes of the 25 patients with persistent LBBB and no PPI at hospital discharge are detailed in Table 5. None of these patients had sudden death at a median of 12 (6 to 24) months. However, the rates of syncope and the need for PPI during the follow-up period were higher in this group than in the rest of the study population (syncope: 16.0% vs. 0.7% [$p = 0.001$]; PPI: 20.0% vs. 0.7%, $p < 0.001$). The individual characteristics of the patients requiring PPI during the follow-up period are shown in Table 6. At 1-year follow-up, patients with persistent LBBB had a poorer New York Heart Association functional class compared to patients with no or transient LBBB ($p = 0.034$) (Fig. 4).

Echocardiographic data. Valve hemodynamics of the patients with and without new-onset LBBB are shown in Figure 5. The changes in LVEF throughout the study period are shown in Figure 6. Patients with persistent

Table 2	Baseline and Procedural Findings, According to the Occurrence of New-Onset LBBB Following TAVI			
	No LBBB (n = 141)	Transient LBBB (n = 23)	Persistent LBBB (n = 38)	p Value*
Baseline characteristics				
Age (yrs)	81 ± 8	79 ± 6	77 ± 9†	0.019
Female	83 (58.9)	17 (73.9)	21 (55.3)	0.328
Body mass index (kg/m²)	26 ± 5	26 ± 5	28 ± 6	0.125
Comorbidities				
Hypertension	119 (84.4)	22 (95.7)	37 (97.4)	0.041
Diabetes mellitus	44 (31.2)	8 (34.8)	15 (39.5)	0.615
COPD	35 (24.8)	3 (13.0)	12 (31.6)	0.261
CAD	79 (56.0)	17 (73.9)	22 (57.9)	0.277
eGFR (ml/min)	56.6 ± 22.5	54.6 ± 20.4	59.1 ± 26.3	0.742
Baseline treatment				
Beta-blockers	64 (45.4)	14 (60.9)	16 (42.1)	0.332
Calcium channel blockers	38 (27.0)	8 (34.8)	12 (31.6)	0.648
Amiodarone	8 (5.7)	2 (8.7)	3 (7.9)	0.729
STS-PROM score (%)	7.6 ± 3.8	6.1 ± 3.7	7.4 ± 3.4	0.476
ECG (ms)				
PR interval	176 ± 36	158 ± 23	174 ± 45	0.114
QRS duration	90 ± 10	92 ± 9	96 ± 10†	0.033
Echocardiography				
LVEF (%)	57 ± 12	54 ± 15	58 ± 11	0.440
Mean gradient (mm Hg)	46 ± 17	47 ± 19	49 ± 19	0.696
Aortic valve area (cm²)	0.65 ± 0.22	0.63 ± 0.28	0.61 ± 0.17	0.547
Computed tomography				
Aortic valve calcification (Agatston units)	2,544 (1,600–4,442)	2,045 (1,666–4,209)	3,150 (1,944–5,358)	0.412
Procedural variables				
Approach				0.335
Transapical	79 (56.0)	12 (52.2)	26 (68.4)	
Transfemoral	62 (44.0)	11 (47.8)	12 (31.6)	
Ratio aortic prosthesis size/aortic annulus	1.16 ± 0.07	1.18 ± 0.09	1.18 ± 0.07	0.097
Prosthesis ventricular depth‡ (mm)	1.64 ± 2.85	1.22 ± 2.23	3.04 ± 1.72†§	0.028

Values are mean ± SD, n (%), or median (interquartile range). *One-way analysis of variance for continuous variables and Fisher exact test for categorical variables. †p < 0.05 versus no LBBB by Tukey post-hoc test. ‡Distance between the hinge point of the mitral valve and the ventricular end of the valve prosthesis frame (TEE, long-axis view). §p < 0.05 versus transient LBBB by Tukey post-hoc test.
Abbreviations as in Table 1.

