Interventional Cardiology

Left Bundle-Branch Block Induced by Transcatheter Aortic Valve Implantation Increases Risk of Death

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Background—Transcatheter aortic valve implantation (TAVI) is a novel therapy for treatment of severe aortic stenosis. Although 30% to 50% of patients develop new left bundle-branch block (LBBB), its effect on clinical outcome is unclear.

Methods and Results—Data were collected in a multicenter registry encompassing TAVI patients from 2005 until 2010. The all-cause mortality rate at follow-up was compared between patients who did and did not develop new LBBB. Of 679 patients analyzed, 387 (57.0%) underwent TAVI with the Medtronic CoreValve System and 292 (43.0%) with the Edwards SAPIEN valve. A total of 233 patients (34.3%) developed new LBBB. Median follow-up was 449.5 (interquartile range, 174–834) days in patients with and 450 (interquartile range, 253–725) days in patients without LBBB (P=0.90). All-cause mortality was 37.8% (n=88) in patients with LBBB and 24.0% (n=107) in patients without LBBB (P=0.002). By multivariate regression analysis, independent predictors of all-cause mortality were TAVI-induced LBBB (hazard ratio [HR], 1.54; confidence interval [CI], 1.12–2.10), chronic obstructive lung disease (HR, 1.56; CI, 1.15–2.10), female sex (HR, 1.39; CI, 1.04–1.85), left ventricular ejection fraction ≤50% (HR, 1.38; CI, 1.02–1.86), and baseline creatinine (HR, 1.32; CI, 1.19–1.43). LBBB was more frequent after implantation of the Medtronic CoreValve System than after Edwards SAPIEN implantation (51.1% and 12.0%, respectively; P<0.001), but device type did not influence the mortality risk of TAVI-induced LBBB.

Conclusions—All-cause mortality after TAVI is higher in patients who develop LBBB than in patients who do not. TAVI-induced LBBB is an independent predictor of mortality. (Circulation. 2012;126:720-728.)

Key Words: conduction ■ heart failure ■ left bundle-branch block ■ mortality ■ transcatheter aortic valve implantation

Transcatheter aortic valve implantation (TAVI) is a relatively new, less invasive treatment for severe, symptomatic aortic stenosis and is advocated as an alternative to conventional surgical aortic valve replacement in patients who do not qualify for surgery. In the latter patient category, the PARTNER trial (Placement of AoRTic traNschatehER valve trial) has demonstrated that TAVI significantly reduces all-cause mortality, repeat hospitalization, and cardiac symptoms compared with standard therapy, including balloon valvuloplasty.1 For patients at high risk for surgery, survival after TAVI was comparable to that of surgical replacement, albeit with different periprocedural risks.2

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Recent studies state that TAVI can induce cardiac conduction abnormalities, the most frequent one being left bundle-branch block (LBBB). The incidence of TAVI-induced LBBB has been reported to vary between 7% and 83% and appears to depend on the device being used.3–6

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Although LBBB may appear to be a fairly harmless side effect in light of valve implantation, LBBB leads to abnormal ventricular contraction and compromised cardiac pump function.7–9 Clinical studies have shown that LBBB is associated with increased morbidity and mortality in a broad population, which varies from healthy individuals to patients after myocardial infarction to patients with established heart failure.10 The aim of the present study was to investigate the impact of a new LBBB after TAVI on all-cause mortality in a series of 679 patients who underwent TAVI between November 2005 and December 2010 in 8 centers in the Netherlands.

Methods

Study Population

All patients who underwent TAVI with either the self-expandable Medtronic CoreValve System (MCS; Medtronic Inc) or the balloon-expandable Edwards SAPIEN valve (ES; Edwards Lifesciences LLC) between November 2005 and December 2010 in any of the 8 participating centers were reviewed. The study population was defined by use of prospectively collected clinical and procedural data that were entered into the dedicated TAVI database of each center. If necessary, additional information was collected retrospectively by analysis of medical records or telephone review.

