



Pre-Existing Right Bundle Branch Block Increases Risk for Death After Transcatheter Aortic Valve Replacement With a Balloon-Expandable Valve

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ABSTRACT

OBJECTIVES The aim of this study was to determine the impact of pre-existing right bundle branch block (RBBB) on clinical outcomes after transcatheter aortic valve replacement (TAVR).

BACKGROUND The impact of pre-existing RBBB on clinical outcomes after TAVR is unknown.

METHODS Between October 2013 and August 2015, 749 patients undergoing TAVR using the Edwards SAPIEN XT prosthesis were prospectively enrolled in the OCEAN-TAVI (Optimized Transcatheter Valvular Intervention) registry from 8 Japanese centers. Electrocardiograms were obtained at baseline. After the procedure, follow-up outpatient visits or telephone interviews were conducted at 30 days, 6 months, and yearly.

RESULTS A total of 102 patients (13.6%) had pre-existing RBBB. The incidence of new pacemaker implantation was significantly higher in the RBBB group (17.6% vs. 2.9%; $p < 0.01$). The Kaplan-Meier analysis revealed that cardiovascular survival probability was significantly lower in the RBBB group than the no-RBBB group (log-rank $p < 0.01$). Patients with RBBB and without pacemakers were at higher risk for cardiovascular mortality in the early phase after discharge, and patients with RBBB and pacemakers had higher cardiovascular mortality at mid-term follow-up (log-rank $p = 0.01$). A multivariate Cox regression model indicated that pre-existing RBBB (hazard ratio: 2.59; 95% confidence interval: 1.15 to 5.85; $p < 0.01$) was an independent predictor of cardiovascular mortality.

CONCLUSIONS Patients with RBBB demonstrated an increased risk for cardiovascular mortality after TAVR, and patients with RBBB and without pacemakers were at higher risk for cardiac death early after discharge. Patients with prior RBBB should be carefully monitored after undergoing TAVR. (J Am Coll Cardiol Intv 2016;9:2210-6)
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In recent years, transcatheter aortic valve replacement (TAVR) has evolved from its position as an emerging technology to a mainstream therapy for treating patients with severe symptomatic aortic stenosis (1-3). As a result, the number of patients undergoing TAVR worldwide has increased

steadily, and the complications related to valve implantation have become well recognized.

New conduction disturbances like left bundle branch block (LBBB) and atrioventricular block (AVB) requiring permanent pacemaker implantation are common and clinically important events (4,5).

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Patients with pre-existing right bundle branch block (RBBB) have an increased risk for post-procedural bradycardia and episodes of high-degree AVB that require treatment with permanent pacemaker implantation (6-9). However, the prognostic value of pre-existing RBBB in patients undergoing TAVR has not been well studied.

The purpose of this study was to determine the impact of a pre-existing RBBB on clinical outcomes in a multicenter cohort of patients who underwent TAVR with a balloon-expandable valve.

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METHODS

STUDY POPULATION AND DESIGN. The OCEAN-TAVI (Optimized Transcatheter Valvular Intervention) registry is a Japanese multicenter prospective registry. This registry was initiated to observe and document the procedural results and post-procedural outcomes of patients who undergo TAVR. The OCEAN-TAVI registry is maintained independent of any industry influence.

Between October 2013 and August 2015, a total of 749 consecutive high-risk Japanese patients with symptomatic, severe aortic stenosis undergoing TAVR using the Edwards SAPIEN XT prosthesis (Edwards Lifesciences, Irvine, California) were prospectively enrolled in the OCEAN-TAVI registry. The patients were treated at the Teikyo University School of Medicine (Tokyo, Japan; n = 78), Kokura Memorial Hospital (Fukuoka, Japan; n = 121), Sendai Kousei Hospital (Miyagi, Japan; n = 123), Saiseikai Yokohama-City Eastern Hospital (Kanagawa, Japan; n = 63), New Tokyo Hospital (Chiba, Japan; n = 61), Shonan Kamakura General Hospital (Kanagawa, Japan; n = 83), Toyohashi Heart Center (Aichi, Japan; n = 65), Nagoya Heart Center (Aichi, Japan; n = 13), and Keio University School of Medicine (Tokyo, Japan; n = 142). Inclusion criteria were the presence of symptomatic, degenerative aortic stenosis with New York Heart Association functional class II or greater; a mean gradient >40 mm Hg or a jet velocity >4.0 m/s, or an aortic valve area <1.0 cm² (or an effective orifice area index <0.6 cm²/m²). Patients for whom TAVR was deemed the best treatment option were selected on the basis of the clinical consensus of a multidisciplinary team of cardiac surgeons, interventional cardiologists, anesthesiologists, and imaging specialists. The primary exclusion criteria were bicuspid or noncalcified aortic valve, failed surgical bioprosthesis implantation, severe aortic regurgitation, and dialysis dependence. The prosthesis size (20, 23, 26, or 29 mm) was determined on the basis of the pre-procedural echocardiographic

