Asso

# Transcatheter Heart Valve Selection and Permanent Pacemaker Implantation in Patients With Pre-Existent Right Bundle Branch Block

Lennart van Gils, MD; Didier Tchetche, MD; Thibault Lhermusier, MD; Masieh Abawi, BSc; Nicolas Dumonteil, MD; Ramón Rodriguez Olivares, MD; Javier Molina-Martin de Nicolas, MD; Pieter R. Stella, MD, PhD; Didier Carrié, MD, PhD; Peter P. De Jaegere, MD, PhD; Nicolas M. Van Mieghem, MD, PhD

**Background**—Right bundle branch block is an established predictor for new conduction disturbances and need for a permanent pacemaker (PPM) after transcatheter aortic valve replacement. The aim of the study was to evaluate the absolute rates of transcatheter aortic valve replacement related PPM implantations in patients with pre-existent right bundle branch block and categorize for different transcatheter heart valves.

Methods and Results-We pooled data on 306 transcatheter aortic valve replacement patients from 4 high-volume centers in Europe and selected those with right bundle branch block at baseline without a previously implanted PPM. Logistic regression was used to evaluate whether PPM rate differed among transcatheter heart valves after adjustment for confounders. Mean age was  $83\pm7$  years and 63% were male. Median Society of Thoracic Surgeons score was 6.3 (interquartile range, 4.1–10.2). The following transcatheter valve designs were used: Medtronic CoreValve (n=130; Medtronic, Minneapolis, MN); Edwards Sapien XT (ES-XT; n=124) and Edwards Sapien 3 (ES-3; n=32; Edwards Lifesciences, Irvine, CA); and Boston Scientific Lotus (n=20; Boston Scientific Corporation, Marlborough, MA). Overall permanent pacemaker implantation rate post-transcatheter aortic valve replacement was 41%, and per valve design: 75% with Lotus, 46% with CoreValve, 32% with ES-XT, and 34% with ES-3. The indication for PPM implantation was total atrioventricular block in 98% of the cases. Lotus was associated with a higher PPM rate than all other valves. PPM rate did not differ between ES-XT and ES-3. Ventricular paced rhythm at 30-day and 1-year follow-up was present in 81% at 89%, respectively.

Conclusions—Right bundle branch block at baseline is associated with a high incidence of PPM implantation for all transcatheter heart valves. PPM rate was highest for Lotus and lowest for ES-XT and ES-3. Pacemaker dependency remained high during followup. (J Am Heart Assoc. 2017;6:e005028. DOI: 10.1161/JAHA.116.005028.)

Key Words: aortic stenosis • bundle-branch block • pacemaker • predictors • right bundle branch block • transcatheter aortic valve implantation • transcatheter aortic valve replacement

atients with severe aortic stenosis and a higher operative risk for mortality are good candidates for transcatheter aortic valve replacement (TAVR).<sup>1-4</sup> TAVR involves placement of a transcatheter heart valve (THV) that protrudes into the left ventricular outflow tract. As such, the THV radial force may impose on the adjacent conduction system and result in conduction disturbances.<sup>5,6</sup> Incidence of new left bundle branch block (LBBB) and high-grade atrioventricular block (AV block) varies according to patient demographics, anatomical characteristics, and selected THV. New LBBB and permanent pacemaker (PPM) implantation post-TAVR varies from 4% to 81% and from 0% to 49%, respectively, and is consistently higher with the self-expanding CoreValve compared to balloon-expandable Sapien valves.<sup>5,7,8</sup>

New THV designs have focussed on profile refinement, paravalvular leak prevention, and the intrinsic feature of partial or complete repositionability and retrievability,<sup>9-11</sup> yet conduction disorders remain common. Right bundle branch block (RBBB) at baseline is considered a dominant predictor for highdegree AV block and PPM post-TAVR.<sup>7,12–16</sup> Frequency of RBBB at baseline in current TAVR practice ranges from 4% to 21%.<sup>7</sup>

From the Erasmus Medical Center, Rotterdam, The Netherlands (L.v.G., P.P.D.J., N.M.V.M.); Clinique Pasteur, Toulouse, France (D.T., N.D., J.M.-M.d.N.); Hôpital Rangueil, Toulouse, France (T.L., D.C.); University Medical Center Utrecht, Utrecht, The Netherlands (M.A., R.R.O., P.R.S.).

Accompanying Tables S1 and S2 are available at http://jaha.ahajournals.org/c ontent/6/3/e005028/DC1/embed/inline-supplementary-material-1.pdf

Correspondence to: Nicolas M. Van Mieghem, MD, PhD, FESC, Department of Interventional Cardiology, Thoraxcenter, ErasmusMC, Room Bd 171, 's Gravendijkwal 230, 3015 CE Rotterdam, The Netherlands. E-mail: n.vanmieghem@erasmusmc.nl

Received November 17, 2016; accepted February 2, 2017.

<sup>© 2017</sup> The Authors. Published on behalf of the American Heart Association, Inc., by Wiley Blackwell. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

Knowledge of the respective PPM rates for different THV designs in patients with RBBB may guide patient-tailored THV selection. This multicenter collaboration sought to further elucidate TAVR-related PPM rates in patients with pre-existent RBBB and categorize for different THV designs.

# Methods

# **Patient Selection**

Between May 2008 and February 2016, 2845 patients underwent TAVR in 4 tertiary care European institutions. All patients were screened for RBBB (and absence of a PPM) before the TAVR procedure and were included in a joint database collecting: baseline demographics; TAVR procedure characteristics; new conduction disorders within 24 hours; PPM at 30 days; and electrocardiographic and clinical-follow-up data at 30 days and 1 year. THV selection was per institution's discretion. A minimum of 10 available cases per THV was a predefined requirement for further analysis, to secure solidity of data.

The 4 THVs used were CoreValve (Medtronic, Minneapolis, MN), Sapien XT (ES-XT) and Sapien 3 (ES-3; Edwards Lifesciences, Irvine, CA), and Lotus (Boston Scientific Corporation, Marlborough, MA). Figure 1 displays the patient flow diagram. All patients provided written informed consent for the procedure and data analysis for research purposes per institutional review board approval.

