ORIGINAL RESEARCH

# Pacemaker Implantation and Dependency After Transcatheter Aortic Valve Replacement in the REPRISE III Trial

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***Background*—**As transcatheter aortic valve replacement expands to younger and/or lower risk patients, the long-term consequences of permanent pacemaker implantation are a concern. Pacemaker dependency and impact have not been methodically assessed in transcatheter aortic valve replacement trials. We report the incidence and predictors of pacemaker implantation and pacemaker dependency after transcatheter aortic valve replacement with the Lotus valve.

***Methods and Results*—**A total of 912 patients with high/extreme surgical risk and symptomatic aortic stenosis were randomized 2:1 (Lotus:CoreValve) in REPRISE III (The Repositionable Percutaneous Replacement of Stenotic Aortic Valve through Implantation of Lotus Valve System—Randomized Clinical Evaluation) trial. Systematic assessment of pacemaker dependency was pre-specified in the trial design. Pacemaker implantation within 30 days was more frequent with Lotus than CoreValve. By multivariable analysis, predictors of pacemaker implantation included baseline right bundle branch block and depth of implantation; diabetes mellitus was also a predictor with Lotus. No association between new pacemaker implantation and clinical outcomes was found. Pacemaker dependency was dynamic (30 days: 43%; 1 year: 50%) and not consistent for individual patients over time. Predictors of pacemaker dependency at 30 days included baseline right bundle branch block, female sex, and depth of implantation. No differences in mortality or stroke were found between patients who were pacemaker dependent or not at 30 days. Rehospitalization was higher in patients who were not pacemaker dependent versus patients without a pacemaker or those who were dependent.

***Conclusions*—**Pacemaker implantation was not associated with adverse clinical outcomes. Most patients with a new pacemaker at 30 days were not dependent at 1 year. Mortality and stroke were similar between patients with or without pacemaker dependency and patients without a pacemaker.

***Clinical Trial Registration*—**URL: https://www.clinicaltrials.gov/. Unique identifier NCT02202434. **(*J Am Heart Assoc*. 2019;8: e012594. DOI: 10.1161/JAHA.119.012594.)**

**Key Words:** aortic valve stenosis • pacemaker dependency • permanent pacemaker • transcatheter aortic valve replacement

Despite the rapid adoption of transcatheter aortic valve replacement (TAVR) for the treatment of aortic stenosis, the high frequency of conduction disturbances and subsequent requirement for permanent pacemaker remains a challenge. Because of the proximity of the aortic annulus with the atrioventricular conduction system, replacement of the aortic valve may result in bundle branch block or high degree atrioventricular block, with consequent permanent pacemaker implantation.[1] A lack of consensus or specific guidelines for pacemaker implantation after TAVR have led to

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Accompanying Data S1, Tables S1 through S8 and Figures S1 through S3 are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.119.012594

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## Clinical Perspective

### What Is New?

- Patients with a pre-existing permanent pacemaker were at the highest risk of death and no association was found between new pacemaker implantation and worse clinical outcomes; risks for new pacemaker implantation at 30 days following transcatheter aortic valve replacement included baseline right bundle branch block, depth of valve implantation, and medically treated diabetes mellitus.
- A prospective, systematic approach to evaluate pacemaker dependency was used; 1-year mortality and stroke were similar between patients in the pacemaker dependent and not dependent groups compared with patients without a pacemaker.
- Predictors of pacemaker dependency at 30 days included right bundle branch block, female sex, and mean depth of implantation and at 1 year included right bundle branch block and left ventricular outflow tract overstretch.

### What Are the Clinical Implications?

- Patients with pre-existing pacemakers and with baseline conduction disturbances (including right bundle branch block) should be carefully monitored after undergoing transcatheter aortic valve replacement.

wide variation in implantation patterns.[2,3] TAVR-related conduction system injury/inflammation is dynamic and may resolve over time but the incidence of pacemaker dependency over the course of follow-up has been poorly studied. Although long-term pacemaker dependency rates of 27% to 68% following TAVR have been reported, these studies have not systematically assessed pacemaker dependency using a consistent protocol-driven algorithm. Finally, data regarding the impact of pacemaker implantation and dependency on left ventricular function, arrhythmias, and survival are limited and could influence expansion of TAVR into younger, low-surgical risk cohorts.

REPRISE III (The Repositionable Percutaneous Replacement of Stenotic Aortic Valve through Implantation of Lotus Valve System—Randomized Clinical Evaluation) is the first large-scale randomized comparison of 2 different TAVR platforms: the Lotus mechanically-expanded valve and the CoreValve self-expanding bioprosthesis.[4] Systematic assessment of pacemaker dependency using a defined algorithm was pre-specified in the trial design.

We report the incidence, timing, and predictors for pacemaker requirement to 30 days after TAVR. Further, we evaluated the proportion of patients who were pacemaker dependent after TAVR as well as predictors and long-term clinical impact of pacemaker dependency.

## Methods

Additional methods can be found in Data S1.

### Study Population

The design, inclusion and exclusion criteria, and primary results of the REPRISE III trial have been reported.[4] Patients with symptomatic aortic stenosis and Society of Thoracic Surgeons predicted risk of mortality ≥8% or another indicator of high or extreme risk were eligible for enrollment. Patients were randomized 2:1 to Lotus (Boston Scientific Corporation, Marlborough, MA) or CoreValve (CoreValve Classic or EvolutR; Medtronic, Dublin, Ireland).[4] Study flow is shown in Figure 1A.[4] The protocol was approved by institutional review boards at each site; all patients provided written informed consent. The data for this clinical trial may be made available to other researchers in accordance with the Boston Scientific Data Sharing Policy (http://www.bostonscientific.com/en-US/data-sharing-requests.html). For the current analysis, patients who were randomized and received the assigned valve were included (Figure 1A).

### Pacemaker Dependency Algorithm

At 30 days and 1 year, patients with a new permanent pacemaker were evaluated for dependence via pacemaker interrogation using a pre-specified algorithm (Figure S1). Pacing rate was decreased by 10 beats per minute (bpm) until: (1) observation of native rhythm; (2) symptom onset; or (3) 30 bpm was reached. Pacemaker dependent patients were defined as patients who were symptomatic or did not have a native rhythm. The percentage of paced ventricular beats was captured.

### Definitions

Clinical outcomes were based on the Valve Academic Research Consortium end points[5] and were analyzed between 31 days and 1 year to avoid bias stemming from patients not receiving a pacemaker because of early death. An independent core laboratory analyzed all echocardiograms. Health status was assessed by the Kansas City Cardiomyopathy Quality of Life and the short form 12 (SF-12) health survey questionnaires.