and multidetector computed tomographic findings. The devices were delivered via the transfemoral, transiliac, or transapical approach. The selection of either the femoral, iliac, or apical approach was determined on the basis of the iliofemoral artery diameter, calcifications, and tortuosity. Procedural success and procedural complications during the TAVR procedure were evaluated according to the Valve Academic Research Consortium 2 criteria (10). This trial is registered with the University Hospital Medical Information Network (UMIN000020423).

ABBREVIATIONS AND ACRONYMS

- AVB** = atrioventricular block
- CI** = confidence interval
- HR** = hazard ratio
- IQR** = interquartile range
- LBBB** = left bundle branch block
- RBBB** = right bundle branch block
- TAVR** = transcatheter aortic valve replacement

TABLE 1 Study Population

	RBBB (n = 102)	No RBBB (n = 647)	p Value
Age, yrs	85.0 (81.0-89.0)	85.0 (82.0-88.0)	0.43
Male	40 (39.2)	213 (32.9)	0.21
Height, cm	148.1 (141.5-154.7)	149.5 (143.5-155.6)	0.63
Weight, kg	49.8 (40.8-58.8)	48.4 (41.4-55.4)	0.31
BSA, m ²	1.41 (1.28-1.54)	1.40 (1.29-1.51)	0.51
BMI, kg/m ²	22.2 (19.5-24.9)	21.7 (19.3-24.1)	0.09
Diabetes	27 (26.4)	162 (25.0)	0.93
Hyperlipidemia	37 (36.3)	283 (43.7)	0.16
Smoking	21 (20.6)	129 (19.9)	0.96
Hypertension	82 (80.4)	484 (74.8)	0.14
NYHA functional class III/IV	53 (52.0)	305 (47.1)	0.21
Coronary artery disease	28 (28.0)	156 (24.2)	0.46
Previous MI	10 (9.8)	54 (8.3)	0.63
Previous CABG	11 (10.8)	48 (7.4)	0.24
Previous PCI	28 (27.5)	177 (27.4)	0.99
Peripheral artery disease	19 (18.6)	100 (15.5)	0.42
Cerebrovascular disease	22 (21.6)	84 (13.0)	0.02
COPD	22 (21.6)	131 (20.2)	0.76
eGFR, ml/min/1.73 m ²	48.1 (37.5-58.6)	49.0 (36.2-61.8)	0.61
Logistic EuroSCORE, %	13.7 (7.4-20.0)	12.8 (6.2-19.4)	0.98
STS score, %	6.8 (4.4-9.0)	6.9 (4.5-9.3)	0.98
EuroSCORE II, %	3.7 (1.4-6.0)	3.9 (2.0-5.8)	0.97
Aortic valve area, cm ²	0.64 (0.49-0.79)	0.62 (0.50-0.79)	0.30
Aortic valve area index, cm ² /m ²	0.44 (0.37-0.52)	0.43 (0.35-0.51)	0.60
Mean pressure gradient, mm Hg	47.5 (35.0-60.0)	48.0 (36.4-59.6)	0.72
LVEF, %	62.0 (55.0-69.0)	61.0 (53.0-69.0)	0.69
Annular area by CT, mm ²	398.7 (356.4-441.0)	378.0 (335.0-421.0)	<0.01
Medications			
Aspirin	82 (80.4)	473 (73.1)	0.12
Thienopyridine	51 (50.0)	336 (52.0)	0.71
Warfarin	15 (14.7)	101 (15.6)	0.81
ACE inhibitors/ARBs	47 (46.1)	360 (55.6)	0.07
Beta blocker	32 (31.4)	213 (33.0)	0.75

Values are median (interquartile range) or n (%).
 ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; BMI = body mass index; BSA = body surface area; CABG = coronary artery bypass graft; COPD = chronic obstructive pulmonary disease; CT = computed tomography; eGFR = estimated glomerular filtration rate; EuroSCORE = European System for Cardiac Operative Risk Evaluation; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; RBBB = right bundle branch block; STS = Society of Thoracic Surgeons.