#### Outcomes

The primary outcome was implantation of a PPM within 30 days after the TAVR procedure. Secondary outcomes were new-onset conduction disturbances within 24 hours: (1) third-degree atrioventricular block (AV3B) and (2) alternating bundle branch block (ie, change from RBBB to LBBB). The decision for PPM was per treating physician's discretion, but, in general, in compliance with contemporary European Society of Cardiology Guidelines on PPM.<sup>17</sup> Clinical outcomes were reported using the revised Valve Academic Research Consortium criteria.<sup>18</sup>

# **Statistical Analysis**

Continuous variables are presented as mean $\pm$ SD or median (interquartile range; IQR). Distribution of continuous variables was assessed for normality with histograms and the Shapiro– Wilk test. Continuous variables were compared using a Student *t* test or Mann–Whitney *U* test, when applicable. Categorical variables are expressed as percentages plus absolute numbers and were tested with the chi-square test for trend.

Logistic regression was performed to identify predictors for the primary outcome (ie, PPM). THVs were included in the univariate analysis plus potential confounders in regard to the



ORIGINAL RESEARCH

**Figure 1.** Flow chart of study inclusion. ES-3 indicates Edwards Sapien 3; ES-XT, Edwards Sapien XT; PPM, permanent pacemaker; RBBB, right bundle branch block; THVs, transcatheter heart valves.

primary outcome. The number of variables in the univariate model was limited by the established rule of thumb of 10 events per variable.<sup>19</sup> All selected variables were evaluated using univariate logistic regression for inclusion in the multivariate model, considering a *P* value of <0.20 as an entry criterion. These variables remained in the multivariate model, regardless of *P* value after adjustment. We controlled for the interaction between valve type and alternative access, because alternative access was seldom used with CoreValve and Lotus. All statistical analyses were performed with SPSS software (version 21.0.01; IBM Corp, Armonk, NY). A 2-sided value of *P*<0.05 was considered statistically significant.

# Results

A total of 2845 consecutive patients underwent TAVR at 4 European centers. For the purpose of this study, 306 (11%)

patients with pre-existent RBBB (without a PPM in situ) were extracted and further analyzed (Figure 1). Patient characteristics are listed in Table 1. Mean age was  $83\pm7$  years, the majority was male (194; 63%), and the median predicted risk of mortality (Society of Thoracic Surgeons [STS] score) was 6.3% (IOR, 4.1–10.2). The CoreValve and Sapien-XT were used in the majority of patients (42% and 41%, respectively). An alternative access was used in  $\approx$ 20% with the balloon expandable ES-XT and ES-3 and 9% with CoreValve and not with Lotus. Antiarrhythmic agents were commonly used; 13% of patients used amiodarone and 4% digoxin.

# **Clinical Outcomes**

All-cause mortality—within 48 hours following the procedure—was 3% (n=10). Thirty-day mortality rate was 7% (n=20) and 30-day stroke rate was 2% (n=5). One-year mortality rate was 18% (n=44).

#### **PPM Implantation**

Conduction changes are summarized in Table 2. The primary outcome—PPM implantation within 30 days—occurred in

 Table 1. Patient Characteristics

41% of patients. The univariate analysis is summarized in Table S1. The following variables were included in the multivariate analysis: valve type; alternative access; body mass index (BMI); sex; and an interaction term for valve type×alternative access (because alternative access was not applied with Lotus). Results from the multivariate analysis are displayed in Figure 2. By multivariate analysis, PPM was more common with Lotus than with the other THVs. Lotus was associated with a significantly higher PPM rate than all other individual transcatheter heart valves (Lotus versus CoreValve: odds ratio [OR], 3.69 [95% CI, 1.13-12.04]; P=0.030; Lotus versus ES-XT: OR, 6.79 [95% CI, 2.05-22.52]; P=0.002; Lotus versus ES-3: OR, 5.24 [95% CI, 1.30-21.25]; P=0.020). On the contrary, PPM rate was lower with the ES-XT valve versus CoreValve and Lotus (ES-XT vs CoreValve: OR, 0.54 [95% Cl, 0.31-0.95]; P=0.033; ES-XT vs Lotus: OR, 0.15 [95% Cl, 0.04-0.49]; P=0.002). PPM rate between the balloon expandable valves did not differ (ES-XT vs ES-3: OR, 0.91 [95% Cl, 0.40-2.07]; P=0.820). Another independent predictor for PPM in the multivariable model was a higher BMI before TAVR (multivariate OR, 1.08 per 1 kg/m<sup>2</sup> increment [95% Cl, 1.02-1.14]; P=0.013). Alternative access was associated with a lower rate of PPM in the univariate model (OR, 0.32 [95% Cl,

	CoreValve (N=130)	ES-XT (N=124)	Lotus (N=20)	ES-3 (N=32)	Overall (306)	P Value	
Age, mean $\pm$ SD	83±6	83±8	83±6	81±6	83±7	0.301	
Male sex, n (%)	79 (61)	83 (67)	12 (60)	20 (63)	194 (63)	0.761	
BMI in kg/m <sup>2</sup> , mean±SD	26±5	27±4	29±7	27±4	27±5	0.319	
Diabetes mellitus, n (%)	33 (25)	38 (31)	9 (45)	13 (41)	93 (30)	0.161	
STS score in %, median [IQR]	6.5 [4.5–10.4]	7.0 [4.0–10.1]	5.9 [5.2–7.8]	4.5 [3.0–10.5]	6.3 [4.1–10.2]	0.186	
PVD, n (%)	28 (22)	36 (29)	6 (30)	7 (22)	77 (22)	0.526	
COPD, n (%)	41 (32)	40 (33)	5 (25)	7 (22)	93 (30)	0.634	
Atrial fibrillation, n (%)	21 (16)	27 (22)	4 (20)	8 (25)	60 (20)	0.584	
NYHA class ≥III, % (n)	101 (78)	103 (83)	14 (74)	17 (53)	235 (77)	0.005	
History of stroke, n (%)	18 (14)	12 (10)	4 (20)	3 (9)	36 (12)	0.613	
History of CABG, n (%)	15 (12)	19 (15)	5 (25)	10 (31)	49 (16)	0.033	
History of PCI, n (%)	49 (38)	53 (43)	6 (30)	10 (31)	118 (39)	0.513	
History of SAVR, n (%)	4 (3)	3 (2)	0 (0)	2 (6)	9 (3)	0.581	
Digoxin use, n (%)	4 (3)	5 (4)	2 (13)	0 (0)	11 (4)	0.187	
Amiodarone use, n (%)	18 (14)	16 (13)	2 (13)	2 (7)	38 (13)	0.792	
Access, n (%)							
Transfemoral	119 (91)	98 (79)	20 (100)	25 (78)	262 (86)	0.005	
Transsubclavian	10 (8)	14 (11)	0 (0)	1 (3)	25 (8)		
Transapical	1 (1)	12 (10)	0 (0)	6 (19)	19 (6)		