LBBB at hospital discharge exhibited a decrease in LVEF of 4.75 ± 8.02% (95% CI: 0.99 to 8.50; p = 0.031) at 1-year follow-up, whereas patients with no/transient LBBB had an increase in LVEF of 2.52 ± 11.32% (95% CI: 0.27 to 4.77; p = 0.0014 [p = 0.0012 between groups]). The LVEF at

Table 3	In-Hospital Outcomes, According to the Occurrence of New-Onset LBBB		
Variable	New-Onset LBBB (n = 61)	No LBBB (n = 142)	p Value
Complete AVB	8 (13.1)	6 (4.3)	0.023
Need for PPI	8 (13.1)	6 (4.3)	0.023
Major vascular complications	4 (6.6)	3 (2.1)	0.202
Major bleeding	9 (14.8)	14 (9.9)	0.194
Myocardial infarction	0	2 (1.4)	0.998
Stroke	3 (4.9)	1 (0.7)	0.083
Death	6 (9.8)	8 (5.7)	0.285
Hospital length of stay (days)	8 (5–13)	7 (6–9)	0.091

Values are n (%) or median (interquartile range).
AVB = atrioventricular block; other abbreviations as in Table 1.

1-year follow-up was lower in the persistent LBBB group compared to the no/transient LBBB group (53 ± 13% vs. 62 ± 9%; p = 0.0014). The changes in LVEF over time depending on baseline and procedural variables are shown in Table 7. In the multivariate linear regression analysis, the occurrence of persistent LBBB was the only independent predictive factor of decreased LVEF at 1-year follow-up (point estimate ± standard error: −8.6 ± 2.6; R^2: 0.14; p = 0.001).

Discussion

New-onset LBBB has been reported in 29% to 65% of the patients following TAVI with a self-expandable valve (1–8), and in 12% to 18% following TAVI with a balloon-expandable valve (3,7,9,10). The rate of 30% of new-onset LBBB observed in the present study might have been related mainly to the exclusion of patients with conduction abnormalities (including LBBB) or pacemaker prior to TAVI. In fact, the rate of new-onset LBBB in previous studies would have increased up to ~75% and 30% for
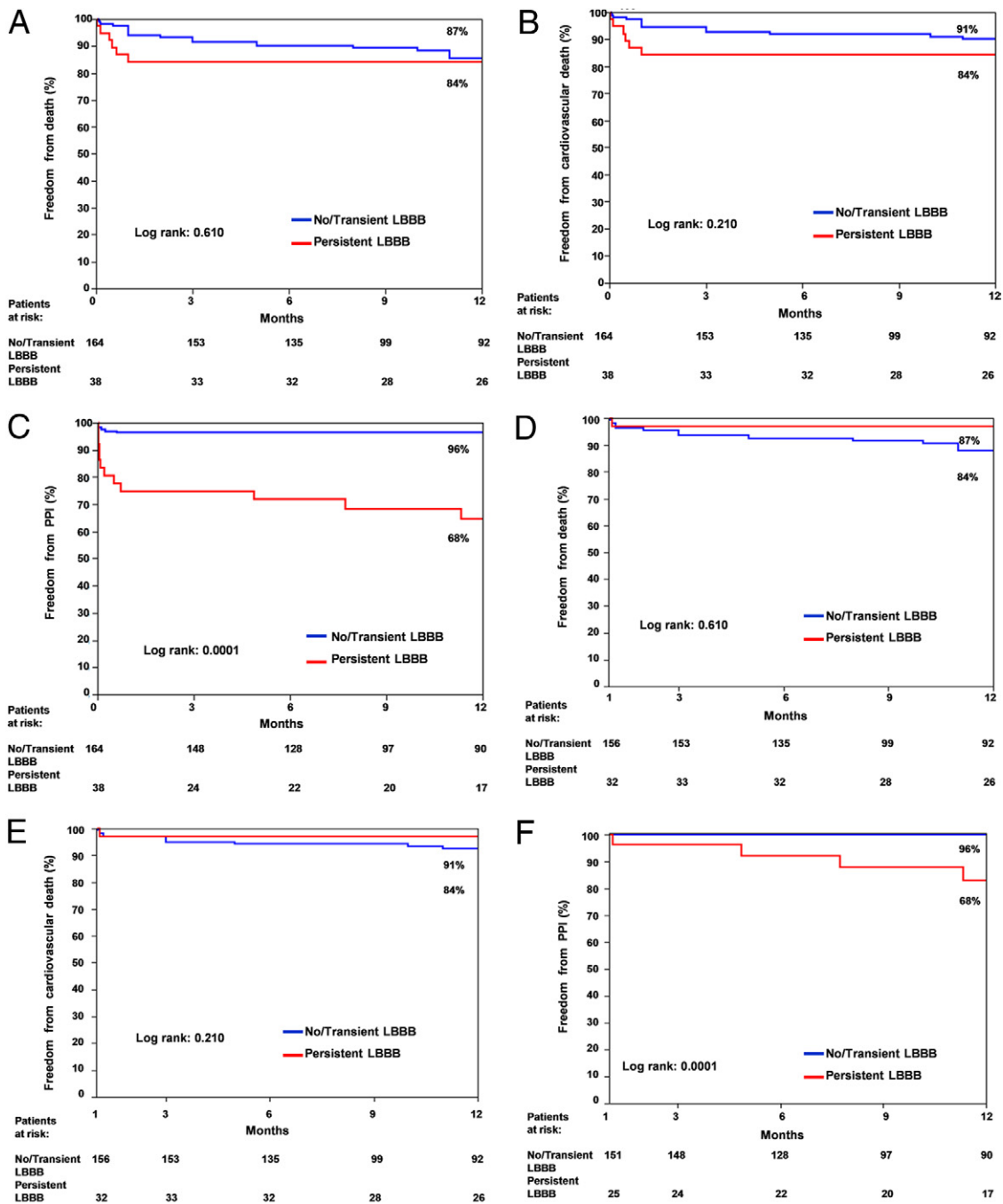
Figure 3   Survival Curves and Landmark Analysis Survival Curves at 30-Day Follow-Up in Patients With and Without Persistent LBBB Following TAVI