### Statistical Analyses

Continuous variables are expressed as mean±SD and compared with the Student *t* test. Discrete variables were reported as n (%), differences were assessed using chi-square or Fisher exact tests. Time-to-event analyses were performed using the Kaplan–Meier method and compared with the

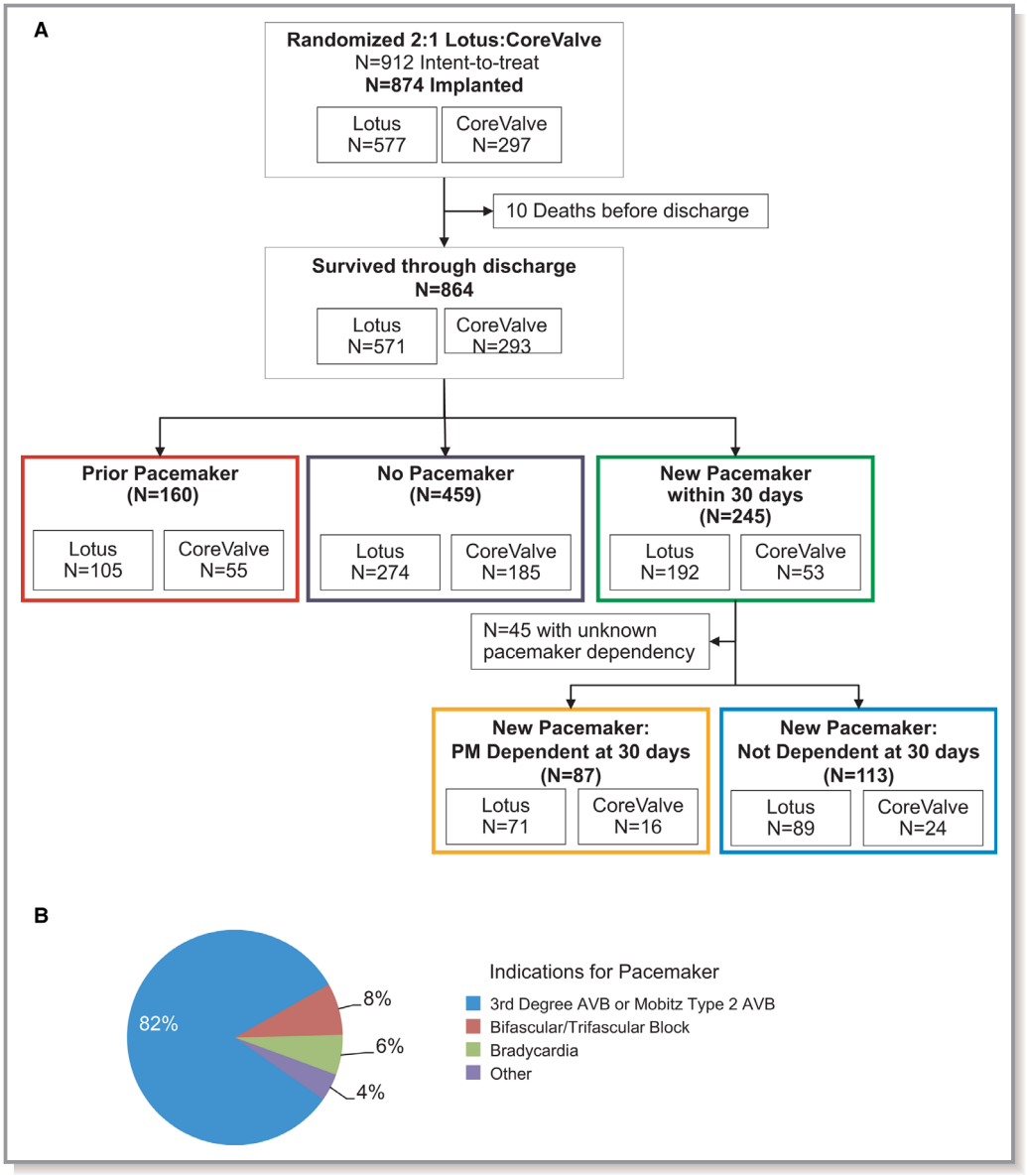


**Figure 1.** Patient flow and pacemaker indications. **A**, Patient flow. **B**, Other/unknown indications: 6 other, 5 left bundle branch block, 3 second degree atrioventricular block type 1 and 1 first degree atrioventricular block. AVB indicates atrioventricular block

log-rank test. Odds ratios and 95% CI for the adjusted risk of receiving a pacemaker after TAVR or being pacemaker dependent were generated using multivariate logistic regression. Parameters entered in the multivariate model included demographics (sex, age, body mass index), medical history (history of chronic obstructive pulmonary disease, diabetes mellitus, hyperlipidemia, hypertension, myocardial infarction, percutaneous coronary intervention, coronary artery bypass graft surgery, coronary artery disease, atrial fibrillation or flutter, stroke, transient ischemic attack, carotid artery stenosis/endarterectomy/stenting, severe liver disease/cirrhosis, renal failure, congestive heart failure, peripheral vascular disease, prior balloon aortic valvuloplasty, or current immunosuppressive therapy), Society of Thoracic Surgeons Score, baseline conduction disturbances (right bundle branch block [RBBB], left bundle branch block [LBBB], left anterior fascicular block, first degree atrioventricular block), procedural and echocardiographic characteristics (valve type [Lotus, CoreValve Classic, EvolutR], depth of implantation, left ventricular outflow tract (LVOT) and annulus overstretch, valve area, annulus area, mean aortic valve gradient, aortic valve area, LVOT area, and left ventricular ejection fraction <40%, coronary cusp calcification), and baseline laboratory values (serum albumin, platelet count, and serum creatinine). Parameters with a univariate $P<0.2$ were modeled in a multivariate analysis using a stepwise procedure in a logistic