Categorical variables are displayed as counts (percentages) and differences were tested using a chi-square test for trend. Continuous variables are displayed as mean±SD or median [IQR] and were tested with a Student *t* test or Mann–Whitney *U* test, depending on distribution. BMI indicates body mass index; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; ES-3, Edwards Sapien 3; ES-XT, Edwards Sapien XT; IQR, interquartile range; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; SAVR, surgical aortic valve replacement; STS, Society of Thoracic Surgeons.

#### Table 2. Permanent Pacemaker Implantations and Conduction-Related Outcomes

	CoreValve (N=130)	ES-XT (N=124)	Lotus (N=20)	ES-3 (N=32)	Overall (N=306)	P Value
New AV3B <24 hours, n (%)	48 (39)	30 (27)	13 (68)	10 (39)	101 (36)	0.004
Alternating BBB <24 hours*, n (%)	10 (8)	7 (6)	3 (17)	3 (12)	23 (8)	0.457
New PPM, n (%)	60 (46)	40 (32)	15 (75)	11 (34)	126 (41)	0.001
Days to PPM, median [IQR]	2 [1–5]	3 [1–5]	1 [1–2]	2 [1–5]	2 [1–5]	0.546
Indication for PPM, n (%) <sup>†</sup>						
AV3B	59 (98)	39 (97)	14 (93)	11 (100)	123 (98)	0.489
AV2B	1 (2)	0 (0)	1 (7)	0 (0)	2 (2)	
Sick sinus syndrome	0 (0)	1 (3)	0 (0)	0 (0)	1 (1)	
Ventricular paced rhythm at 30 days <sup>‡</sup> , n (%)	38 (81)	24 (92)	9 (69)	8 (73)	79 (81)	0.275
Ventricular paced rhythm at 1 year <sup>‡</sup> , n (%)	21 (91)	15 (94)	2 (67)	3 (75)	41 (89)	0.415

Categorical variables are displayed as counts (percentages) and differences were tested using a chi-square test for trend. Continuous variables are displayed as median [IQR] and were tested with a Mann–Whitney *U* test. AV2B indicates second-degree atrioventricular block; AV3B, third-degree atrioventricular block; BBB, bundle branch block; ES-3, Edwards Sapien3; ES-XT, Edwards Sapien XT; IQR, interquartile range; PPM, permanent pacemaker.

\*Alternating bundle branch block was considered as a new left bundle branch block in this patient population with pre-existent right bundle branch block.

<sup>†</sup>Percentage indicates the proportion of patients who received a permanent pacemaker.

<sup>‡</sup>Follow-up electrocardiograms were missing in 29 patients (23%) at 30 days and in 80 (64%) at 1 year.

0.15–0.69]; *P*=0.004), but not in the multivariate model (OR, 0.26 [95% CI, 0.05–1.27]; *P*=0.095). There was an important interaction between alternative access and valve type, attributed to the fact that Lotus was not performed with alternative access. The association between alternative access and PPM was nonsignificant with any of the valve types (CoreValve: OR, 0.234 [95% CI, 0.048–1.128]; *P*=0.070; with ES-XT: OR, 0.565 [95% CI, 0.207–1.539]; *P*=0.264; with ES-3: OR, 0.250 [95% CI, 0.0262–2.403]; *P*=0.230).

#### **New-Onset Conduction Disturbances**

Alternating bundle branch block within 24 hours was documented in 23 patients (8%). New-onset AV3B within 24 hours was documented in 101 patients (36%). Univariate and multivariate analysis addressing new AV3B are summarized in Table S2. New AV3B was more common with Lotus than with other individual THVs by multivariate analysis (Lotus vs ES-XT: OR, 6.01 [95% CI, 1.93–18.67]; P=0.002; Lotus vs ES-XT: OR, 3.88 [95% CI, 1.02–14.82]; P=0.047; Lotus vs CoreValve: OR, 3.80 [95% CI, 1.25–11.52]; P=0.018). New AV3B was less common with the ES-XT valve than with Lotus (OR, 0.17 [95% CI, 0.05–0.52]; P=0.002). New AV3B rate between the balloon expandable valves was similar (ES-XT vs ES-3: univariate OR, 0.59 [95% CI, 0.24–1.43]; P=0.240).

Of all patients with new AV3B within 24 hours of the TAVR procedure, 91% received a PPM. One in 4 of these permanent pacemakers were implanted more than 4 days after the TAVR procedure. The documented indication for PPM implantation was almost exclusively AV3B (98%). Follow-up electrocardiograms at 30 days and 1 year confirmed ventricular pacing in 81% and 89%, respectively.

# Discussion

The present study showed that tailored valve choice may reduce rates of PPM implantations in patients with preexistent RBBB. Overall PPM rate post-TAVR in patients with RBBB was 41% and was highest with Lotus (75%). More than 80% of patients with a PPM remained pacemaker dependent at 30-day and 1-year follow-up.