Kaplan-Meier curves up to 1-year follow-up for **(A)** overall mortality, **(B)** cardiac mortality, and **(C)** permanent pacemaker implantation in patients with and without new-onset persistent LBBB following transcatheter aortic valve implantation. Kaplan-Meier curves from 30 days following TAVI to 12 months for **(D)** overall mortality, **(E)** cardiac mortality, and **(F)** permanent pacemaker implantation (PPI) in patients with and without persistent LBBB. Abbreviations as in Figure 1.

self-expandable and balloon-expandable valves, respectively, if patients with complete bundle branch block and/or pacemaker had been excluded (1–6,8–10). Importantly, and in accordance with prior studies using balloon-expandable valves, a significant number of these conduction abnormal-

ities resolved within the first few days following the intervention (9,10). In a further step, this study also shows that up to about one-half of the cases of new-onset LBBB present at hospital discharge (median: 7 days after TAVI) had resolved at 1-year follow-up. This finding clearly differs

Table 4	Baseline and Procedural Findings, According to the Need for PPI (In-Hospital or During the Follow-Up Period)			
	PPI (Cumulative) (n = 20)	No PPI (n = 182)	HR (95% CI)	p Value
Clinical characteristics				
Age (yrs)	81 ± 6	80 ± 8	1.02 (0.96–1.09)	0.454
Female	12 (60.0)	109 (59.9)	0.90 (0.37–2.22)	0.803
Body mass index (kg/m²)	27 ± 6	27 ± 5	1.01 (0.92–1.11)	0.762
Comorbidities				
Hypertension	17 (85.0)	161 (88.5)	0.59 (0.17–2.04)	0.406
Diabetes mellitus	6 (30.0)	61 (33.5)	0.96 (0.37–2.51)	0.938
COPD	5 (25.0)	45 (24.7)	1.16 (0.42–3.22)	0.778
CAD	11 (55.0)	107 (58.8)	0.95 (0.39–2.30)	0.903
eGFR (ml/min)	51.9 ± 20.6	57.3 ± 23.2	0.99 (0.97–1.01)	0.343
Baseline treatment				
Beta-blockers	8 (40.0)	86 (47.3)	0.70 (0.28–1.72)	0.434
Calcium channel blockers	8 (40.0)	50 (27.5)	1.64 (0.67–4.01)	0.281
Amiodarone	2 (10.0)	11 (6.0)	1.80 (0.41–7.81)	0.433
STS-PROM score	6.9 ± 2.8	7.6 ± 3.8	0.94 (0.79–1.11)	0.457
ECG (ms)				
PR interval	191 ± 59	172 ± 35	1.01 (0.99–1.02)	0.354
QRS duration	94 ± 10	92 ± 10	1.02 (0.97–1.07)	0.500
Echocardiography				
LVEF (%)	62 ± 8	57 ± 12	1.03 (0.99–1.08)	0.137
Mean gradient (mm Hg)	44 ± 21	47 ± 17	0.99 (0.97–1.02)	0.491
Aortic valve area (cm²)	0.61 ± 0.19	0.64 ± 0.22	0.50 (0.40–6.26)	0.591
Computed tomography				
Aortic valve calcification (Agatston units)	3,362 ± 2,345	3,209 ± 2,104	—	0.854
Procedural variables				
Approach			1.66 (0.63–4.33)	0.303
Transapical	14 (70.0)	103 (56.6)	—	—