**Table 1.** Baseline Characteristics in Patients Who Received a New Pacemaker Within 30 days of the Index Procedure

| | No Pacemaker (n=459) | New Pacemaker (n=245) | *P* Value |
|---|---|---|---|
| Age, y | 82±8 | 83±7 | 0.48 |
| Female sex | 236 (51) | 123 (50) | 0.76 |
| Body mass index, kg/m$^2$ | 29±7 | 31±8 | 0.001 |
| STS score | 6.5±4.2 | 6.8±3.6 | 0.33 |
| EuroSCORE II | 5.9±4.5 | 6.5±5.7 | 0.14 |
| Extreme surgical risk | 111 (24) | 45 (18) | 0.08 |
| LVEF <40% | 40 (8.8) | 11 (4.5) | 0.04 |
| Atrial fibrillation | 124 (27) | 78 (32) | 0.18 |
| Atrial flutter | 14 (3.1) | 11 (4.6) | 0.31 |
| Diabetes mellitus | 136 (30) | 82 (34) | 0.29 |
| History of coronary artery disease | 321 (70) | 176 (72) | 0.63 |
| History of myocardial infarction | 75 (17) | 44 (18) | 0.54 |
| History of percutaneous coronary intervention | 138 (30) | 79 (32) | 0.55 |
| History of coronary artery bypass graft surgery | 110 (24) | 60 (25) | 0.85 |
| Congestive heart failure | 349 (77) | 182 (76) | 0.80 |
| Annulus area, mm$^2$ | 446±68 | 450±67 | 0.45 |
| LVOT area, mm$^2$ | 427±80 | 427±76 | 0.99 |
| Aortic valve area, cm$^2$ | 0.7±0.2 | 0.7±0.2 | 0.001 |
| Mean aortic valve gradient, mm Hg | 45±14 | 45±13 | 0.77 |
| Baseline RBBB | 17 (3.7) | 68 (28) | <0.0001 |
| Baseline LBBB | 36 (7.9) | 20 (8.2) | 0.91 |
| Baseline LAFB | 70 (15) | 51 (21) | 0.07 |
| Baseline first degree atrioventricular block | 31 (6.8) | 25 (10) | 0.11 |
| Mean depth of valve implantation, mm | 5.7±2.2 | 6.2±2.3 | 0.01 |
| Annulus overstretch | 125±20 | 118±17 | <0.0001 |
| LVOT overstretch | 132±26 | 126±22 | 0.002 |
| Current immunosuppressive therapy | 48 (11) | 22 (9.1) | 0.57 |
| Hypertension | 420 (92) | 231 (94) | 0.18 |
| Prior balloon aortic valvuloplasty | 28 (6.1) | 17 (7.1) | 0.63 |
| Chronic obstructive pulmonary disease (≥moderate) | 71 (16) | 50 (21) | 0.08 |
| Prior stroke | 60 (13) | 28 (12) | 0.54 |
| Right carotid artery stenosis (≥80%) | 11 (3.0) | 3 (1.6) | 0.40 |
| Left carotid artery stenosis (≥80%) | 9 (2.5) | 2 (1.1) | 0.35 |
| Prior carotid endarterectomy/ carotid artery stenting | 37 (8.2) | 16 (6.6) | 0.47 |
| History of peripheral vascular disease | 127 (28) | 72 (30) | 0.58 |
| History of dialysis-dependent renal failure | 5 (1.1) | 0 (0) | 0.17 |
| Severe liver disease/cirrhosis | 6 (1.3) | 4 (1.7) | 0.74 |
| Platelet count <150 (10$^9$/L) | 81 (18) | 45 (18) | 0.34 |
| Serum creatinine, mg/dL | 1.1±0.40 | 1.1±0.42 | 0.64 |
| Serum albumin, g/dL | 3.8±0.43 | 3.8±0.48 | 0.55 |
| Moderate or greater calcification of left coronary cusp | 86 (19) | 46 (19) | 0.20 |
| Moderate or greater calcification of right coronary cusp | 13 (2.8) | 4 (1.6) | >0.99 |

Continued

**Table 1.** Continued

| | No Pacemaker (n=459) | New Pacemaker (n=245) | *P* Value |
|---|---|---|---|
| Moderate or greater calcification of non-coronary cusp | 331 (72) | 173 (71) | 0.79 |
| Depth of implant from left coronary sinus, mm | 6.3±2.5 | 6.7±2.6 | 0.02 |
| Depth of implant from posterior aortic sinus of the ascending aorta, mm | 5.1±2.7 | 5.7±2.8 | 0.03 |

% unless indicated. Calcification graded by computed tomographic imaging core laboratory as none/mild, moderate, or severe. Annulus overstretch indicates valve area/annulus area [by CTA]; LAFB, left anterior fascicular block; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; LVOT overstretch, valve area/LVOT area [by CTA]; LVOT, left ventricular outflow tract; RBBB, right bundle branch block; STS, Society of Thoracic Surgeons.

regression model. The significance level thresholds for entry and exit of independent variables into the multivariate model was set at 0.1. Statistical analyses were performed with SAS software, version 9.2 or later.

## Results

A total of 912 patients with high/extreme surgical risk and severe, symptomatic aortic stenosis were randomized (2:1,