Study Design

We compared patients who developed new LBBB within 7 days after TAVI with patients who did not. For this purpose, all ECGs before and within 7 days after implantation were collected and reviewed by 2 of the authors (P.H. and T.T.P.) to extract heart rhythm, PR and QRS interval, and QRS axis. Newly developed LBBB was defined as a postprocedural V1-negative QRS complex with a duration of >120 ms and a notched or slurred R wave in at least 1 of the lateral leads (I, aVL, V5, V6), according to established guidelines.11 As a surrogate for the extent of left ventricular hypertrophy, we measured the amplitude of the R wave in aVL and V6/V5, as well as the amplitude of the S wave in V1, based on the Sokolow-Lyon criteria.12 An absent Q wave in V6 was regarded as an indicator of septal fibrosis.13,14

Exclusion criteria for the study were an aborted procedure without valve implantation, preexisting permanent pacemaker (PPM), or preexisting LBBB. All patients who required postprocedural PPM implantation were excluded from analysis (regardless of whether or not they developed LBBB), because a pacemaker intervention protects against bradyarrhythmic cardiac death, thereby influencing mortality. Moreover, it is known that intrinsic atrioventricular conduction apparently recovers within time, because some patients who have been implanted with a permanent pacemaker do not require ventricular pacing at long-term follow-up.15 As a result, these patients have intrinsic ventricular activation and do not exhibit the dysynchronous activation of right ventricular pacing. Cause of death was classified into 3 categories: Cardiovascular, noncardiovascular, and sudden. Death was defined as cardiovascular if it was caused by pump failure (acute or chronic), coronary artery disease, or cerebrovascular disease. The cause of death was categorized as sudden if a patient died suddenly.

Primary End Point

The primary end point was all-cause mortality at follow-up and was collected by consulting the Dutch civil registry. This governmental controlled registry contains vital records of the entire population, including date of death.

Statistical Analysis

The primary hypothesis of the present study was that TAVI-induced LBBB affects all-cause mortality of TAVI patients. This idea arose from studies that showed a reduced mortality caused by cardiac resynchronization therapy (CRT) in LBBB patients. For patients with New York Heart Association class I or II, the MADIT-CRT trial (Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy) demonstrated a 31% reduction in ventricular tachyarrhythmias or death caused by CRT.16 Overall 1-year mortality after TAVI in previous reports ranges from 24% to 31%.17 Assuming a 30% incidence of LBBB and a 1-year mortality of 30% and 20% in patients with and without TAVI-induced LBBB, respectively, we estimated that a minimum sample size of 231 patients with new LBBB and 462 patients without would be needed (2-sided α=0.05 and a power of 0.8).

Baseline variables were compared between groups. Categorical variables are presented as numbers and proportions and were compared with the Fisher exact test. For continuous variables, normality of distribution was assessed with the Kolmogorov-Smirnov test. Normal and skewed continuous variables are presented as means with SD and medians with interquartile range (IQR), respectively, and were compared accordingly with either an unpaired t test or the Mann-Whitney U test. A 2-sided probability value <0.05 was considered to be statistically significant. Survival was estimated by the Kaplan-Meier method. The log-rank test was used to compare mortality between patients with and without TAVI-induced LBBB. All variables with P<0.20 in univariate Cox regression analysis were entered into a multivariate Cox regression analysis by the enter method to determine the effect of TAVI-induced LBBB, adjusted for other potential predictors of the primary end point. To evaluate whether TAVI-induced LBBB was subject to a learning curve, consecutive patients at each center were ranked according to their entry time into the local TAVI program. Next, patients were grouped into strata of 20 patients according to their ranking number. The sixth and last stratum consisted of case number 100 and higher. Subsequently, data from all centers were combined. The aforementioned ranking and stratification were performed separately for both the MCS and the ES device. For descriptive purposes, we performed analysis of subsets with and without LBBB with use of the Breslow-Day test for heterogeneity testing. All statistical analyses were performed with the Statistical Package for Social Sciences (SPSS), version 17 (IBM SPSS, Chicago, IL).