Transfemoral	6 (30.0)	79 (43.4)	—	—
Ratio prosthesis/aortic annulus	1.17 ± 0.09	1.16 ± 0.07	—	0.407
Ventricular depth of prosthesis* (mm)	3.19 ± 1.65	1.71 ± 2.68	1.27 (0.96–1.68)	0.100
Residual AR ≥2	1 (5.0)	27 (14.8)	1.02 (0.79–1.31)	0.877
New-onset LBBB	14 (70.0)	47 (25.8)	5.99 (2.29–15.61)	<0.001

Values are mean ± SD or n (%). *Distance between the hinge point of the mitral valve and the ventricular end of the valve prosthesis frame (TEE, long-axis view).

AR = aortic regurgitation; CI = confidence interval; HR = hazard ratio; other abbreviations as in Table 1.

from the experience with the self-expandable valve system, in which LBBB persisted in the vast majority of patients up to 6-month follow-up (15). Nuis et al. (8) showed that about 50% of conduction disturbances occurring during the TAVI procedure took place before valve implantation and were related to wire manipulation or balloon valvuloplasty. It is therefore not surprising that in the absence of permanent damage or mechanical stress of the left bundle branch, a significant number of these conduction disturbances resolve within the few days following the procedure. Another

Table 5	Late Clinic Outcomes, According to the Presence of New-Onset, Persistent LBBB (With No Pacemaker Implantation) at Hospital Discharge			
Outcome	Overall (n = 176)	Persistent LBBB (n = 25)	No/Transient LBBB (n = 151)	p Value
Follow-up (months)*	12 (6–24)	12 (5–24)	12 (5–24)	0.164
Syncope	5 (2.8)	4 (16.0)	1 (0.7)	0.001
Heart failure requiring hospitalization	26 (14.8)	7 (28.0)	19 (12.6)	0.124
PPI	6 (3.4)	5 (20.0)	1 (0.7)	<0.001
Death				
Overall	32 (18.2)	4 (16.0)	28 (18.5)	0.998
Cardiac death	14 (8.0)	1 (4.0)	13 (8.6)	0.696
Sudden death	1 (0.6)	0	1 (0.7)	0.999

Values are median (interquartile range) or n (%). *Median (IQR).

Abbreviations as in Table 1.

Table 6	**Individual Characteristics of the Patients Requiring PPI During the Follow-Up Period**			
Age (yrs)	**STS-PROM (%)**	**Persistent LBBB**	**Timing of PPI (months)**	**Reason for PPI**
69	6.8	Yes	7	Complete AVB (+ syncope)
70	5.2	Yes	4	Complete AVB (+ heart failure)
76	3.5	No	19	Complete AVB (+ pre-syncope)
77	4.5	Yes	1	Complete AVB (+ syncope)
78	7.9	Yes	11	Complete AVB (+ syncope)
79	10.8	Yes	43	Complete AVB (+ syncope)

Abbreviations as in Tables 1 and 3.

important finding of the present study is the fact that no new intraventricular conduction disturbances were observed either after day 2 in the periprocedural period or later during the follow-up period.