	RBBB (n = 102)	No RBBB (n = 647)	p Value
Transfemoral	80 (78.4)	508 (78.5)	0.15
Transapical	22 (21.6)	119 (18.4)	
Transiliac	0 (0)	20 (3.1)	
Valve size			
SAPIEN XT 20 mm	0 (0)	9 (1.4)	0.50
SAPIEN XT 23 mm	66 (64.7)	426 (65.8)	
SAPIEN XT 26 mm	32 (31.4)	197 (30.4)	
SAPIEN XT 29 mm	4 (3.9)	15 (2.3)	
Area oversizing ratio	1.14 (1.05-1.23)	1.18 (1.10-1.26)	<0.01
Post-dilation	23 (22.5)	155 (24.0)	0.75

Values are n (%) or median (interquartile range).
RBBB = right bundle branch block.

ELECTROCARDIOGRAPHIC DATA. Electrocardiographic records were obtained from all patients at baseline and immediately after valve implantation. Electrocardiographic records were analyzed by a cardiologist at each center. The diagnosis of intraventricular conduction abnormalities was on the basis of the American Heart Association, American

College of Cardiology Foundation, and Heart Rhythm Society recommendations for the standardization and interpretation of electrocardiograms (11).

INDICATIONS FOR NEW PACEMAKER IMPLANTATION.

In agreement with the American College of Cardiology, American Heart Association, and Heart Rhythm Society recommendations, new pacemaker implantation was indicated if third-degree or advanced second-degree AVB at any anatomic level occurred and was not expected to resolve or in the presence of sinus node dysfunction and documented symptomatic bradycardia (12). The selection of a single-chamber or dual-chamber pacemaker was left to the implanting physician at each center.

FOLLOW-UP. Study follow-up was completed via outpatient visits or telephone interviews at 30 days, 6 months, and yearly after the procedure. No patient was lost to follow-up, and the median follow-up period was 492 days (interquartile range [IQR]: 323.5 to 660.5 days). All events were defined according to the Valve Academic Research Consortium 2 criteria, and any death was recorded and classified to indicate whether it was due to a cardiovascular or noncardiovascular cause (10). Any death of unknown cause was defined as death due to a cardiovascular cause, as recommended by the Valve Academic Research Consortium 2 criteria, and sudden cardiac death was defined as any unexpected death due to a cardiac cause. Late mortality was defined as mortality between 30 days and 1 year, and mid-term mortality was defined as all-cause mortality after 1 year.

STATISTICAL ANALYSIS. Continuous variables were assessed for normal distribution using the Shapiro-Wilk test and are expressed as mean \pm SD or as median and IQR, as appropriate. Categorical variables are expressed as numeric values and percentages. Comparison of continuous variables was performed using the unpaired Student *t* test or the Wilcoxon rank sum test, depending on the variable distribution. The chi-square test or Fisher exact test was used to compare categorical variables. Kaplan-Meier analysis was performed using the log-rank test to compare survival rates between the RBBB and no-RBBB groups. Univariate logistic regression analysis was performed to obtain the odds ratio for all-cause mortality. Thereafter, a Cox logistic regression analysis was performed using the variables with *p* values <0.10 in the univariate analysis, to examine their independent associations with all-cause mortality. The data were analyzed using PASW Statistics 22.0 (SPSS, Chicago, Illinois).

	RBBB (n = 102)	No RBBB (n = 647)	p Value
Major vascular complication	6 (5.9)	45 (7.0)	0.44
Minor vascular complication	5 (4.9)	32 (4.9)	0.99
Life-threatening bleeding	12 (11.8)	39 (6.0)	0.03
Major bleeding	13 (12.7)	82 (12.7)	0.98
Minor bleeding	14 (13.7)	109 (16.8)	0.43
Myocardial infarction	0 (0)	8 (1.2)	0.61
Coronary obstruction	2 (2.0)	8 (1.2)	0.41
Cardiac tamponade	3 (2.9)	9 (1.4)	0.22
Valve migration	0 (0)	0 (0)	NS
Conversion to open heart surgery	3 (2.9)	7 (1.1)	0.14
Stroke	2 (2.0)	16 (2.5)	1.00
Transfusion	36 (35.3)	216 (33.4)	0.70
Stage 3 acute kidney injury	4 (3.9)	13 (2.0)	0.19
Post-implantation			
Mean pressure gradient, mm Hg	10.0 (7.5-12.5)	10.0 (7.5-12.5)	0.78
LVEF, %	61.4 (54.9-67.9)	61.0 (54.5-66.5)	0.73
Aortic regurgitation moderate or greater	3 (2.9)	14 (2.2)	0.41
New atrial fibrillation	4 (3.9)	22 (3.4)	0.48
New pacemaker	18 (17.6)	19 (2.9)	<0.01
Early safety endpoint (30 days)	23 (22.5)	116 (17.9)	0.27
30-day survival	95 (96.0)	624 (98.6)	0.09
Late mortality*	12 (11.8)	37 (5.7)	
Sudden cardiac death	2 (2.0)	2 (0.3)	
Death due to heart failure	4 (3.9)	6 (0.9)	
1-yr mortality†	17.7 \pm 3.8	9.4 \pm 1.2	0.03
1-yr cardiovascular mortality†	10.1 \pm 3.0	2.9 \pm 0.7	<0.01