Prevalence of RBBB in the general population ranges from 0.5% to 1.5%, has a male predominance, and increases with age to 2.2% in patients above 55 years old.<sup>20,21</sup> Prevalence of pre-existent RBBB is 4% in patients undergoing surgical aortic valve replacement (SAVR) with a mean age of 69 years<sup>22</sup> and is 10% in patients undergoing TAVR with a mean age of 81.7 RBBB is a dominant predictor for PPM after both TAVR and SAVR.<sup>7,9,11,23,24</sup> Not unexpectedly, patients with pre-existent RBBB are more vulnerable for high-grade AV block given that the conduction system is already impaired. With TAVR, the radial force of a stented frame may impose pressure on the conduction system embedded in the interventricular septum within a couple of millimeters from the aortic annulus and may further compromise the left bundle branch.<sup>14</sup> Before patients with RBBB evolve toward total AV block, an alternating bundle branch can sometimes be recognized, as illustrated in Figure 3. In our population, an alternating bundle branch block within 24 hours post-TAVR could be detected in 8% of patients.

According to a recent meta-analysis, TAVR with the selfexpanding CoreValve is associated with a higher PPM rate compared with the balloon expandable ES-XT.<sup>7</sup> PPM rate with newer-generation THVs varies and definitely remains a clinical issue, in particular with the mechanically expanded Lotus.



**Figure 2.** Forest plot displaying odds ratios (OR) for permanent pacemaker implantation after multivariate analysis. The following variables were included in the multivariate model: valve type, sex, body mass index (BMI), alternative access, and an interaction term valve type × alternative access. \*Odds ratio per 1 kg/m<sup>2</sup> increment of BMI. <sup>†</sup>An interaction term for the interaction between alternative access and valve type was included in the model to adjust for the fact that alternative access was not applied with Lotus. ES-3 indicates Edwards Sapien 3; ES-XT, Edwards Sapien XT; NA, not applicable; PPM, permanent pacemaker.

Also, the latest balloon expandable ES-3 THV has a higher reported PPM rate compared with its predecessor, ES-XT. $^{25}$ 

Prevalence of RBBB in this study was similar to what has been reported in the literature. Our findings demonstrate a higher incidence of PPM in patients with pre-existent RBBB compared to what generally is reported in a random TAVR population. In patients with pre-existent RBBB treated with CoreValve in this study, almost half required a PPM as compared to 20% in the randomized US CoreValve High Risk Study and 28% in the meta-analysis by Siontis et al.<sup>7,26</sup> PPM rate in patients with ES-XT was 31% and is significantly higher than the 6% in the meta-analysis and 9% in the randomized PARTNER 2 (Placement of Aortic Transcatheter Valves 2) trial.<sup>3</sup> In our study, also with newer generation THVs in patients with pre-existent RBBB, the PPM rate was consistently higher than what is reported in high-risk TAVR patients: ES-3 34% versus  $10\%^{27}$  and Lotus 75% versus 27%,<sup>9</sup> respectively.

Multivariate analysis confirmed a higher incidence of PPM with Lotus than with other THV designs. Conversely, ES-XT was associated with the lowest PPM risk. Interestingly, a higher BMI before TAVR also predicted PPM implantation, although the effect was modest. Previous studies reported the impact of BMI on outcomes post-TAVR, but did not show an enhanced rate of PPM implantations.<sup>4,28</sup> The exact pathophysiology is unclear. However, BMI may pose particular hurdles from a procedure execution perspective and maybe result in less-accurate (and maybe deeper) valve implants. Alternative access (ie, transsubclavian or transapical access) was associated with a lower PPM rate in the univariate model. However, this effect was absent in the multivariate model, suggesting the effect of the balloon expandable valves that were used in the majority (75%) of alternative access procedures.

The high rate of PPM with Lotus could hypothetically be caused by (1) a higher radial force of the stented frame compared to other THVs, which potentially forces the native annulus in a circular shape, and (2) the Lotus frame remains in contact with the wall of the left ventricular outflow tract throughout the process of foreshortening and locking, which could be more harmful to the conduction system. Depth of transcatheter valve implantation is an established predictor for CoreValve, ES-XT, and ES-3,<sup>29–31</sup> in particular with an implantation depth of more than 6 mm below the native aortic



**Figure 3.** Two-lead electrocardiogram derived from continuous rhythm monitoring within 24 hours after transcatheter aortic valve replacement, illustrating the typical cascade from RBBB to a total atrioventricular block. \*Intermittent sinus beats with LBBB. BBB indicates bundle branch block; LBBB, left bundle branch block; RBBB, right bundle branch block.

valve. Methodology to determine depth of implantation is not standardized and was not collected in this study. However, depth of implantation could affect the need for PPM with any THV and warrants further detailed analysis.

Previous reports suggested the transient nature of TAVRinduced conduction disorders given that up to half of patients with new pacemakers post-TAVR were no longer pacemaker dependent at follow-up.<sup>13,32,33</sup> In contrast, our study demonstrates a paced rhythm in 89% of patients at 1 year in patients who received a PPM, underscoring a less-resilient conduction system in these patients. Similarly, patients with pre-existent RBBB who developed AV3B within 24 hours after the procedure received a PPM in 91% of the cases, with 1 in 4 receiving the pacemaker more than 4 days post-TAVR, underscoring the persistence of this conduction disorder. In aggregate, conduction recovery post-TAVR in patients with pre-existent RBBB is unlikely, and therefore the decision to proceed with PPM implantation could be made early after TAVR to minimize hospital stay.

In our study—involving patients with pre-existent RBBB and a relatively high rate of PPM implantations—the mortality rate (7% at 30 days and 18% at 1 year) is on par with recently published trials and registry data.<sup>26,31,34–38</sup> Conflicting data link new conduction disorders in general and PPM implantation in particular to impaired TAVR-related outcome, including less improvement in LV function or quality of life, more rehospitalizations, and increased 1-year mortality.<sup>13,39–41</sup>

Hypothetically, PPM implantation in patients with RBBB levels out mortality attributed to the high incidence of—potentially lethal—total heart blocks.