Predictive factors of new-onset, persistent LBBB. Unlike all prior studies evaluating the predictive factors of LBBB (transient and persistent) following TAVI, this study specifically focused in the prediction of persistent LBBB compared with transient or absent LBBB. Of note, no predictive factors were encountered for transient LBBB, whereas both a lower (ventricular) valve positioning and longer QRS duration were associated with persistent LBBB following balloon-expandable valve implantation. A longer QRS duration might be associated with an early stage of the conduction system disease which, in turn, can increase the vulnerability of this system to any trauma during the TAVI procedure (16,17). A more ventricular positioning of the valve prosthesis might increase the risk for mechanical stress and direct damage of the conduction system, leading to a higher risk for conduction disturbances. In accordance with the results of this study, a lower positioning of the valve prosthesis has been shown to be a predictor of conduction disturbances and PPI in patients following TAVI with the self-expandable device (1,6,7).

Prognostic value of new-onset, persistent LBBB. This study showed that the occurrence of new-onset, persistent LBBB following TAVI is associated with a much higher risk for complete AVB requiring PPI. It is of high clinical relevance that the higher risk for complete AVB started very soon (hours to days) after the appearance of LBBB, and
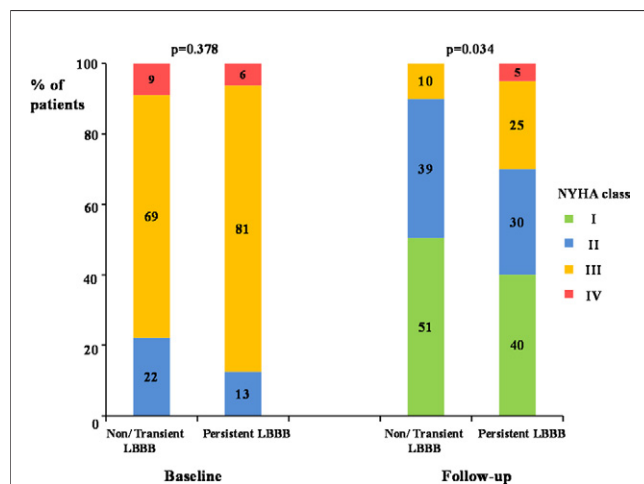