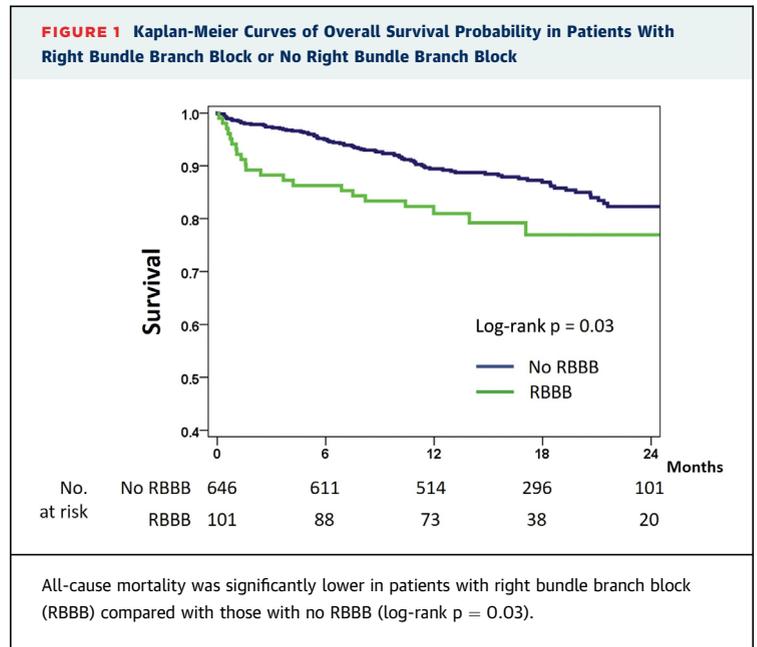
Values are n (%), median (interquartile range), or mean \pm SD. *All-cause mortality between day 30 and 1 year.
†Cumulative Kaplan-Meier estimates at 1 year.
Abbreviations as in Table 1.

RESULTS

PATIENT CHARACTERISTICS. A total of 102 patients (13.6%) had RBBB at the baseline evaluation. The baseline characteristics of the RBBB and no-RBBB groups are presented in **Table 1**. The prevalence of previous cerebrovascular disease was higher in the RBBB group (21.6% vs. 13.0%; $p = 0.02$). A larger annular area was observed in the RBBB group than in the no-RBBB group (398.7 mm² [IQR: 356.4 to 441.0 mm²] vs. 378.0 mm² [IQR: 335.0 to 421.0 mm²]; $p < 0.01$). Other baseline comorbidities were similar between the 2 groups.

PROCEDURAL CHARACTERISTICS. The transfemoral approach was implemented in 78.4% of the patients in the RBBB group and in 78.5% in the no-RBBB group. The most commonly used implant was the Edwards SAPIEN XT 23-mm valve, which was used in 64.7% of the RBBB group and in 67.2% of the no-RBBB group. No significant difference was observed between the 2 groups in the rate of post-dilation (**Table 2**).

POST-PROCEDURAL OUTCOMES AND FOLLOW-UP. Post-procedural outcomes and follow-up are shown in **Table 3**. The incidence of life-threatening bleeding was higher in the RBBB group than in the no-RBBB group (11.8% vs. 6.0%; $p = 0.03$). The incidences of major vascular complications, minor vascular complications, major bleeding, and minor bleeding were similar between the RBBB and no-RBBB groups. The incidences of myocardial infarction, coronary obstruction, cardiac tamponade, valve migration, conversion to open heart surgery, stroke, transfusion, and stage 3 acute kidney injury were similar in both groups. The incidence of new pacemaker implantation was significantly higher among patients with RBBB (17.6% vs. 2.9%; $p < 0.01$). Between the RBBB and no-RBBB groups, there was a trend toward lower 30-day survival in the RBBB group (96.0% vs. 98.6%; $p = 0.09$) and the rate of early safety endpoints (30 days, 22.5% vs. 17.9%; $p = 0.27$). The incidences of moderate or greater post-procedural aortic regurgitation (2.9% vs. 2.2%; $p = 0.41$), post-procedural mean pressure gradient (10.0 mm Hg [IQR: 7.5 to 12.5 mm Hg] vs. 10.0 mm Hg [IQR: 7.5 to 12.5 mm Hg]; $p = 0.78$) and left ventricular ejection fraction (61.4% [IQR: 54.9% to 67.9%] vs. 61.0% [IQR: 54.5% to 66.5%]; $p = 0.73$) were similar in both groups. The rates of late mortality, cardiovascular mortality, and death due to heart failure were higher in the RBBB group than in the no-RBBB group.