#### Limitations

This multicenter study has an observational design and may suffer from inherent bias in terms of THV selection and confounders. Depth of implantation-which is known to be associated with PPM—was not collected in this study. Indeed, given that balloon expandable devices have less TAVR-related conduction disorders, operators may already favor this THV for patients with pre-existent RBBB and avoid mechanically expanded valves on the other hand. Nonetheless, only THVs with at least 10 patients in the database were eligible for further analysis, and the number of events was sufficient to allow for adequate multivariate analysis to adjust for confounders. We acknowledge that the Lotus valve is relatively under-represented in the present study, and therefore avoidance of this valve cannot be strongly recommended. However, we believe that there is a clear signal that this valve is associated with the highest PPM rate. The decision to implant a PPM was at the treating physician's discretion, but was most often for high-degree AV block and thus conforms to current international guidelines.<sup>17</sup>

# Conclusion

Postprocedural PPM rate in this cohort of patients with preexistent RBBB was consistently higher than described in the literature for all THVs. PPM rate was highest with Lotus and lowest with the balloon expandable ES-XT and ES-3. Pacemaker dependency remained high at both 30-day and 1-year follow-up.

# Sources of Funding

Dr Van Mieghem has received research grants from Claret Medical, Boston Scientific, Medtronic, and Edwards Lifesciences.

# Disclosures

Prof Dr De Jaegere is proctor for Boston Scientific. The remaining authors have nothing to disclose in relation to this topic.

#### References

 Reinohl J, Kaier K, Reinecke H, Schmoor C, Frankenstein L, Vach W, Cribier A, Beyersdorf F, Bode C, Zehender M. Effect of availability of transcatheter aorticvalve replacement on clinical practice. N Engl J Med. 2015;373:2438–2447.

- Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Brown DL, Block PC, Guyton RA, Pichard AD, Bavaria JE, Herrmann HC, Douglas PS, Petersen JL, Akin JJ, Anderson WN, Wang D, Pocock S; Investigators PT. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med.* 2010;363:1597–1607.
- Leon MB, Smith CR, Mack MJ, Makkar RR, Svensson LG, Kodali SK, Thourani VH, Tuzcu EM, Miller DC, Herrmann HC, Doshi D, Cohen DJ, Pichard AD, Kapadia S, Dewey T, Babaliaros V, Szeto WY, Williams MR, Kereiakes D, Zajarias A, Greason KL, Whisenant BK, Hodson RW, Moses JW, Trento A, Brown DL, Fearon WF, Pibarot P, Hahn RT, Jaber WA, Anderson WN, Alu MC, Webb JG; Investigators P. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. N Engl J Med. 2016;374:1609–1620.
- 4. Yamamoto M, Mouillet G, Oguri A, Gilard M, Laskar M, Eltchaninoff H, Fajadet J, lung B, Donzeau-Gouge P, Leprince P, Leuguerrier A, Prat A, Lievre M, Chevreul K, Dubois-Rande JL, Teiger E; Investigators FR. Effect of body mass index on 30- and 365-day complication and survival rates of transcatheter aortic valve implantation (from the French Aortic National Corevalve and Edwards 2 [FRANCE 2] Registry). *Am J Cardiol.* 2013;112:1932–1937.
- van der Boon RM, Nuis RJ, Van Mieghem NM, Jordaens L, Rodes-Cabau J, van Domburg RT, Serruys PW, Anderson RH, de Jaegere PP. New conduction abnormalities after TAVI–frequency and causes. *Nat Rev Cardiol.* 2012;9:454– 463.
- 6. Nuis RJ, Van Mieghem NM, Schultz CJ, Tzikas A, Van der Boon RM, Maugenest AM, Cheng J, Piazza N, van Domburg RT, Serruys PW, de Jaegere PP. 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;32:2067–2074.
- Siontis GC, Juni P, Pilgrim T, Stortecky S, Bullesfeld L, Meier B, Wenaweser P, Windecker S. Predictors of permanent pacemaker implantation in patients with severe aortic stenosis undergoing TAVR: a meta-analysis. J Am Coll Cardiol. 2014;64:129–140.
- Houthuizen P, van der Boon RM, Urena M, Van Mieghem N, Brueren GB, Poels TT, Van Garsse LA, Rodes-Cabau J, Prinzen FW, de Jaegere P. Occurrence, fate and consequences of ventricular conduction abnormalities after transcatheter aortic valve implantation. *EuroIntervention*. 2014;9:1142–1150.
- Meredith Am IT, Walters DL, Dumonteil N, Worthley SG, Tchetche D, Manoharan G, Blackman DJ, Rioufol G, Hildick-Smith D, Whitbourn RJ, Lefevre T, Lange R, Muller R, Redwood S, Allocco DJ, Dawkins KD. Transcatheter aortic valve replacement for severe symptomatic aortic stenosis using a repositionable valve system: 30-day primary endpoint results from the REPRISE II study. J Am Coll Cardiol. 2014;64:1339–1348.
- Schofer J, Colombo A, Klugmann S, Fajadet J, DeMarco F, Tchetche D, Maisano F, Bruschi G, Latib A, Bijuklic K, Weissman N, Low R, Thomas M, Young C, Redwood S, Mullen M, Yap J, Grube E, Nickenig G, Sinning JM, Hauptmann KE, Friedrich I, Lauterbach M, Schmoeckel M, Davidson C, Lefevre T. Prospective multicenter evaluation of the direct flow medical transcatheter aortic valve. J Am Coll Cardiol. 2014;63:763–768.
- Willson AB, Rodes-Cabau J, Wood DA, Leipsic J, Cheung A, Toggweiler S, Binder RK, Freeman M, DeLarochelliere R, Moss R, Nombela-Franco L, Dumont E, Szummer K, Fontana GP, Makkar R, Webb JG. Transcatheter aortic valve replacement with the St. Jude Medical Portico valve: first-in-human experience. J Am Coll Cardiol. 2012;60:581–586.
- Rivard L, Schram G, Asgar A, Khairy P, Andrade JG, Bonan R, Dubuc M, Guerra PG, Ibrahim R, Macle L, Roy D, Talajic M, Dyrda K, Shohoudi A, le Polain de Waroux JB, Thibault B. Electrocardiographic and electrophysiological predictors of atrioventricular block after transcatheter aortic valve replacement. *Heart Rhythm.* 2015;12:321–329.
- Nazif TM, Dizon JM, Hahn RT, Xu K, Babaliaros V, Douglas PS, El-Chami MF, Herrmann HC, Mack M, Makkar RR, Miller DC, Pichard A, Tuzcu EM, Szeto WY, Webb JG, Moses JW, Smith CR, Williams MR, Leon MB, Kodali SK; Office PP. Predictors and clinical outcomes of permanent pacemaker implantation after transcatheter aortic valve replacement: the PARTNER (placement of aortic transcatheter valves) trial and registry. *JACC Cardiovasc Interv.* 2015;8:60–69.
- 14. Khawaja MZ, Rajani R, Cook A, Khavandi A, Moynagh A, Chowdhary S, Spence MS, Brown S, Khan SO, Walker N, Trivedi U, Hutchinson N, De Belder AJ, Moat N, Blackman DJ, Levy RD, Manoharan G, Roberts D, Khogali SS, Crean P, Brecker SJ, Baumbach A, Mullen M, Laborde JC, Hildick-Smith D. Permanent pacemaker insertion after CoreValve transcatheter aortic valve implantation: incidence and contributing factors (the UK CoreValve Collaborative). *Circulation*. 2011;123:951–960.
- 15. van der Boon RM, Houthuizen P, Urena M, Poels TT, van Mieghem NM, Brueren GR, Altintas S, Nuis RJ, Serruys PW, van Garsse LA, van Domburg RT, Cabau JR, de Jaegere PP, Prinzen FW. Trends in the occurrence of new conduction abnormalities after transcatheter aortic valve implantation. *Catheter Cardiovasc Interv.* 2015;85:144–152.