Results

Study Population

Between November 15, 2005 and December 23, 2010, 1013 patients underwent TAVI in the 8 participating centers in the Netherlands. Not eligible were 197 patients because of an aborted procedure without valve implantation (n=11) and preexisting LBBB or preexisting PPM (n=186). In addition, another 118 patients were excluded because of postprocedural PPM implantation (Figure 1). There were 19 patients who died shortly after implantation, so that no follow-up ECG was available; as a consequence, it was not possible to categorize these patients. Therefore, a total of 679 patients were eligible for analysis. Baseline characteristics of the total study population and of patients with and without TAVI-induced LBBB are outlined in Table 1. Patients were septuagenarians and octogenarians with an almost even sex distribution. Baseline QRS duration was slightly but significantly shorter in patients with TAVI-induced LBBB. On the basis of ECG indices, there was no significant difference in left ventricular hypertrophy or septal fibrosis. All other baseline variables did not differ significantly between groups.

Procedural Outcomes

In 387 patients (57.0%), an MCS device was implanted (valve size 26 mm [n=192] and 29 mm [n=195]), and in 292 patients (43.0%), an ES device was implanted (valve size 23 mm [n=109] and 26 mm [n=183]). Access was trans-
Primary End Point

Median follow-up was 449.5 days (IQR, 174–834 days) in patients with new LBBB and 450 days (IQR, 253–725 days) in patients without new LBBB (P=0.90). At 30 days, the all-cause mortality rate was 12.9% (n=30) in patients who developed new LBBB compared with 8.7% (n=39) in patients who did not (log-rank P=0.09). At 1 year after implantation, the end point had occurred in 62 patients with new LBBB (26.6%) and 78 patients without new LBBB (17.5%; log-rank P=0.006), which indicates an increment in absolute and relative mortality risk for new LBBB of 9.1% and 52.0%, respectively. During total follow-up, the primary end point of all-cause mortality was reached in 37.8% (n=88) of patients with and 24.0% (n=107) of patients without new LBBB (log-rank P=0.002). Kaplan-Meier estimates of survival indicate a continuous worsening of outcome in patients with TAVI-induced LBBB (Figure 2). For the subset of 118 patients excluded from analysis because of PPM implantation, the mortality rate was 4.2% (n=5), 16.9% (n=20), and 28.8% (n=34) at 30 days, 1 year, and total follow-up, respectively.

Determinants of all-cause mortality at total follow-up are shown in Table 2. By univariate analysis, the following variables significantly predicted the end point, in descending order of hazard ratio (HR): Chronic obstructive lung disease (HR, 1.52; 95% confidence interval [CI], 1.13–2.05), TAVI-induced LBBB (HR, 1.55; 95% CI, 1.17–2.06), female sex (HR, 1.52; 95% CI, 1.15–2.03), left ventricular ejection fraction ≤50% (HR, 1.46; 95% CI, 1.09–1.96), use of MCS prosthesis (HR, 1.41; 95% CI, 1.05–1.90), and baseline creatinine (HR, 1.29; 95% CI, 1.18–1.42). By multivariate analysis, TAVI-induced LBBB was one of the strongest independent predictors of all-cause mortality (HR, 1.54; 95% CI, 1.12–2.10), together with chronic obstructive lung disease (HR, 1.56; 95% CI, 1.15–2.10), followed by female sex (HR, 1.39; 95% CI, 1.04–1.85), left ventricular ejection fraction ≤50% (HR, 1.38; 95% CI, 1.02–1.86), and baseline creatinine (HR, 1.32; 95% CI, 1.19–1.43).

Descriptive subset analysis showed that the effect of TAVI-induced LBBB on mortality was constant throughout different subgroups, except for chronic obstructive lung disease. The mortality risk of new LBBB was similar in patients who received an MCS or ES device (Figure 3).

The cause of death was cardiovascular in 42 patients without TAVI-induced LBBB (39.3%) and in 42 (47.7%) with TAVI-induced LBBB. Death was noncardiovascular in 47 (43.9%) and 31 patients (35.2%) without and with TAVI-induced LBBB, respectively, whereas the cause of death was sudden in 18 (16.8%) and 15 patients (17.0%) without and with new LBBB, respectively. In other words, the cardiovascular mortality rate was 9.4% for patients without and 18.0% for patients with TAVI-induced LBBB (log-rank P<0.001), whereas the noncardiac mortality rate was 10.5% and 13.3%, respectively (log-rank P=0.20). The mortality rate for sudden death was 4.0% for patients without and 6.4% for patients with TAVI-induced LBBB (log-rank P=0.13).