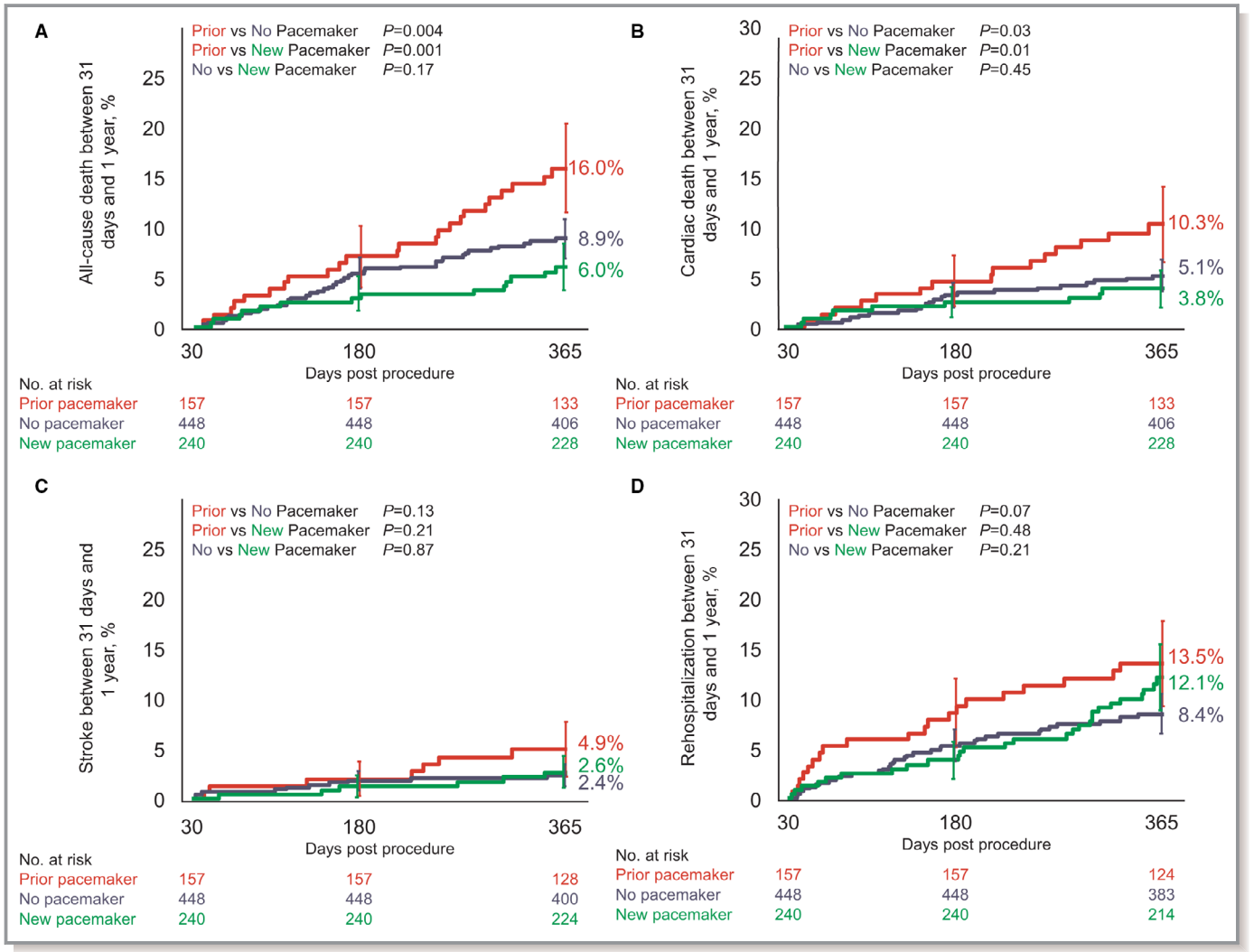


**Figure 2.** Clinical impact of pacemaker implantation. **A**, all-cause death, (**B**) cardiac death, (**C**) all stroke, and (**D**) hospitalization for valve-related symptoms/worsening congestive heart failure (New York Heart Association class III/IV) in patients with a prior pacemaker at baseline (red), patients who did not receive a pacemaker (purple), and patients who received a pacemaker within 30 days of the index procedure (green). Event rates between 31 and 365 days were calculated with Kaplan–Meier methods. Error bars indicate standard error. AVB indicates atrioventricular block

Lotus:CoreValve) and 874 received the assigned device (577 Lotus, 297 CoreValve; Figure 1A). The first-generation Lotus was used throughout the study while the second-generation EvolutR was introduced during study enrollment leading to 51.5% (153/297) CoreValve Classic and 48.5% (144/297) EvolutR.

Pre-existing pacemakers were present in 18% of Lotus patients (105/571) and 19% of CoreValve patients (55/293). In patients who survived through discharge (n=864), the need for pacemaker implantation within 30 days was greater with Lotus than CoreValve among pacemaker naïve patients (Lotus 34% [192/571] and CoreValve 18% [53/293], $P<0.001$). The 30-day pacemaker implantation rate in patients treated with CoreValve Classic (20%) and EvolutR (16%) were not significantly different; therefore, patients were analyzed together in the 'CoreValve' cohort. Median time to pacemaker implantation was 2 days post-TAVR; 90% were implanted within 1 week. More than 80% received a pacemaker because of high degree atrioventricular block (Figure 1B).

Baseline characteristics are shown in Table 1 and Table S1. Patients who received a new pacemaker within 30 days had higher weight and body mass index and were more likely to have baseline RBBB and hyperlipidemia compared with patients who did not. Depth of valve implantation was greater whereas left ventricular ejection fraction <40%, effective orifice area and overstretch were lower in patients who received a new pacemaker versus those who did not (Table 1). Patients who had a pacemaker before the index procedure were older and had more comorbidities (higher EuroSCORE, increased history of coronary artery disease, congestive heart failure, prior myocardial infarction, percutaneous coronary intervention, atrial flutter/fibrillation, and left ventricular ejection fraction <40%) compared with patients without a pacemaker.

## Outcomes in Patients With a New Pacemaker

Patients with a pre-existing pacemaker had higher clinical event rates than patients who did or did not receive a pacemaker (death: prior pacemaker 15.3% versus no pacemaker 8.7%; $P=0.02$; versus new pacemaker 5.8%, $P=0.002$, Table S2). Comparing patients without a pacemaker to those who received a new pacemaker, the frequency of death and stroke between 31 days and 1 year were similar (Figure 2, Table S2). Rates of re-hospitalization and other clinical outcomes were also similar in patient without and with a new pacemaker (Table S2). Left ventricular ejection fraction was slightly lower in patients who received a pacemaker (1 year: 54±10) compared with those who did not (57±11, $P=0.004$; Table 3). Both new and no pacemaker patients experienced significant improvements in health status post-TAVR as measured by the KCCQ (Kansas City Cardiomyopathy Questionnaire) (Figure S2). The extent of improvement in the physical composite score of the short form 12 (SF-12) health survey was somewhat smaller in patients who received a new pacemaker compared with those without a pacemaker (3.9 versus 5.4, $P=0.08$).

## Predictors of Pacemaker Requirement

Valve type was a significant predictor of 30-day pacemaker requirement overall. The independent multivariate predictors of 30-day pacemaker implantation in the Lotus and CoreValve cohorts are shown in Table 2 (and Tables S3 and S4). Baseline RBBB was the strongest predictor of pacemaker implantation in both Lotus and CoreValve-treated patients; mean depth of valve implantation was also a significant predictor. Medically treated diabetes mellitus was associated with an increased likelihood of pacemaker implantation in Lotus-treated patients.

## Incidence of Pacemaker Dependency

In patients who received a new pacemaker, the percentage of ventricular paced beats was 65% at 30 days and 57% at 1 year (Table S5). Of the patients without a preexisting pacemaker at baseline, 35% (n=245) received a pacemaker and 65% (n=459) did not receive a pacemaker within 30 days of the index procedure (Figure 3A). At 30 days, 40% of new pacemaker patients who had dependency data were considered dependent based on the pre-specified algorithm (n=87); at 1 year 50% of these patients were pacemaker dependent (Figure 3A). Approximately 83% of dependent patients at 30 days remained dependent at 1 year; 17% were no longer dependent. Of patients who received a new pacemaker but were not dependent at 30 days, three-quarters remained that way while one-quarter became dependent by 1 year (Figure 3B). A break down by valve type is shown in Figure S3.