KAPLAN-MEIER SURVIVAL CURVES OF MID-TERM SURVIVAL.

The Kaplan-Meier analysis revealed that the overall survival probability was significantly lower (log-rank $p = 0.03$) (**Figure 1**) and the cardiovascular survival probability significantly lower (log-rank $p < 0.01$) (**Figure 2**) in the RBBB group compared with the no-RBBB group. The Kaplan-Meier overall and cardiovascular survival curves also revealed that there were significant differences between the groups, RBBB or no RBBB, and permanent pacemaker or no pacemaker (log-rank

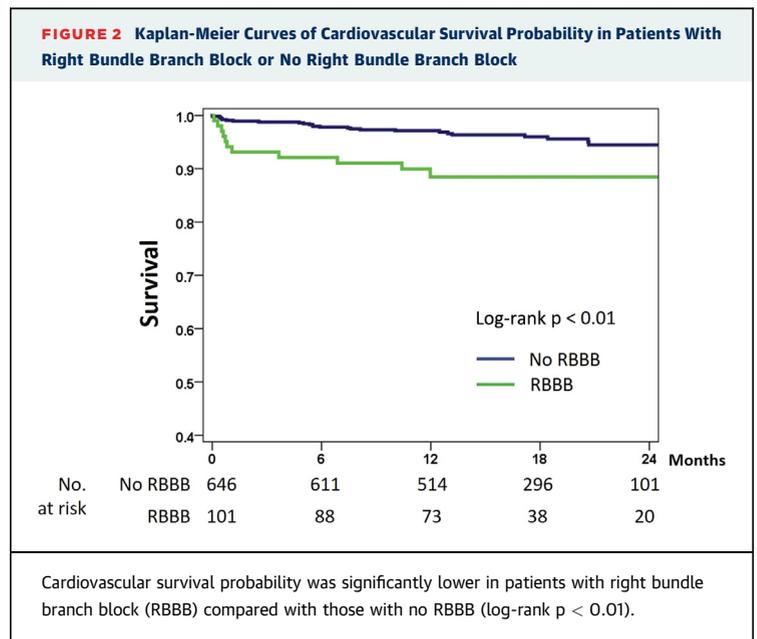
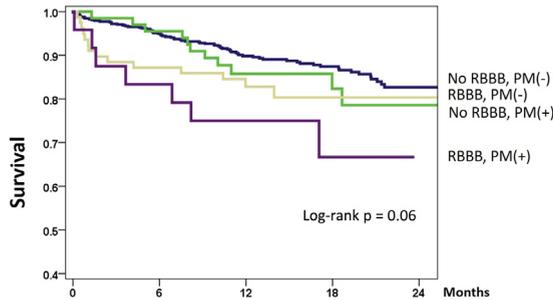


FIGURE 3 Kaplan-Meier Curves of Overall Survival Probability in Patients With Right Bundle Branch Block or No Right Bundle Branch Block and Permanent Pacemaker or No Pacemaker



No. at risk	No RBBB, PM(-)	RBBB, PM(-)	No RBBB, PM(+)	RBBB, PM(+)
578	547	466	268	91
67	64	48	28	10
77	68	59	29	16
23	20	14	9	4

Overall survival probability was different in 4 groups of patients with right bundle branch block (RBBB) or no RBBB and permanent pacemaker (PM) or no PM (log-rank $p = 0.06$).

$p = 0.06$ and $p = 0.01$, respectively) (Figures 3 and 4). Patients with RBBB and without pacemakers were at higher risk for cardiovascular mortality in the early phase after discharge, and patients with RBBB and pacemakers had higher mortality in the mid-term outcomes.

PREDICTORS OF CARDIOVASCULAR MORTALITY. In the univariate analysis, pre-existing RBBB, male sex, New York Heart Association functional

class III or IV, prior coronary artery bypass grafting, prior peripheral artery disease, and life-threatening bleeding (in-hospital) were significant predictors of all-cause mortality. The multivariate Cox regression model indicated that pre-existing RBBB (hazard ratio [HR]: 2.59; 95% confidence interval [CI]: 1.15 to 5.85; $p = 0.021$), male sex (HR: 3.40; 95% CI: 1.63 to 7.11; $p = 0.001$), NYHA functional class III or IV (HR: 3.41; 95% CI: 1.52 to 7.71; $p = 0.003$), previous coronary artery bypass grafting (HR: 3.56; 95% CI: 1.47 to 8.64; $p = 0.005$), and life-threatening bleeding (HR: 7.76; 95% CI: 3.38 to 17.80; $p < 0.001$) were the only independent predictors of all-cause mortality (Table 4).