Determinants of TAVI-Induced LBBB

A binary logistic regression analysis was performed to identify baseline variables associated with the development of TAVI-induced LBBB. The use of the MCS prosthesis contributed significantly to the occurrence of LBBB in univariate analysis (HR, 7.69; 95% CI, 5.13–11.54). By multivariate analysis, this interaction persisted (HR, 8.51; 95% CI, 5.53–13.11; Table 3).

Comparison of Devices

After MCS implantation, a new LBBB occurred in 198 (51.1%) of 387 patients, as opposed to 35 (12.0%) of 292 patients in whom an ES valve had been implanted (P<0.001). Implantation of 26- and 29-mm MCS devices resulted in new LBBB in 95 (49.5%) of 192 and 103 (52.8%) of 195 patients, respectively (P=0.54). For the ES device, new LBBB occurred less frequently with 23-mm valves (7 [6.4%] of 109) than with 26-mm valves (28 [15.3%] of 183; P=0.03). Table 4 shows the difference in mortality rate between patients with and without LBBB for the entire study population and for subpopulations who received the MCS and ES device. Mor-
...tality rate did not differ significantly between MCS and ES for patients with or without TAVI-induced LBBB (log-rank \( P = 0.85 \) and 0.23, respectively). The frequency of LBBB development after MCS implantation decreased with increasing entry time, from \( 60\% \) to \( 40\% \). Entry time did not affect frequency of LBBB development after ES implantation (Figure 4). In the 2 centers implanting both the MCS and ES devices, the frequency of new LBBB was significantly higher with MCS implantations than with ES implantations (46.7\% and 15.9\%, respectively; \( P < 0.001 \)). In addition, LBBB occurred in 53.7\% of cases in the MCS-implanting centers compared with 10.3\% of cases in the ES-implanting centers \( (P<0.001) \). Of the 118 patients who required postprocedural PPM implantation, 102 (86.4\%) required the procedure after

MCS implantation and 16 (13.6\%) after ES implantation. In this patient category, the distribution of the different valve types was 5.9\% (n=7), 7.6\% (n=9), 42.4\% (n=50), and 44.1\% (n=52) for the ES 23-mm, ES 26-mm, MCS 26-mm, and MCS 29-mm valve, respectively.

### Discussion

The present study shows that all-cause mortality is significantly higher in TAVI patients who develop LBBB than in TAVI patients who do not. The higher all-cause mortality is largely determined by a significantly higher rate of cardiovascular deaths among patients with LBBB. TAVI-induced LBBB is one of the strongest predictors of all-cause mortality in...
TAVI patients, and this effect remains after adjustment for all potential confounders. Because the PARTNER trial showed that TAVI reduced all-cause mortality at 1 year by 38% compared with standard therapy, the 60% increase in 1-year mortality caused by new-onset LBBB in the present study suggests that the benefit of valve replacement by TAVI is largely neutralized when LBBB develops. In the broader perspective, the strong influence of abnormal conduction on clinical outcome in patients with valvular heart disease indicates that proper impulse conduction and valvular function are approximately equally important for normal cardiac function.

TAVI-Induced LBBB as a Risk Factor for Mortality

Previous TAVI-related studies have cited LBBB as a complication but did not mention its possible clinical relevance, because little is known about the impact of LBBB in the setting of valvular heart disease. However, multivariate analysis of the present data indicate that TAVI-induced LBBB is an independent and important risk factor for all-cause mortality after TAVI. Although it is not possible to completely exclude that LBBB is a surrogate for another baseline or procedural characteristic, we think that the present data strongly indicate that TAVI-induced LBBB itself is a risk factor for mortality.