**Table 2.** Multivariate Predictors of 30-Day Pacemaker Implantation

| Lotus Patients | Odds Ratio (95% CI) | *P* Value |
|---|---|---|
| RBBB at baseline | 21.6 (8.3– 56.6) | <0.0001 |
| Mean depth of valve implantation | 1.17 (1.04–1.32) | 0.008 |
| Medically treated diabetes mellitus | 1.66 (1.03–2.67) | 0.04 |
| CoreValve patients | | |
| RBBB at baseline | 5.42 (1.89–15.6) | 0.002 |
| Mean depth of valve implantation | 1.15 (1.01–1.32) | 0.04 |

Included patients who did or did not receive a new pacemaker within 30 days of the index procedure (excluded patients with a prior pacemaker) and analyzed in each treatment group (Lotus or CoreValve). RBBB indicates right bundle branch block.

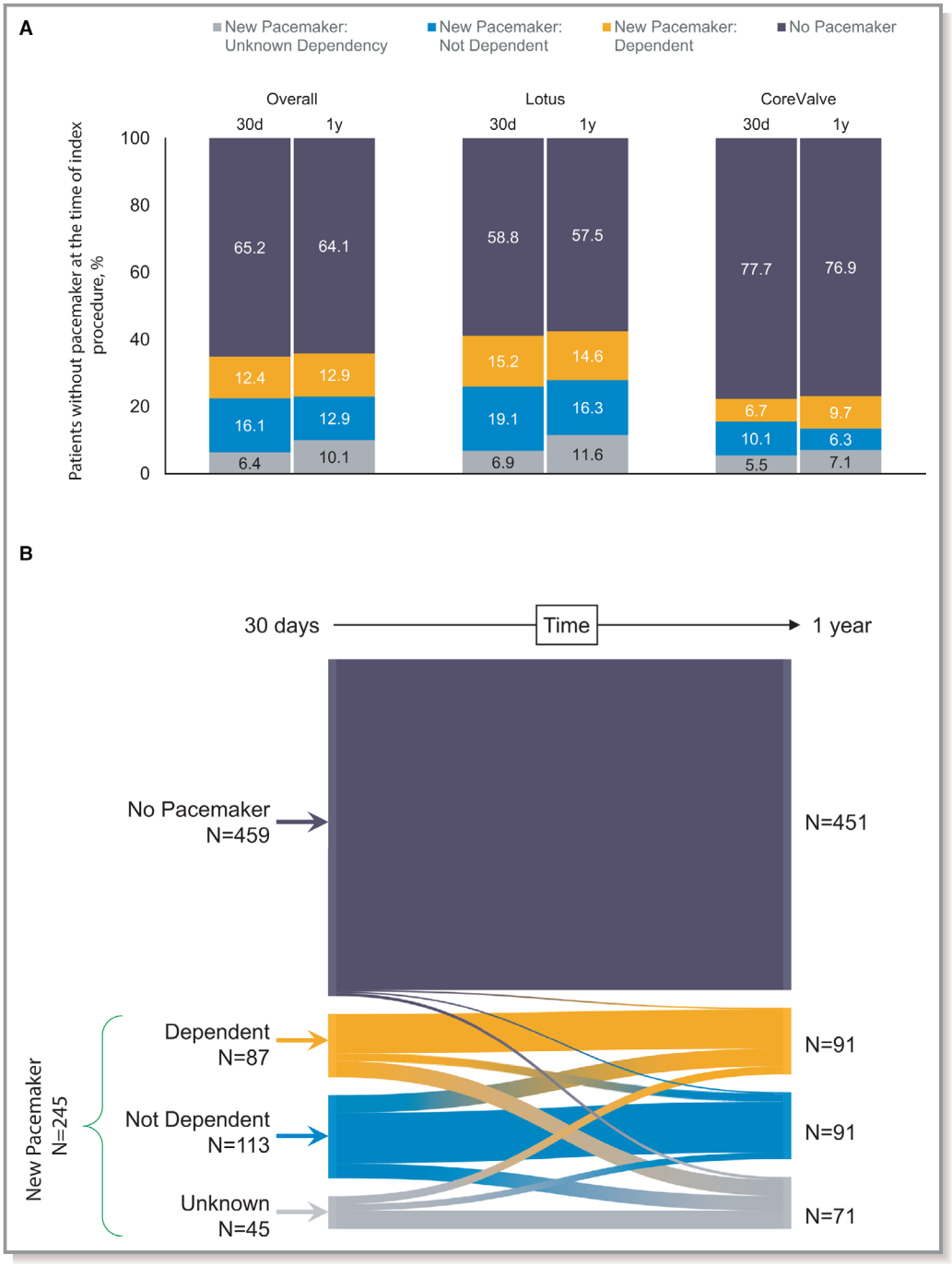


**Figure 3.** Pacemaker dependency at 30 days and 1 year. **A**, Pacemaker status and dependency in patients who did not have a prior pacemaker at baseline. **B**, Change in pacemaker status and dependency between 30 days and 1 year.

## Outcomes by Pacemaker Dependency

No differences in death or stroke between 31 days and 1 year were observed among the no pacemaker, dependent, and not dependent cohorts (Figure 4, Table S6). Patients who received a new pacemaker but were not dependent had higher re-hospitalization rates (18.3%) compared with patients who did not receive a pacemaker (8.4%; *P*=0.007) or were dependent (6.1%, *P*=0.02). The rate of bleeding was higher in patients without a pacemaker (6.0%) compared with patients who received a new pacemaker but were not dependent (0.9%; *P*=0.02); pacemaker dependent patients had a bleeding rate of 5.8% (Table S6). Left ventricular ejection fraction was similar between patients who were or were not pacemaker dependent (Table 3).