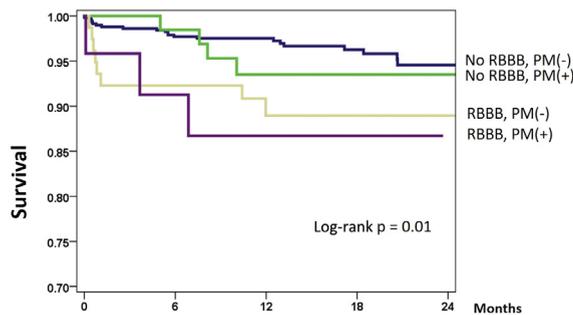
DISCUSSION

This study is the first of its kind to demonstrate the impact of pre-existing RBBB on clinical outcomes after TAVR using the balloon-expandable Edwards SAPIEN XT prosthesis. From a multicenter registry of 749 patients, 102 patients (13.6%) had RBBB on baseline electrocardiography. The incidence of new pacemaker implantation was higher among patients with pre-existing RBBB. The Kaplan-Meier survival curves indicated that pre-existing RBBB was associated with increased all-cause and cardiovascular mortality. Pre-existing RBBB was 1 of the independent predictors of all-cause mortality.

Prior evidence has shown that asymptomatic RBBB in the general population is benign, is not associated with future cardiovascular events, and does not require further evaluation (13,14). However, previous studies have shown that the prevalence of RBBB increases with age and is higher in men, patients with diabetes, and patients with hypertension (15,16). Among patients with heart failure, RBBB has been associated with an adverse prognosis (17,18). Recent data from the Copenhagen City Heart Study demonstrated that RBBB was associated with an increased risk for all-cause mortality and adverse cardiovascular outcomes (16). Our study demonstrated that pre-existing RBBB was associated with mid-term cardiac mortality after TAVR. One potential explanation for this finding is that the pre-existing RBBB reflected a high-risk concomitant condition, but in our study, the other baseline patient characteristics were not significantly different between the RBBB and no-RBBB groups.

Another possible explanation for why pre-existing RBBB was associated with a worse prognosis after TAVR may be related to the development of new conduction disturbances. The incidence of new conduction disturbances, especially new-onset LBBB, is 1 of the most frequent complications after TAVR. The

FIGURE 4 Kaplan-Meier Curves of Cardiovascular Survival Probability in Patients With Right Bundle Branch Block or No Right Bundle Branch Block and Permanent Pacemaker or No Pacemaker



No. at risk	No RBBB, PM(-)	RBBB, PM(-)	No RBBB, PM(+)	RBBB, PM(+)
578	547	466	268	91
67	64	48	28	10
77	68	59	29	16
23	20	14	9	4

Cardiovascular survival probability was significantly different in 4 groups of patients with right bundle branch block (RBBB) or no RBBB and permanent pacemaker (PM) or no pacemaker (log-rank $p = 0.01$).

rate of new-onset LBBB in patients is 12% to 20% after TAVR (5,19-22). Previous studies have shown that a larger size of valve implantation or valve implantation more on the ventricular side can cause direct trauma or mechanical damage to the His bundle at the region of the membranous septum and right trigone beneath the noncoronary and right coronary cusps and lead to the incidence of new conduction abnormalities and complete AVB after TAVR (22-25). A recent study reported that new-onset LBBB after TAVR performed with a balloon-expandable valve was associated with a higher rate of permanent pacemaker implantation but was not associated with an increased risk for overall mortality, cardiovascular mortality, or rehospitalization at mid-term follow-up (5).

A few studies have evaluated pre-existing conduction disturbances and their relationship to the risk for permanent pacemaker implantation after TAVR (19,20,23). Pre-existing RBBB or LBBB has been associated with an increased risk for new pacemaker implantation after TAVR (6,7,22,23); complete AVB and symptomatic bradycardia were the main indications for pacemaker implantation after TAVR. The present study also revealed that RBBB was related to an increased incidence of new pacemaker implantation. A total of 18% of the patients with prior RBBB developed complete AVB and needed permanent pacemaker implantation after TAVR, compared with only 2.9% of the patients with no prior RBBB. However, new pacemaker implantation did not increase mortality after TAVR on the basis of the results of a previous study (26).