Figure 4   **Changes in Functional Class Following TAVI**

Changes in New York Heart Association functional class in patients with and without persistent LBBB following TAVI. Abbreviations as in Figure 1.
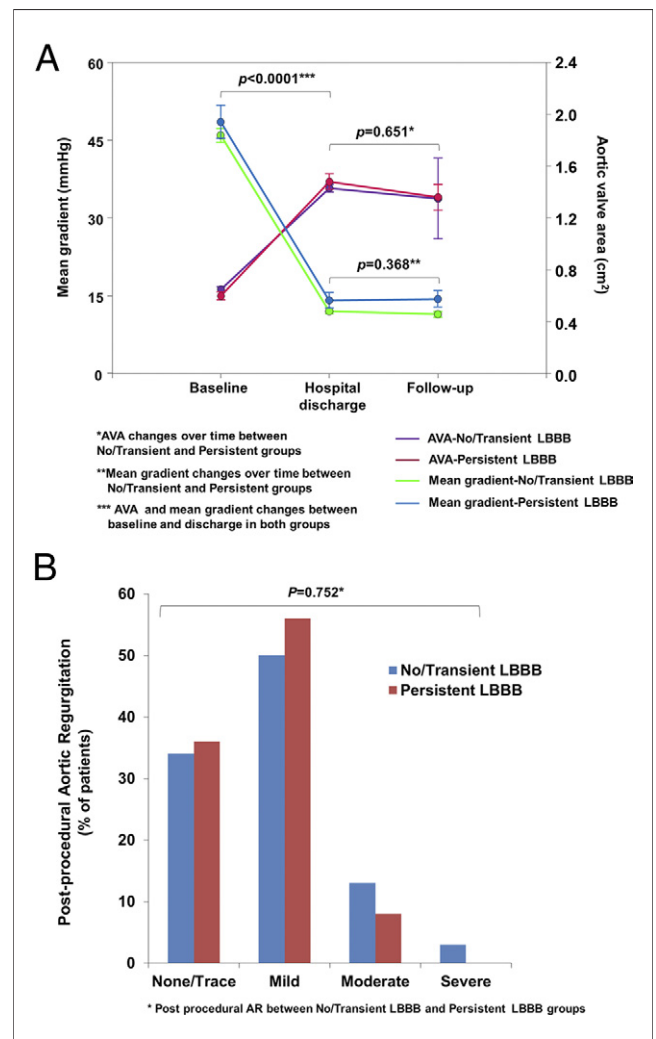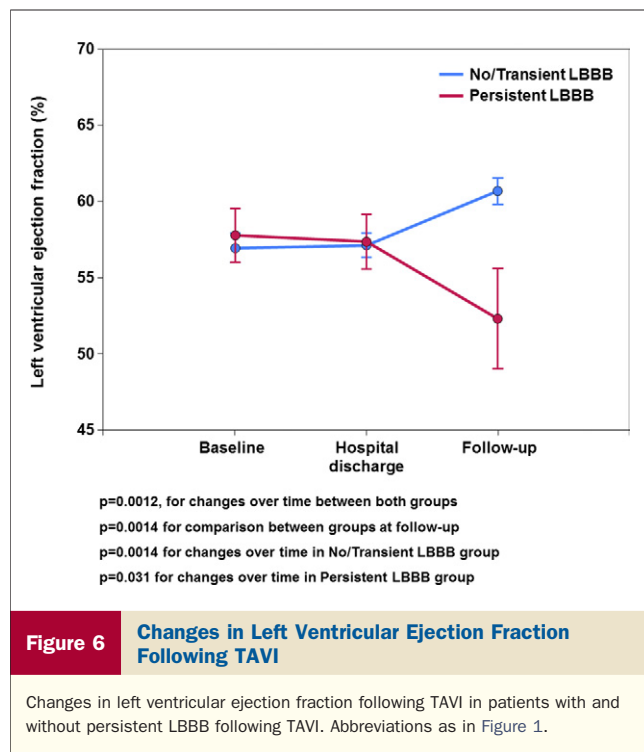

Figure 5   **Valve Hemodynamics Following TAVI**

(A) Changes in mean transvalvular gradient and aortic valve area, according to the occurrence on new-onset LBBB. **(B)** Degree of residual aortic regurgitation, according to the presence of new-onset LBBB. Abbreviations as in Figure 1.

Figure 6 Changes in Left Ventricular Ejection Fraction Following TAVI

Changes in left ventricular ejection fraction following TAVI in patients with and without persistent LBBB following TAVI. Abbreviations as in Figure 1.

Annotations within figure:
p=0.0012, for changes over time between both groups
p=0.0014 for comparison between groups at follow-up
p=0.0014 for changes over time in No/Transient LBBB group
p=0.031 for changes over time in Persistent LBBB group