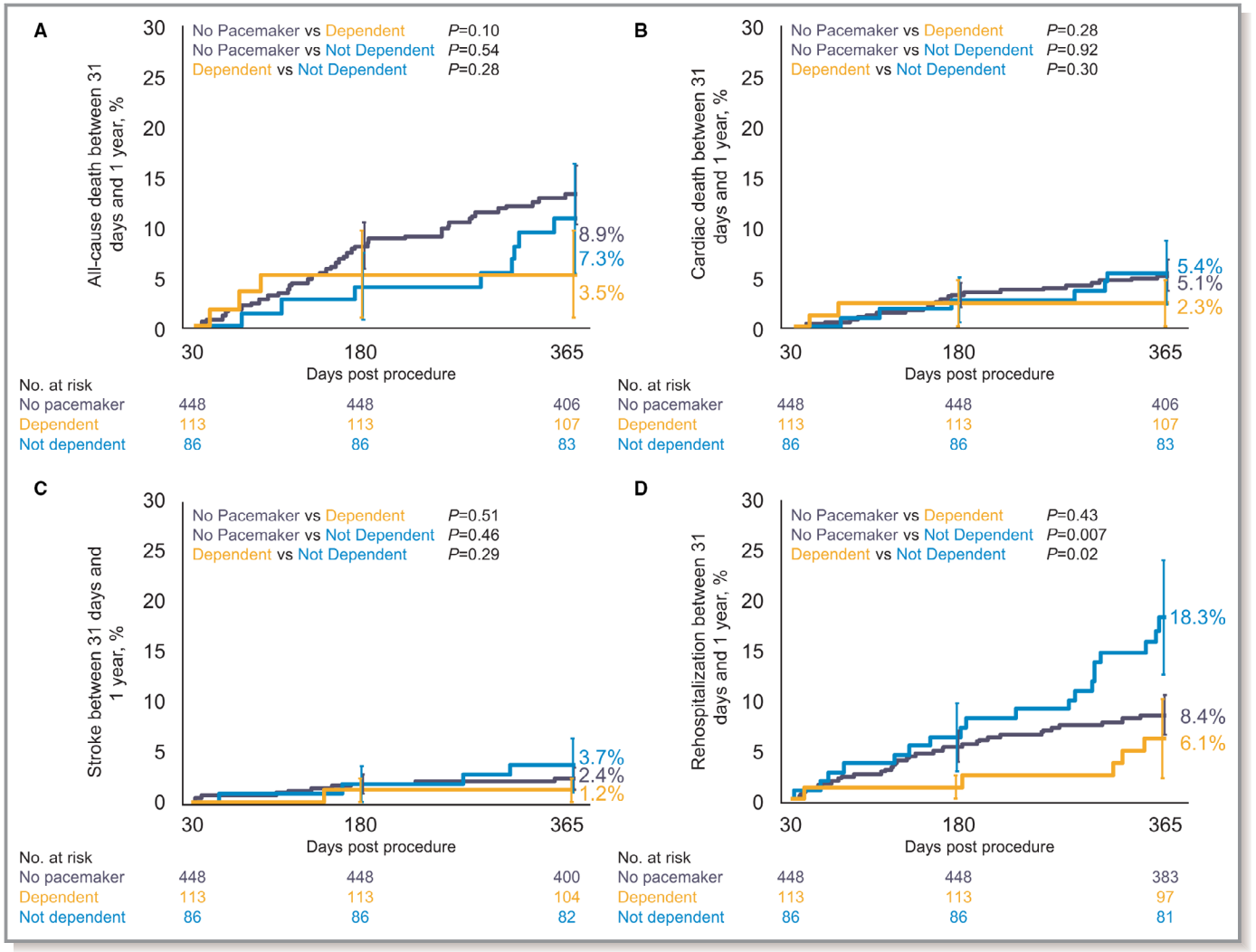


**Figure 4.** Clinical impact of pacemaker dependency. **A**, All-cause death, (**B**) cardiac death, (**C**) all stroke, and (**D**) hospitalization for valve-related symptoms/worsening congestive heart failure (New York Heart Association class III/IV) in patients without a pacemaker at baseline (purple) and in patients who received a pacemaker within 30 days of the index procedure who were pacemaker dependent (orange) or not pacemaker dependent (blue) at 30 days. Event rates between 31 and 365 days were calculated with Kaplan–Meier methods. Error bars indicate standard error.

## Predictors of Pacemaker Dependency

Multivariate predictors of pacemaker dependency at 30 days included baseline RBBB and depth of valve implantation; male sex was protective (Table 4; Table S7). Baseline RBBB and LVOT overstretch were significant multivariate predictors of pacemaker dependency at 1 year (Table 4; Table S8). Valve type was not a significant predictor of pacemaker dependency in patients who received a pacemaker at either timepoint.

## Discussion

The major findings of our study include: (1) patients with pre-existing pacemakers were at highest risk of death post-TAVR; new pacemaker implantation was not associated with worse 1-year outcomes. (2) Multivariate predictors of new pacemaker implantation included baseline RBBB and depth of valve implantation; diabetes mellitus was a predictor for Lotus. (3) Pacemaker dependency was dynamic; 20% to 25% of new pacemaker patients switched dependency status between 30 days and 1 year. (4) Pacemaker dependent patients did not have worse clinical outcomes at 1 year compared with patients without a pacemaker. (5) Pacemaker dependency at both time points was predicted by baseline RBBB; depth of valve implantation and female sex predicted 30-day dependency whereas LVOT overstretch predicted 1-year dependency.

Pacemaker implantation post-TAVR occurs in 2% to 50% of patients depending on valve type, patient population, and

**Table 3.** Left Ventricular Ejection Fraction Over Time Stratified by Pacemaker Status at 30 days

| Pacemaker Status | 30 D | 6 Mo | 1 Y |
|---|---|---|---|
| Prior pacemaker | 52±11 (119)* | 54±11 (97) | 52±11 (91)* |
| No pacemaker | 55±11 (344) | 56±11 (298) | 57±11 (288) |
| New pacemaker | | | |
| Overall | 54±11 (194) | 54±11 (172)* | 54±10 (167)* |
| Not dependent | 54±10 (96) | 54±11 (81) | 53±10 (77) |
| Dependent | 53±12 (67) | 53±12 (61) | 53±11 (63) |

The "Overall pacemaker" group included patients without pacemaker dependency information. Dependency was measured at 30 days.
*$P$<0.05 vs the no pacemaker group.

other factors.[1,2] Rates in patients treated with the first-generation Lotus valve range between 25% and 41%.[6–8] The first-generation Lotus frame may travel deeper into the LVOT during implantation than other valves; subsequent studies using optimized implantation depth and newer versions of the Lotus device suggest lower rates of pacemaker implantation are achievable.[8,9] The most consistent independent predictor of new pacemaker implantation, unrelated to device, is pre-existing RBBB which is associated with poorer clinical outcomes.[10] Depth of valve implantation was a significant predictor of pacemaker implantation in this population as well. Other factors which increase the likelihood of receiving a pacemaker after TAVR can be grouped into pre-existing conduction abnormalities and anatomic factors (LBBB, annulus/LVOT calcification), procedural factors (overstretch, diameter), and clinical characteristics or demographics.[11]