- 16. Saia F, Lemos PA, Bordoni B, Cervi E, Boriani G, Ciuca C, Taglieri N, Mariani J Jr, Filho RK, Marzocchi A. Transcatheter aortic valve implantation with a selfexpanding nitinol bioprosthesis: prediction of the need for permanent pacemaker using simple baseline and procedural characteristics. *Catheter Cardiovasc Interv.* 2012;79:712–719.
- 17. Brignole M, Auricchio A, Baron-Esquivias G, Bordachar P, Boriani G, Breithardt OA, Cleland J, Deharo JC, Delgado V, Elliott PM, Gorenek B, Israel CW, Leclercq C, Linde C, Mont L, Padeletti L, Sutton R, Vardas PE; Guidelines ESCCFP, Zamorano JL, Achenbach S, Baumgartner H, Bax JJ, Bueno H, Dean V, Deaton C, Erol C, Fagard R, Ferrari R, Hasdai D, Hoes AW, Kirchhof P, Knuuti J, Kolh P, Lancellotti P, Linhart A, Nihoyannopoulos P, Piepoli MF, Ponikowski P, Sirnes PA, Tamargo JL, Tendera M, Torbicki A, Wijns W, Windecker S, Document R, Kirchhof P, Blomstrom-Lundqvist C, Badano LP, Aliyev F, Bansch D, Baumgartner H, Bsata W, Buser P, Charron P, Daubert JC, Dobreanu D, Faerestrand S, Hasdai D, Hoes AW, Le Heuzey JY, Mavrakis H, McDonagh T, Merino JL, Nawar MM, Nielsen JC, Pieske B, Poposka L, Ruschitzka F, Tendera M, Van Gelder IC, Wilson CM. 2013 ESC guidelines on cardiac pacing and resynchronization therapy in the Task Force on cardiac pacing and resynchronization therapy the European Society of Cardiology (ESC). Developed in collaboration with the European Heart Rhythm Association (EHRA). *Eur Heart J.* 2013;34:2281–2329.
- 18. Kappetein AP, Head SJ, Genereux P, Piazza N, van Mieghem NM, Blackstone EH, Brott TG, Cohen DJ, Cutlip DE, van Es GA, Hahn RT, Kirtane AJ, Krucoff MW, Kodali S, Mack MJ, Mehran R, Rodes-Cabau J, Vranckx P, Webb JG, Windecker S, Serruys PW, Leon MB. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. *Eur Heart J.* 2012;33:2403–2418.
- Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. *J Clin Epidemiol*. 1996;49:1373–1379.
- 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;34:138–146.
- Haataja P, Nikus K, Kahonen M, Huhtala H, Nieminen T, Jula A, Reunanen A, Salomaa V, Sclarovsky S, Nieminen MS, Eskola M. Prevalence of ventricular conduction blocks in the resting electrocardiogram in a general population: the Health 2000 Survey. *Int J Cardiol.* 2013;167:1953–1960.
- 22. Van Mieghem NM, Head SJ, de Jong W, van Domburg RT, Serruys PW, de Jaegere PP, Jordaens L, Takkenberg JJ, Bogers AJ, Kappetein AP. Persistent annual permanent pacemaker implantation rate after surgical aortic valve replacement in patients with severe aortic stenosis. *Ann Thorac Surg.* 2012;94:1143–1149.
- Meredith IT, Worthley SG, Whitbourn RJ, Antonis P, Montarello JK, Newcomb AE, Lockwood S, Haratani N, Allocco DJ, Dawkins KD. Transfemoral aortic valve replacement with the repositionable Lotus Valve System in high surgical risk patients: the REPRISE I study. *EuroIntervention*. 2014;9:1264–1270.
- 24. Epstein AE, DiMarco JP, Ellenbogen KA, Estes NA III, Freedman RA, Gettes LS, Gillinov AM, Gregoratos G, Hammill SC, Hayes DL, Hlatky MA, Newby LK, Page RL, Schoenfeld MH, Silka MJ, Stevenson LW, Sweeney MO, Smith SC Jr, Jacobs AK, Adams CD, Anderson JL, Buller CE, Creager MA, Ettinger SM, Faxon DP, Halperin JL, Hiratzka LF, Hunt SA, Krumholz HM, Kushner FG, Lytle BW, Nishimura RA, Ornato JP, Page RL, Riegel B, Tarkington LG, Yancy CW; American College of Cardiology/American Heart Association Task Force on Practice G, American Association for Thoracic S, Society of Thoracic S. ACC/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing committee to revise the ACC/AHA/NASPE 2002 guideline update for implantation of cardiac pacemakers and antiarrhythmia devices) developed in collaboration with the American Association for Thoracic Surgeons. J Am Coll Cardiol. 2008;51:e1–e62.
- Toggweiler S, Gurvitch R, Leipsic J, Wood DA, Willson AB, Binder RK, Cheung A, Ye J, Webb JG. Percutaneous aortic valve replacement: vascular outcomes with a fully percutaneous procedure. J Am Coll Cardiol. 2012;59:113–118.
- Adams DH, Popma JJ, Reardon MJ. Transcatheter aortic-valve replacement with a self-expanding prosthesis. N Engl J Med. 2014;371:967–968.
- Nijhoff F, Abawi M, Agostoni P, Ramjankhan FZ, Doevendans PA, Stella PR. Transcatheter aortic valve implantation with the new balloon-expandable Sapien 3 versus Sapien XT valve system: a propensity score-matched singlecenter comparison. *Circ Cardiovasc Interv.* 2015;8:e002408.
- Abramowitz Y, Chakravarty T, Jilaihawi H, Cox J, Sharma RP, Mangat G, Nakamura M, Cheng W, Makkar RR. Impact of body mass index on the outcomes following transcatheter aortic valve implantation. *Catheter Cardiovasc Interv.* 2016;88:127–134.
- Binder RK, Webb JG, Toggweiler S, Freeman M, Barbanti M, Willson AB, Alhassan D, Hague CJ, Wood DA, Leipsic J. Impact of post-implant SAPIEN XT geometry and position on conduction disturbances, hemodynamic