Table 7	Changes in LVEF Between Hospital Discharge and 6- to 12-Month Follow-Up, According to Baseline and Procedural Variables	
	Δ LVEF	p Value
Clinical characteristics		
Age		0.907
≥ Median (81 yrs)	1.18 ± 9.42	
< Median (81 yrs)	1.42 ± 12.68	
Sex		0.824
Male	1.64 ± 9.14	
Female	1.15 ± 11.98	
Comorbidities		
Hypertension		0.035
Yes	0.56 ± 11.10	
No	7.46 ± 9.80	
Diabetes mellitus		0.104
Yes	0.26 ± 10.53	
No	3.94 ± 12.34	
COPD		0.202
Yes	2.04 ± 10.57	
No	−1.00 ± 12.71	
CAD		0.385
Yes	2.50 ± 14.06	
No	0.51 ± 8.70	
Baseline eGFR		0.235
≥ Median (55 ml/min)	2.54 ± 12.02	
< Median (55 ml/min)	0.11 ± 10.19	
STS-PROM score (%)		0.655
≥ Median (7.20 %)	1.11 ± 10.39	
< Median (7.20%)	2.01 ± 9.62	
ECG		
PR interval		0.974
≥ Median (168 ms)	2.07 ± 9.27	
< Median (168 ms)	2.14 ± 11.92	
QRS duration		0.645
≥ Median (92 ms)	0.80 ± 10.86	
< Median (92 ms)	1.75 ± 11.46	
Echocardiography		
LVEF		0.420
≥ Median (60%)	0.63 ± 9.79	
< Median (60%)	2.51 ± 13.27	
Mean gradient		0.784
≥ Median (43 mm Hg)	1.03 ± 11.57	
< Median (43 mm Hg)	1.59 ± 10.78	
Aortic valve area		0.424
≥ Median (0.60 cm²)	0.95 ± 8.18	
< Median (0.60 cm²)	2.47 ± 11.96	
Procedural variables		
Transcatheter approach		0.784
Transapical	1.10 ± 10.70	
Transfemoral	1.69 ± 12.05	
New-onset LBBB		0.001
No/Transient LBBB	2.52 ± 11.32	
Persistent LBBB	−4.75 ± 8.02	
Residual aortic regurgitation		0.625
≥2	1.09 ± 11.38	
<2	2.50 ± 9.88	
Peak CK-MB		0.446
≥ Median (19.30 μg/dl)	0.95 ± 10.95	
< Median (19.30 μg/dl)	2.59 ± 7.73	
Peak troponin T		0.092
≥ Median (0.50 μg/dl)	0.20 ± 9.64	
< Median (0.50 μg/dl)	3.97 ± 9.91	

Values are mean ± SD.
CK-MB = creatinine kinase–myocardial band; IVS = interventricular septum; other definitions as in Table 1.

continued during the follow-up period in those patients with persistent LBBB. In fact, all but 1 case of complete AVB leading to PPI during the follow-up period occurred in patients with persistent LBBB, and syncope was the clinical presentation in most patients. While we found no relationship between the occurrence of LBBB and acute or late mortality following TAVI, and no cases of sudden death were reported among the patients with persistent LBBB. The potential usefulness of a closer follow-up (serial ECGs, 24- to 48-h ECG monitoring within the first months following TAVI), and/or systematic electrophysiologic studies in such cases should probably be investigated in the future.

Patients with persistent LBBB had a significant impairment in LVEF during the follow-up period and exhibited a poorer functional status compared to those with no/transient LBBB. Tzikas et al. (18) reported a lack of post-procedural improvement in LVEF in patients with new-onset conduction disturbances (LBBB and/or pacemaker implantation) after self-expandable valve implantation. It is known that the presence of LBBB generates a ventricular contraction asynchrony secondary to an abnormal electrical activation, which in turn causes left ventricular remodeling and further ventricular dysfunction (19). The potential beneficial effects of resynchronization therapy (20) might merit evaluation in future studies.

Study limitations. The results regarding the lack of a relationship between persistent LBBB and cardiac mortality, and particularly sudden death, should be interpreted with caution due to the relatively small sample size. These

results will therefore have to be confirmed in larger studies in the future.

Conclusions

In patients with aortic stenosis and no prior conduction abnormalities, new-onset LBBB occurred in up to 30% of patients following TAVI with a balloon-expandable valve, although this conduction disturbance was persistent in less than half of patients at 6- to 12-month follow-up. The ventricular depth of the prosthesis and QRS duration predicted the occurrence of persistent LBBB, which was associated with a higher rate of AVB and PPI, and poorer functional status and ventricular function at midterm follow-up. These results highlight the importance of close monitoring and follow-up of patients with persistent LBBB following TAVI and support the performance of larger studies to further evaluate the prognostic value of these conduction abnormalities following TAVI.

Reprint requests and correspondence: Dr. Josep Rodés-Cabau, Quebec Heart & Lung Institute, Laval University, 2725 chemin Ste-Foy, G1V 4G5 Quebec City, Quebec, Canada. E-mail: josep.rodes@criucpq.ulaval.ca.