Most studies have shown no significant association between post-TAVR pacemaker implantation and death.[1,12,13] Two exceptions are the Society of Thoracic Surgeons/ACC (American College of Cardiology) Transcatheter Valve Therapy registry which found 1-year overall mortality was increased among patients who received a pacemaker after TAVR and there was a trend toward increased mortality at 5 years in the Nordic Aortic Valve Intervention trial (new pacemaker 38.2% versus no pacemaker 21.7%; $P$=0.07).[14,15] In our study, implantation of a new pacemaker was not associated with adverse outcomes compared with patients who did not receive a pacemaker and, in fact, was associated with numerically fewer adverse outcomes to 1 year. Patients with a pacemaker before TAVR had a higher mortality rate compared with patients who never received a pacemaker. Implantation of a pacemaker post-TAVR has also been shown to increase hospital length of stay, rehospitalization rates, and be associated with less improvement in left ventricular function.[16] Finally, there are complications and financial considerations related to the pacemaker itself.[1,12,13,16] These results are primarily derived from higher risk populations; the clinical consequences of new pacemaker implantation in lower risk patients has been less well studied.

**Table 4.** Multivariate Predictors of Pacemaker Dependency

| 30 D | Odds Ratio (95% CI) | $P$ Value |
|---|---|---|
| RBBB at baseline | 4.47 (2.11– 9.5) | <0.0001 |
| Male sex | 0.39 (0.19–0.78) | 0.008 |
| Mean depth of valve implantation, mm | 1.18 (1.01–1.38) | 0.03 |
| 1 y | | |
| RBBB at baseline | 3.46 (1.70–7.06) | 0.0006 |
| LVOT overstretch* (%) | 1.02 (1.01–1.04) | 0.005 |

Included patients who received a new pacemaker within 30 days of the index procedure (excluded patients with a prior pacemaker). LVOT indicates left ventricular outflow tract; RBBB, right bundle branch block.
*Valve area/LVOT area [by CTA].

Pacemaker dependency post-TAVR has not been rigorously or consistently evaluated. Conduction disturbances after TAVR may resolve over time; between one- and two-thirds of patients who require a permanent pacemaker after TAVR are not dependent at subsequent follow-up.[7,17–20] In REPRISE III, 38% were pacemaker dependent at 30 days and 44% were dependent at 1 year, which is within the wide range observed in other studies (27% and 68%).[7,17–23] The change in dependency during follow-up underscores the possibility that some conduction disturbances may improve or progress with time. There may be differences among TAVR valves though additional studies are needed to better assess this.

Previous studies have found a number of independent predictors for long-term pacemaker dependence including pre-existing RBBB, first-degree atrioventricular block, left anterior hemiblock, porcelain aorta, and implantation depth of the prosthesis.[17,20,24,25] RBBB and depth of implantation were confirmed as independent predictors of pacemaker dependency with LVOT overstretch identified as an additional predictor in the REPRISE III patient population. Male sex was associated with a decreased likelihood of pacemaker dependency.

We found no differences in mortality or stroke between patients who were or were not dependent on the new pacemaker. Few studies have reported outcomes in these patient groups. One small single-center study showed similar rates of clinical outcomes between dependent and not dependent patients through 1-year post-TAVR.[17] The rate of rehospitalization was lowest in pacemaker dependent patients compared with patients without a pacemaker or those who were not dependent. The findings related to pacemaker dependency do not necessarily support changing the indication for permanent pacemaker implantation after TAVR, but predictors of short-term or persistent pacemaker dependency may help in selecting patients who would benefit most from receiving a pacemaker. Techniques or devices that

help with short-term pacing or diagnosis of arrhythmic events, including implantable cardiac monitors,[26] could help ensure the optimal use and best outcomes of permanent pacemaker implantation. Our results support periodic examination and adjustment of pacemaker settings to ensure normal conduction while minimizing the risks of long-term pacing and associated left ventricular dysfunction. Leadless pacemakers and permanent His bundle pacing may contribute to less morbidity in these patients in the future.[27,28]

This current study has limitations. The control arm included 2 generations of CoreValve. The study was not designed or powered to compare clinical outcomes in patients with and without a pacemaker. Additionally, atrial fibrillation burden was not prospectively documented by protocol and invasive electrophysiological tests were not performed. Pacemaker dependency is likely to be dynamic and was assessed at only 2 time points and the small number of patients did not allow an analysis of pacemaker dependency by valve type. As such, intervening moments of pacemaker dependency may have been missed. Follow-up beyond 1-year is not yet available.

## Conclusions

Patients with a pre-existing permanent pacemaker were at the highest risk of adverse clinical outcomes. No associations between new pacemaker implantation and clinical outcomes were found. Most patients with a new pacemaker were not dependent at 1 year. Pacemaker dependent patients did not have worse outcomes compared with either those without pacemaker dependency or patients without a pacemaker.

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# Supplemental Material

**Data S1.**

## Supplemental Methods

Parameters entered in the multivariate model included demographics (sex, age, BMI), medical history (history of chronic obstructive pulmonary disease, diabetes, hyperlipidemia, hypertension, myocardial infarction, percutaneous coronary intervention, coronary artery bypass graft surgery, coronary artery disease, atrial fibrillation or flutter, stroke, transient ischemic attack, carotid artery stenosis/endarterectomy/stenting, severe liver disease/cirrhosis, renal failure, congestive heart failure, peripheral vascular disease, prior balloon aortic valvuloplasty, or current immunosuppressive therapy), risk assessments (STS Score, EuroSCORE), baseline conduction disturbances (right bundle branch block [RBBB], left bundle branch block [LBBB], LAFB [left anterior fascicular block], first degree AV block), procedural and echocardiographic characteristics (valve type [Lotus, CoreValve Classic, EvolutR], depth of implantation, LVOT and annulus overstretch, valve area, annulus area, mean aortic valve gradient, aortic valve area, LVOT Area, and left ventricular ejection fraction <40%, coronary cusp calcification), and baseline laboratory values (serum albumin, platelet count, and serum creatinine). Parameters with a univariate P value <0.2 were modeled in a multivariate analysis using a stepwise procedure in a logistic regression model. The significance level thresholds for entry and exit of independent variables into the multivariate model was set at 0.1.