performance, and paravalvular regurgitation.  $\it JACC$  Cardiovasc Interv. 2013;6:462–468.

- Husser O, Pellegrini C, Kessler T, Burgdorf C, Thaller H, Mayr NP, Kasel AM, Kastrati A, Schunkert H, Hengstenberg C. Predictors of permanent pacemaker implantations and new-onset conduction abnormalities with the SAPIEN 3 balloon-expandable transcatheter heart valve. *JACC Cardiovasc Interv.* 2016;9:244–254.
- 31. Petronio AS, Sinning JM, Van Mieghem N, Zucchelli G, Nickenig G, Bekeredjian R, Bosmans J, Bedogni F, Branny M, Stangl K, Kovac J, Schiltgen M, Kraus S, de Jaegere P. Optimal implantation depth and adherence to guidelines on permanent pacing to improve the results of transcatheter aortic valve replacement with the Medtronic CoreValve System: the CoreValve prospective, international, post-market ADVANCE-II study. *JACC Cardiovasc Interv.* 2015;8:837–846.
- Roten L, Stortecky S, Scarcia F, Kadner A, Tanner H, Delacretaz E, Meier B, Windecker S, Carrel T, Wenaweser P. Atrioventricular conduction after transcatheter aortic valve implantation and surgical aortic valve replacement. *J Cardiovasc Electrophysiol.* 2012;23:1115–1122.
- van der Boon RM, Van Mieghem NM, Theuns DA, Nuis RJ, Nauta ST, Serruys PW, Jordaens L, van Domburg RT, de Jaegere PP. Pacemaker dependency after transcatheter aortic valve implantation with the self-expanding Medtronic CoreValve System. *Int J Cardiol.* 2013;168:1269–1273.
- 34. Linke A, Wenaweser P, Gerckens U, Tamburino C, Bosmans J, Bleiziffer S, Blackman D, Schafer U, Muller R, Sievert H, Sondergaard L, Klugmann S, Hoffmann R, Tchetche D, Colombo A, Legrand VM, Bedogni F, IePrince P, Schuler G, Mazzitelli D, Eftychiou C, Frerker C, Boekstegers P, Windecker S, Mohr FW, Woitek F, Lange R, Bauernschmitt R, Brecker S; Investigators As. Treatment of aortic stenosis with a self-expanding transcatheter valve: the International Multi-centre ADVANCE Study. *Eur Heart J.* 2014;35:2672–2684.
- 35. Schymik G, Lefevre T, Bartorelli AL, Rubino P, Treede H, Walther T, Baumgartner H, Windecker S, Wendler O, Urban P, Mandinov L, Thomas M, Vahanian A. European experience with the second-generation Edwards SAPIEN XT transcatheter heart valve in patients with severe aortic stenosis: 1-year outcomes from the SOURCE XT Registry. *JACC Cardiovasc Interv.* 2015;8:657–669.