REFERENCES

1. Piazza N, Onuma Y, Jesserun E, et al. Early and persistent intraventricular conduction abnormalities and requirements for pacemaking after percutaneous replacement of the aortic valve. J Am Coll Cardiol Intv 2008;1:310–6.
2. Calvi V, Puzzangara E, Pruiti GP, et al. Early conduction disorders following percutaneous aortic valve replacement. Pacing Clin Electrophysiol 2009;32 Suppl 1:S126–30.
3. Roten L, Wenaweser P, Delacretaz E, et al. Incidence and predictors of atrioventricular conduction impairment after transcatheter aortic valve implantation. Am J Cardiol 2010;106:1473–80.
4. Fraccaro C, Buja G, Tarantini G, et al. Incidence, predictors, and outcome of conduction disorders after transcatheter self-expandable aortic valve implantation. Am J Cardiol 2011;107:747–54.
5. Khawaja MZ, Rajani R, Cook A, et al. Permanent pacemaker insertion after CoreValve transcatheter aortic valve implantation: incidence and contributing factors (the UK CoreValve Collaborative). Circulation 2011;123:951–60.
6. Baan J Jr, Yong ZY, Koch KT, et al. Factors associated with cardiac conduction disorders and permanent pacemaker implantation after percutaneous aortic valve implantation with the CoreValve prosthesis. Am Heart J 2010;159:497–503.
7. Aktug O, Dohmen G, Brehmer K, et al. Incidence and predictors of left bundle branch block after transcatheter aortic valve implantation. Int J Cardiol 2012;160:26–30.
8. Nuis RJ, Van Mieghem NM, Schultz CJ, et al. Timing and potential mechanisms of new conduction abnormalities during the implantation of the Medtronic CoreValve System in patients with aortic stenosis. Eur Heart J 2011;32:2067–74.
9. Gutierrez M, Rodes-Cabau J, Bagur R, et al. Electrocardiographic changes and clinical outcomes after transapical aortic valve implantation. Am Heart J 2009;158:302–8.
10. Godin M, Eltchaninoff H, Furuta A, et al. Frequency of conduction disturbances after transcatheter implantation of an Edwards Sapien aortic valve prosthesis. Am J Cardiol 2010;106:707–12.
11. Rodes-Cabau J. Transcatheter aortic valve implantation: current and future approaches. Nat Rev Cardiol 2011;9:15–29.
12. Leon MB, Piazza N, Nikolsky E, et al. Standardized endpoint definitions for Transcatheter Aortic Valve Implantation clinical trials: a consensus report from the Valve Academic Research Consortium. J Am Coll Cardiol 2011;57:253–69.
13. Surawicz B, Childers R, Deal BJ, et al. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part III: intraventricular conduction disturbances. J Am Coll Cardiol 2009;53:976–81.
14. Epstein AE, DiMarco JP, Ellenbogen KA, et al. ACC/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities. J Am Coll Cardiol 2008;51:e1–62.
15. Piazza N, Nuis RJ, Tzikas A, et al. Persistent conduction abnormalities and requirements for pacemaking six months after transcatheter aortic valve implantation. EuroIntervention 2010;6:475–84.
16. Mazzoleni A, Curtin ME, Wolff R, Reiner L, Somes G. On the relationship between heart weights, fibrosis, and QRS duration. J Electrocardiol 1975;8:233–6.
17. Thompson R, Mitchell A, Ahmed M, Towers M, Yacoub M. Conduction defects in aortic valve disease. Am Heart J 1979;98:3–10.
18. Tzikas A, van Dalen BM, Van Mieghem NM, et al. Frequency of conduction abnormalities after transcatheter aortic valve implantation with the Medtronic-CoreValve and the effect on left ventricular ejection fraction. Am J Cardiol 2011;107:285–9.
19. Zannad F, Huvelle E, Dickstein K, et al. Left bundle branch block as a risk factor for progression to heart failure. Eur J Heart Fail 2007;9:7–14.
20. Perrin MJ, Green MS, Redpath CJ, et al. Greater response to cardiac resynchronization therapy in patients with true complete left bundle branch block: a PREDICT substudy. Europace 2012;14:690–5.

Key Words: conduction disturbances ■ left bundle branch block ■ pacemaker ■ transcatheter aortic valve implantation ■ transcatheter aortic valve replacement.