In our study, prior RBBB was related to cardiac or sudden death early after discharge. Our speculation is that the patients with prior RBBB who had died suddenly in the early phase after discharge developed AVB, bradycardia, and subsequent heart failure. Indeed, patients with RBBB and no pacemaker implantation demonstrated a rapid increase in cardiovascular mortality within 1 month after TAVR in the present study (Figure 4). One case report documented a patient with pre-existing RBBB who died suddenly in the early phase after discharge, and the investigators were able to determine at autopsy that the prosthetic valve had compressed the atrioventricular conduction system region at the septum (27). Recent studies have confirmed that early discharge after transfemoral TAVR is feasible and safe (28,29). However, patients at high risk for a new conduction disturbance, such as patients with prior RBBB, should undergo careful monitoring to detect fatal arrhythmic events after discharge and may require prolonged hospitalization.

TABLE 4 Predictors of Cardiovascular Mortality

	Univariate Analysis			Multivariate Analysis		
	OR	95% CI	p Value	HR	95% CI	p Value
RBBB (pre-TAVR)	3.01	1.43-6.32	0.005	2.59	1.15-5.85	0.021
Male	3.28	1.65-6.53	0.001	3.40	1.63-7.11	0.001
NYHA functional class III or IV	3.46	1.61-7.47	0.001	3.41	1.52-7.71	0.003
Previous CABG	4.42	1.97-9.91	0.001	3.56	1.47-8.64	0.005
Peripheral artery disease	2.13	1.00-4.54	0.045			
Life-threatening bleeding (in-hospital)	8.64	4.02-18.56	<0.001	7.76	3.38-17.80	<0.001

CI = confidence interval; HR = hazard ratio; OR = odds ratio; TAVR = transcatheter aortic valve replacement; other abbreviations as in Table 1.

STUDY LIMITATIONS. Our study was conducted on a prospective multicenter TAVR cohort with a relatively small number of patients. The analyses need to be hierarchical, with patients analyzed by center. However, the between-center variability with respect to the outcome was small enough to be considered negligible.

Although the electrocardiograms were evaluated by experienced cardiologists in each center, there was no centralized core laboratory for electrocardiographic analysis. Future studies involving larger groups of patients and longer term follow-up will be required to confirm our results. Follow-up was performed by telephone interview, soliciting information from relatives or local doctors, or direct consultation. At each center in our registry, follow-up was performed primarily by direct consultation. However, systematic errors could exist and should be taken into consideration when evaluating the reported cause of death.

CONCLUSIONS

Pre-existing RBBB was observed in 13.6% of the patients who underwent TAVR and was significantly related to the incidence of new pacemaker implantation. The present study showed that prior RBBB was associated with an increased risk for overall mortality and cardiovascular mortality after TAVR with a balloon-expandable valve. Patients with RBBB and without pacemakers were at higher risk for cardiac death early after discharge. Careful monitoring to detect fatal arrhythmic events after TAVR should be conducted in patients with prior RBBB who are at higher risk for developing new conduction disturbances.

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PERSPECTIVES

WHAT IS KNOWN? The prognostic value of pre-existing RBBB in patients undergoing TAVR is unknown.

WHAT IS NEW? Patients with RBBB demonstrated an increased risk for cardiovascular mortality, and patients

without pacemakers were at higher risk for cardiac death early after discharge.

WHAT IS NEXT? Patients with prior RBBB should be carefully monitored after undergoing TAVR.