### Table 2. Univariate and Multivariate Cox Regression Analysis of the Primary End Point of All-Cause Mortality

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate Analysis</th>
<th>Multivariate Analysis</th>
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<tbody>
<tr>
<td></td>
<td>HR</td>
<td>CI</td>
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<tr>
<td>Age</td>
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<td>Female sex</td>
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<tr>
<td>Baseline creatinine</td>
<td>1.29</td>
<td>1.18–1.42</td>
</tr>
<tr>
<td>Previous MI</td>
<td>1.24</td>
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<td>Previous CABG</td>
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<td>COPD</td>
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<td>LVEF ≤50%</td>
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<td>MCS prosthesis*</td>
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<td>Transfemoral access</td>
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<tr>
<td>TAVI-induced LBBB</td>
<td>1.55</td>
<td>1.17–2.06</td>
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</table>

HR indicates hazard ratio; CI, 95% confidence interval; MI, myocardial infarction; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction; MCS, Medtronic CoreValve System; and TAVI-induced LBBB, new left bundle-branch block induced by transcatheter aortic valve implantation.

*For calculation of the HR, the MCS prosthesis was compared to the Edwards SAPIEN prosthesis.
risk factor for mortality. After all, most baseline characteristics of patients without and with TAVI-induced LBBB were comparable. Notably, in the TAVI-induced LBBB group, there was no higher incidence of left ventricular hypertrophy or septal fibrosis, both of which are known to be associated with a poorer prognosis. There was also no coincidental association of TAVI-induced LBBB with a noncardiovascular cause of death. In logistic binary regression analysis, the use of the MCS prosthesis was a potent predictor of new-onset LBBB; however, in multivariate Cox regression analysis for survival, the device type being used did not predict mortality. This paradox can be explained by the fact that TAVI-induced LBBB is the predominant cause of mortality.

**Possible Mechanism of Increased Mortality**

There are 2 possible explanations for the deleterious effect of TAVI-induced LBBB: The risk of progression to high-degree atrioventricular conduction disorders and the adverse effects of dyssynchrony induced by LBBB. With regard to the latter, this possible effect of LBBB is in concordance with literature on electrocardiography and heart failure management, in which LBBB has increasingly been recognized as an important disorder, especially since the introduction of CRT.\(^\text{10,16}\) Moreover, the Dual Chamber and VVI Implantable Defibrillator (DAVID) trial demonstrated that continuous right ventricular pacing (which results in a left ventricular activation pattern comparable to that of LBBB) increases the combined end point of heart failure hospitalization and death compared with backup pacing only. In that trial with 250 patients in each study arm, the HR for all-cause 1-year mortality was 1.61.\(^\text{19}\)

Both experimental LBBB and clinical right ventricular pacing lead to an early reduction in cardiac pump function followed by worsening over time, caused at least in part by left ventricular remodeling.\(^\text{9,20}\) Recently, a reduction in left ventricular function has also been observed in TAVI patients shortly after development of LBBB.\(^\text{21}\) Timewise similar but directionally opposite changes are known to occur after application of CRT in heart failure patients, in which a rapid improvement in left ventricular function is seen, followed by reverse remodeling and ultimately, reduction in mortality.\(^\text{22–24}\) Therefore, a likely cause for the higher mortality after TAVI-induced LBBB is progression of heart failure as a consequence of left ventricular remodeling induced by the abnormal contraction pattern. This hypothesis is supported by the observed larger percentage of cardiovascular deaths that occurred in patients with TAVI-induced LBBB. This is congruent with observations that in chronic right ventricular pacing, heart failure hospitalization occurs more frequently in patients with depressed cardiac function than in patients with normal cardiac function.\(^\text{25}\) Except for pump failure, patients who develop dyssynchrony-induced left ventricular dysfunction are also susceptible to ventricular tachyarrhythmias,
which could be another possible explanation for the higher mortality in the TAVI-induced LBBB group.

In the present study, we were not able to differentiate between different (cardiac) causes of death. However, it is reasonable to presume that in our setting, the significantly higher rate of cardiovascular death after TAVI-induced LBBB was, in a majority of cases, caused by (dyssynchrony-induced) heart failure. Because there was no significant difference in sudden death, it seems less likely that TAVI-induced LBBB is associated with bradyarrhythmias. Future studies are needed to confirm our hypotheses on the mechanisms of increased mortality by TAVI-induced LBBB. In this way, we will be able to choose a cost-effective treatment strategy (eg, pacemaker or CRT implantation) that will improve quality of life, life expectancy, or both in this patient population composed of septuagenarians and octogenarians.