- 36. Holmes DR Jr, Nishimura RA, Grover FL, Brindis RG, Carroll JD, Edwards FH, Peterson ED, Rumsfeld JS, Shahian DM, Thourani VH, Tuzcu EM, Vemulapalli S, Hewitt K, Michaels J, Fitzgerald S, Mack MJ; Registry SAT. Annual outcomes with transcatheter valve therapy: from the STS/ACC TVT Registry. J Am Coll Cardiol. 2015;66:2813–2823.
- 37. Hamm CW, Mollmann H, Holzhey D, Beckmann A, Veit C, Figulla HR, Cremer J, Kuck KH, Lange R, Zahn R, Sack S, Schuler G, Walther T, Beyersdorf F, Bohm M, Heusch G, Funkat AK, Meinertz T, Neumann T, Papoutsis K, Schneider S, Welz A, Mohr FW; Board GA-E. The german aortic valve registry (GARY): inhospital outcome. *Eur Heart J*. 2014;35:1588–1598.
- Gilard M, Eltchaninoff H, Iung B, Donzeau-Gouge P, Chevreul K, Fajadet J, Leprince P, Leguerrier A, Lievre M, Prat A, Teiger E, Lefevre T, Himbert D, Tchetche D, Carrie D, Albat B, Cribier A, Rioufol G, Sudre A, Blanchard D, Collet F, Dos Santos P, Meneveau N, Tirouvanziam A, Caussin C, Guyon P, Boschat J, Le Breton H, Collart F, Houel R, Delpine S, Souteyrand G, Favereau X, Ohlmann P, Doisy V, Grollier G, Gommeaux A, Claudel JP, Bourlon F, Bertrand B, Van Belle E, Laskar M; Investigators F. Registry of transcatheter aortic-valve implantation in high-risk patients. *N Engl J Med*. 2012;366:1705–1715.
- 39. Nazif TM, Williams MR, Hahn RT, Kapadia S, Babaliaros V, Rodes-Cabau J, Szeto WY, Jilaihawi H, Fearon WF, Dvir D, Dewey TM, Makkar RR, Xu K, Dizon JM, Smith CR, Leon MB, Kodali SK. Clinical implications of new-onset left bundle branch block after transcatheter aortic valve replacement: analysis of the partner experience. *Eur Heart J*. 2014;35:1599–1607.
- 40. Houthuizen P, Van Garsse LA, Poels TT, de Jaegere P, van der Boon RM, Swinkels BM, Ten Berg JM, van der Kley F, Schalij MJ, Baan J Jr, Cocchieri R, Brueren GR, van Straten AH, den Heijer P, Bentala M, van Ommen V, Kluin J, Stella PR, Prins MH, Maessen JG, Prinzen FW. Left bundle-branch block induced by transcatheter aortic valve implantation increases risk of death. *Circulation*. 2012;126:720–728.
- 41. Testa L, Latib A, De Marco F, De Carlo M, Agnifili M, Latini RA, Petronio AS, Ettori F, Poli A, De Servi S, Ramondo A, Napodano M, Klugmann S, Ussia GP, Tamburino C, Brambilla N, Colombo A, Bedogni F. Clinical impact of persistent left bundle-branch block after transcatheter aortic valve implantation with CoreValve Revalving System. *Circulation*. 2013;127:1300–1307.

# **SUPPLEMENTAL MATERIAL**

Table S1. Predictors for permanent pacemaker implantation.

	Univariate OR [95% CI]	P-Value
Type of THV		
Lotus vs. CoreValve	3.50 [1.20-10.20]	.022
Lotus vs. ES-XT	6.30 [2.14-18.55]	.001
Lotus vs. ES-3	5.73 [1.65-19.94]	.006
CoreValve vs. ES-XT	1.80 [1.08-3.00]	.024
CoreValve vs. ES-3	1.64 [0.73-3.67]	. 232
ES-XT vs. ES-3	0.91 [0.40-2.07]	.820
Patient characteristics		
Alternative access	0.32 [0.15-0.69]	.004
Baseline atrial fibrillation	0.79 [0.44-1.42]	.429
Body mass index*	1.08 [1.02-1.14]	.006
Female sex	1.49 [0.93-2.39]	.098
Medication Amiodarone	0.87 [0.43-1.75]	.690
Medication Digitalis	0.86 [0.25-3.00]	.813
NYHA - class ≥ III	0.92 [0.54-1.58]	.765
Prior SAVR	0.40 [0.08-1.95]	.256

Results from univariate logistic regression analysis. Variables in italic were included in the multivariate analysis. \*Odds ratio per 1 kg/m<sup>2</sup> increment of body mass index. Abbreviations: CI = confidence interval; ES-3 = Edwards sapien valve 3; ES-XT = Edwards Sapien XT; NYHA = New York Heart Association; SAVR = surgical aortic valve replacement; THV = transcatheter heart valve.

Table S2. Predictors for new total atrioventricular block <24h.

	Univariate OR (95% Cl)	P-Value	Multivariate OR (95% Cl)	P-Value
Type of THV				
Lotus vs. CoreValve	3.43 (1.22-9.63)	.019	3.80 (1.25-11.52)	.018
Lotus vs. ES-XT	5.92 (2.06-16-99)	.001	6.01 (1.93-18.67)	.002
Lotus vs. ES-3	3.47 (0.99-12.09)	.051	3.88 (1.02-14.82)	.047
CoreValve vs. ES-XT	1.73 (0.99-3.00)	.053	1.58 (0.88-2.85)	.128
CoreValve vs. ES-3	1.01 (0.42-2.41)	.981		
ES-XT vs. ES-3	0.59 (0.24-1.43)	.240	0.17 (0.05-0.52)	.002
Patient characteristics				
Alternative access	0.51 (0.21-1.23)	.133	0.48 (0.13-1.81)	.281
Baseline atrial fibrillation	1.00 (0.53-1.86)	.987		
Body mass index	1.04 (0.99 -1.10)	.126	1.04 (0.98-1.10)	.218
Female sex	1.39 (0.84-2.29)	.200	1.30 (0.77-2.20)	.326
Prior surgical aortic valve replacement	0.89 (0.22-3.63)	.868		

Results from uni- and multivariate logistic regression for new onset third degree atrioventricular block within 24 hours. Variables in italic were included in multivariate regression. Abbreviations: CI = confidence interval; ES-XT = Edwards Sapien XT; ES-3 = Edwards Sapien 3; OR = Odds Ratio; THV = transcatheter heart valve.





# Transcatheter Heart Valve Selection and Permanent Pacemaker Implantation in Patients With Pre –Existent Right Bundle Branch Block

Lennart van Gils, Didier Tchetche, Thibault Lhermusier, Masieh Abawi, Nicolas Dumonteil, Ramón Rodriguez Olivares, Javier Molina-Martin de Nicolas, Pieter R. Stella, Didier Carrié, Peter P. De Jaegere and Nicolas M. Van Mieghem

J Am Heart Assoc. 2017;6:e005028; originally published March 3, 2017; doi: 10.1161/JAHA.116.005028 The Journal of the American Heart Association is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231 Online ISSN: 2047-9980

The online version of this article, along with updated information and services, is located on the World Wide Web at: http://jaha.ahajournals.org/content/6/3/e005028

Subscriptions, Permissions, and Reprints: The *Journal of the American Heart Association* is an online only Open Access publication. Visit the Journal at http://jaha.ahajournals.org for more information.