REFERENCES

- Reinohl J, Kaier K, Reinecke H, et al. Effect of availability of transcatheter aortic-valve replacement on clinical practice. *N Engl J Med* 2015;373:2438-47.
- Adams DH, Popma JJ, Reardon MJ. Transcatheter aortic-valve replacement with a self-expanding prosthesis. *N Engl J Med* 2014;371:967-8.
- Kodali SK, Williams MR, Smith CR, et al. Two-year outcomes after transcatheter or surgical aortic-valve replacement. *N Engl J Med* 2012;366:1686-95.
- Khatri PJ, Webb JG, Rodes-Cabau J, et al. Adverse effects associated with transcatheter aortic valve implantation: a meta-analysis of contemporary studies. *Ann Intern Med* 2013;158:35-46.
- Urena M, Webb JG, Cheema A, et al. Impact of new-onset persistent left bundle branch block on late clinical outcomes in patients undergoing transcatheter aortic valve implantation with a balloon-expandable valve. *J Am Coll Cardiol Intv* 2014;7:128-36.
- Erkaptic D, De Rosa S, Kelava A, Lehmann R, Fichtlscherer S, Hohnloser SH. Risk for permanent pacemaker after transcatheter aortic valve implantation: a comprehensive analysis of the literature. *J Cardiovasc Electrophysiol* 2012;23:391-7.
- Siontis GC, Juni P, Pilgrim T, et al. Predictors of permanent pacemaker implantation in patients with severe aortic stenosis undergoing TAVR: a meta-analysis. *J Am Coll Cardiol* 2014;64:129-40.
- Chorianopoulos E, Krumdorf U, Pleger ST, Katus HA, Bekeredjian R. Incidence of late occurring bradyarrhythmias after TAVI with the self-expanding CoreValve[®] aortic bioprosthesis. *Clin Res Cardiol* 2012;101:349-55.
- Egger F, Nurnberg M, Rohla M, et al. High-degree atrioventricular block in patients with preexisting bundle branch block or bundle branch block occurring during transcatheter aortic valve implantation. *Heart Rhythm* 2014;11:2176-82.
- Kappetein AP, Head SJ, Genereux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. *J Am Coll Cardiol* 2012;60:1438-54.
- 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: a scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society. Endorsed by the International Society for Computerized Electrocardiology. *J Am Coll Cardiol* 2009;53:976-81.
- Epstein AE, DiMarco JP, Ellenbogen KA, et al. 2012 ACCF/AHA/HRS focused update incorporated into the ACCF/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *Circulation* 2013;127:e283-352.
- Aro AL, Anttonen O, Tikkanen JT, et al. Intraventricular conduction delay in a standard 12-lead electrocardiogram as a predictor of mortality in the general population. *Circ Arrhythm Electrophysiol* 2011;4:704-10.
- Thrainsdottir IS, Hardarson T, Thorgeirsson G, Sigvaldason H, Sigfusson N. The epidemiology of right bundle branch block and its association with cardiovascular morbidity—the Reykjavik Study. *Eur Heart J* 1993;14:1590-6.
- Eriksson P, Hansson PO, Eriksson H, Dellborg M. Bundle-branch block in a general male population: the study of men born 1913. *Circulation* 1998;98:2494-500.
- Bussink BE, Holst AG, Jespersen L, Deckers JW, Jensen GB, Prescott E. Right bundle branch block: prevalence, risk factors, and outcome in the general population: results from the Copenhagen City Heart Study. *Eur Heart J* 2013;34:138-46.
- Barsheshet A, Goldenberg I, Garty M, et al. Relation of bundle branch block to long-term (four-year) mortality in hospitalized patients with systolic heart failure. *Am J Cardiol* 2011;107:540-4.
- Abdel-Qadir HM, Tu JV, Austin PC, Wang JT, Lee DS. Bundle branch block patterns and long-term outcomes in heart failure. *Int J Cardiol* 2011;146:213-8.
- 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.
- Godin M, Eltchaninoff H, Furuta A, et al. transcatheter implantation of an Edwards SAPIEN aortic valve prosthesis. *Am J Cardiol* 2010;106:707-12.
- van der Boon RM, Nuis RJ, Van Mieghem NM, et al. New conduction abnormalities after TAVI—frequency and causes. *Nat Rev Cardiol* 2012;9:454-63.
- Urena M, Mok M, Serra V, et al. Predictive factors and long-term clinical consequences of persistent left bundle branch block following transcatheter aortic valve implantation with a balloon-expandable valve. *J Am Coll Cardiol* 2012;60:1743-52.
- Bagur R, Rodes-Cabau J, Gurvitch R, et al. Need for permanent pacemaker as a complication of transcatheter aortic valve implantation and surgical aortic valve replacement in elderly patients with severe aortic stenosis and similar baseline electrocardiographic findings. *J Am Coll Cardiol Intv* 2012;5:540-51.
- 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.
- 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.
- Escarcega RO, Magalhaes MA, Lipinski MJ, et al. Mortality in patients requiring pacemaker implantation following transcatheter aortic valve replacement: insights from a systematic review and meta-analysis. *Int J Cardiol* 2014;174:207-8.
- Saji M, Murai T, Tobaru T, Tabata M, Takanashi S, Takayama M. Autopsy finding of the SAPIEN XT valve from a patient who died suddenly after transcatheter aortic valve replacement. *Cardiovasc Interv Ther* 2013;28:267-71.
- Barbanti M, Capranzano P, Ohno Y, et al. Early discharge after transfemoral transcatheter aortic valve implantation. *Heart* 2015;101:1485-90.
- Genereux P, Demers P, Poulin F. Same day discharge after transcatheter aortic valve replacement: are we there yet? *Catheter Cardiovasc Interv* 2016;87:980-2.

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