Possible Mechanism of TAVI-Induced LBBB
The development of atrioventricular conduction disorders and LBBB observed with aortic valve disease\cite{26} and after TAVI\cite{4,27–29} or surgical aortic valve replacement\cite{30–32} has been explained by the proximity of the atrioventricular node and left bundle branch to the aortic valve.\cite{33} During the TAVI procedure, pressure of the prosthetic skirt on the membranous septum and the nearby atrioventricular node and left bundle branch may cause conduction disorders.\cite{4} Indeed, it has been demonstrated that LBBB development was predicted by deeper MCS prosthesis implantation.\cite{34} Therefore, another possible cause of death for TAVI-induced LBBB is progression to high-degree atrioventricular block, although a post-procedural new LBBB has not been identified as a risk factor for permanent pacemaker implantation, in contrast to preprocedural LBBB.\cite{15}

Comparison of Devices
The present study corroborates data from other studies demonstrating that the incidence of TAVI-induced LBBB is

Table 3. Univariate and Multivariate Binary Logistic Regression Analysis of TAVI-Induced Left Bundle-Branch Block

<table>
<thead>
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<th>Variable</th>
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<td>S(V1) + R(V5/6) &gt;35 mm</td>
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<td>0.97–1.04</td>
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<tr>
<td>Absent Q in V6</td>
<td>1.05</td>
<td>0.72–1.54</td>
<td>0.79</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCS prosthesis*</td>
<td>7.69</td>
<td>5.13–11.54</td>
<td>&lt;0.001</td>
<td>8.51</td>
<td>5.53–13.11</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

TAVI indicates transcatheter aortic valve implantation; HR, hazard ratio; CI, 95% confidence interval; MI, myocardial infarction; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction; and MCS, Medtronic CoreValve System.

*For calculation of the HR, the MCS prosthesis was compared to the Edwards SAPIEN prosthesis.

Table 4. Mortality of Patients Without and With New Left Bundle-Branch Block for the Total Study Population and for Subpopulations Receiving Each Device Type

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>No LBBB</th>
<th>New LBBB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total study population</td>
<td>195/679 (28.7)</td>
<td>107/446 (23.4)</td>
<td>88/233 (37.8)</td>
</tr>
<tr>
<td>Medtronic CoreValve System</td>
<td>128/387 (33.1)</td>
<td>52/189 (27.5)</td>
<td>76/198 (38.4)</td>
</tr>
<tr>
<td>Edwards SAPIEN</td>
<td>67/292 (22.9)</td>
<td>55/257 (21.4)</td>
<td>12/35 (34.3)</td>
</tr>
</tbody>
</table>

LBBB indicates left bundle-branch block. Values are n/N (%).

Figure 4. Incidence of transcatheter aortic valve implantation (TAVI)–induced left bundle-branch block (LBBB) according to valve type. The percentages of patients who developed a TAVI-induced LBBB are shown for both the Medtronic CoreValve System (MCS) and the Edwards SAPIEN (ES) device. Patients were ranked into 6 different categories according to their entry time into the local TAVI program.
higher for the MCS device than for the ES prosthesis.\textsuperscript{5,5,7} A similar difference was observed for requirement of PPM implantation because of high-degree atrioventricular block, which is also in agreement with previous studies.\textsuperscript{4,5} The higher chance of inducing conduction disorders by the MCS device has been attributed to the longer prosthetic skirt of the MCS device.\textsuperscript{28} However, recently it has been shown that during MCS implantation procedures, LBBB develops before actual insertion of the valve device in >50\% of the cases and that contact of the guidewire or compression of the left ventricular outflow orifice by the dilatary balloon may be responsible for some of the damage to the conduction system.\textsuperscript{3,6} For the ES prosthesis, these data are not available. However, there are important differences between the delivery systems (catheters, balloon sizes and shapes) and vascular access route (ie, transapical access, in which there is no need for a curved, stiff guidewire in the left ventricle) that may explain the lower incidence of LBBB in ES implantations. The present data further indicate that the incidence of LBBB in MCS implantations decreases to some extent with increasing experience. Still, even with increasing experience, the frequency of LBBB is 40\% for MCS as opposed to <10\% for the ES prosthesis. Therefore, education on TAVI should not only be directed to optimal valve repair but also to prevention of LBBB. Clearly, there is a great need for better understanding of the origin of TAVI-induced LBBB to develop better tools to prevent this conduction disorder. Our observation that TAVI-induced LBBB increases the risk of mortality, combined with a >4 times higher incidence of LBBB and PPM implantation with MCS implants, should be taken into consideration when making the choice between currently available devices and when obtaining informed consent from the patient.

Study Limitations

The present study is based on a multicenter Dutch registry, with the inherent limitations of such a design. However, this study is composed of consecutive cases over a 5-year period from 8 of 11 TAVI-implanting centers in the Netherlands. To ensure data quality and validity, we chose a hard end point (all-cause mortality). No monitoring board or core laboratory was available for ECG analysis, but we strictly adhered to published guidelines for the diagnosis of LBBB\textsuperscript{11} and scored the presence of LBBB without knowledge of the actual outcome of the patient. The mean 30-day all-cause mortality rate in the present study was higher and the 1-year all-cause mortality rate was lower than that of earlier reports, including the PARTNER trial,\textsuperscript{1,2,17} probably as a result of differences in logistic EuroSCORE (European System for Cardiac Operative Risk Evaluation), patient characteristics, and inclusion and exclusion criteria.

Conclusions

In patients who develop LBBB after TAVI, all-cause mortality is significantly higher than among patients who do not develop LBBB. The excess in mortality is largely determined by a significantly higher rate of cardiovascular deaths in patients with LBBB. The frequency of LBBB is strongly dependent on prosthesis type; however, the mortality risk when LBBB occurs is equal for both devices. These data indicate that LBBB is a serious complication of TAVI that may strongly attenuate the benefit of this procedure. Further research is warranted to clarify the cause of death and the causal factors for TAVI-induced LBBB.

Disclosures

Dr Van Garse is a proctor for Edwards Lifesciences. Dr de Jaegere is a proctor for Medtronic CoreValve. Dr van der Kley is a proctor for Edwards Lifesciences. Dr Schalij has received research grants from Medtronic Inc and Edwards Lifesciences. Dr Cocchieri is a proctor for Edwards Lifesciences. Dr den Heijer is a proctor for Medtronic CoreValve. Dr Stella is a proctor for Edwards Lifesciences. Dr Prinzen has received research grants from Medtronic Inc, EBR Systems, Philips, Enopace Biomedical, and Merck Sharpe & Dohme. The remaining authors report no conflicts.

References

Transcatheter aortic valve implantation (TAVI) has proved to be a valuable treatment in patients with severe, symptomatic aortic valve stenosis who do not qualify for surgery. The TAVI procedure is frequently complicated by new-onset left bundle-branch block (LBBB). Although this complication has been addressed in TAVI literature, no attention has been paid to its clinical relevance, despite ample evidence of unfavorable outcome in other patient populations. Our multicenter study, comprising 679 TAVI patients from 8 centers in the Netherlands, convincingly shows that TAVI-induced LBBB is one of the strongest predictors of all-cause mortality. The observed ~60% increase in mortality caused by TAVI-induced LBBB suggests that the benefit of valve repair is largely neutralized when LBBB develops. Mortality risk of LBBB was independent of the device type used; however, the incidence of LBBB was 4-5 times higher with the use of the Medtronic CoreValve System device than with the Edwards SAPIEN device (51% versus 12%). This is the first study indicating the considerable importance of LBBB in the outcome of TAVI patients. More attention should be paid to avoiding LBBB in TAVI procedures, both by implanters and by vendors of TAVI devices. With an approximately 50% rate of LBBB and an approximately 20% rate of permanent pacemaker implantations, the studied Medtronic CoreValve System prostheses (until 2010) performed significantly worse than the Edwards SAPIEN devices with regard to both patient outcome and healthcare costs. LBBB should be regarded as a serious adverse event when evaluating new TAVI devices.
Left Bundle-Branch Block Induced by Transcatheter Aortic Valve Implantation Increases Risk of Death

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