**Table S1. Additional baseline characteristics by pacemaker status at 30 days.**

| | Prior Pacemaker (N=157) | No Pacemaker (N=448) | New Pacemaker (N=240) | *P* value Prior vs No Pacemaker | *P* value Prior vs New Pacemaker | *P* value No vs New Pacemaker |
|---|---|---|---|---|---|---|
| Current immunosuppressive therapy | 12 (7.5) | 48 (11) | 22 (9.1) | 0.28 | 0.57 | 0.57 |
| Hypertension | 150 (94) | 420 (92) | 231 (94) | 0.36 | 0.82 | 0.18 |
| Prior balloon aortic valvuloplasty | 12 (7.5) | 28 (6.1) | 17 (7.1) | 0.52 | 0.85 | 0.63 |
| Chronic obstructive pulmonary disease (≥moderate) | 33 (21) | 71 (16) | 50 (21) | 0.14 | 0.94 | 0.08 |
| Prior stroke | 19 (12) | 60 (13) | 28 (12) | 0.70 | 0.90 | 0.54 |
| Right carotid artery stenosis (≥80%) | 1 (0.8) | 11 (3.0) | 3 (1.6) | 0.31 | >0.99 | 0.40 |
| Left carotid artery stenosis (≥80%) | 1 (0.8) | 9 (2.5) | 2 (1.1) | 0.46 | >0.99 | 0.35 |
| Prior carotid endarterectomy/ carotid artery stenting | 12 (7.6) | 37 (8.2) | 16 (6.6) | 0.81 | 0.71 | 0.47 |
| History of peripheral vascular disease | 49 (31) | 127 (28) | 72 (30) | 0.47 | 0.82 | 0.58 |
| History of dialysis-dependent renal failure | 0 (0) | 5 (1.1) | 0 (0) | 0.33 | Not evaluable | 0.17 |
| Severe liver disease/cirrhosis | 0 (0) | 6 (1.3) | 4 (1.7) | 0.35 | 0.15 | 0.74 |
| Platelet count <150 ($10^9$/L) | 35 (22) | 81 (18) | 45 (18) | 0.86 | 0.34 | 0.34 |
| Serum creatinine (mg/dL) | 1.2 ± 0.41 | 1.1 ± 0.40 | 1.1 ± 0.42 | 0.18 | 0.42 | 0.64 |
| Serum albumin (g/dL) | 3.8 ± 0.48 | 3.8 ± 0.43 | 3.8 ± 0.48 | 0.89 | 0.75 | 0.55 |
| Moderate or greater calcification of left coronary cusp | 25 (16) | 86 (19) | 46 (19) | 0.28 | 0.84 | 0.20 |
| Moderate or greater calcification of right coronary cusp | 2 (1.3) | 13 (2.8) | 4 (1.6) | 0.58 | 0.49 | >0.99 |
| Moderate or greater calcification of non-coronary cusp | 120 (75) | 331 (72) | 173 (71) | 0.91 | 0.91 | 0.79 |
| Depth of implant from left coronary sinus, mm | 6.6 ± 2.5 | 6.3 ± 2.5 | 6.7 ± 2.6 | 0.54 | 0.03 | 0.02 |
| Depth of implant from posterior aortic sinus of the ascending aorta, mm | 5.4 ± 2.7 | 5.1 ± 2.7 | 5.7 ± 2.8 | 0.60 | 0.19 | 0.03 |

% unless indicated. Calcification graded by Computed Tomographic Imaging core lab as none/mild, moderate or severe.

**Table S2. Outcomes between 31 days and 1 year in patients who had a prior pacemaker, no pacemaker or new pacemaker at 30 days.**

| | Prior Pacemaker (N=157) | No Pacemaker (N=448) | New Pacemaker (N=240) | *P* value Prior vs No Pacemaker | *P* value Prior vs New Pacemaker | *P* value No vs New Pacemaker | *P* value Overall |
|---|---|---|---|---|---|---|---|
| All-cause mortality | 24 (15.3) | 39 (8.7) | 14 (5.8) | 0.02 | 0.002 | 0.18 | 0.005 |
| Cardiovascular | 15 (9.6) | 22 (4.9) | 9 (3.8) | 0.04 | 0.02 | 0.48 | 0.03 |
| Non-cardiovascular | 9 (5.7) | 17 (3.8) | 5 (2.1) | 0.30 | 0.05 | 0.22 | 0.16 |
| Stroke | 7 (4.5) | 10 (2.2) | 6 (2.5) | 0.16 | 0.28 | 0.82 | 0.32 |
| Disabling | 4 (2.5) | 8 (1.8) | 5 (2.1) | 0.52 | 0.74 | 0.78 | 0.76 |
| Non-disabling | 3 (1.9) | 3 (0.7) | 1 (0.4) | 0.18 | 0.32 | >0.99 | 0.30 |
| All-cause mortality or disabling stroke | 26 (16.6) | 43 (9.6) | 16 (6.7) | 0.02 | 0.002 | 0.19 | 0.005 |
| Cardiac death or disabling stroke | 17 (10.8) | 29 (6.5) | 11 (4.6) | 0.08 | 0.02 | 0.31 | 0.05 |
| Major vascular complications | 0 (0) | 1 (0.2) | 1 (0.4) | >0.99 | >0.99 | >0.99 | >0.99 |
| Bleeding | 11 (7.0) | 27 (6.0) | 8 (3.3) | 0.66 | 0.09 | 0.13 | 0.21 |
| Life-threatening or Disabling | 5 (3.2) | 15 (3.3) | 4 (1.7) | 0.92 | 0.33 | 0.20 | 0.43 |
| Myocardial infarction | 6 (3.8) | 12 (2.7) | 6 (2.5) | 0.43 | 0.55 | 0.89 | 0.67 |
| Repeat TAVR | 2 (1.3) | 0 (0) | 1 (0.4) | 0.07 | 0.56 | 0.35 | 0.06 |
| Rehospitalization | 20 (12.7) | 36 (8.0) | 27 (11.3) | 0.08 | 0.65 | 0.16 | 0.16 |
| TAV-in-TAV deployment | 1 (0.6) | 0 (0) | 1 (0.4) | 0.26 | >0.99 | 0.35 | 0.22 |

Rehospitalization for valve-related symptoms or worsening congestive heart failure (NYHA class III or IV). Abbreviations: TAV=transcatheter aortic valve; TAVR= transcatheter aortic valve replacement

**Table S3. Left Ventricular Ejection Fraction over Time.**

| | Prior Pacemaker (N=157) | No Pacemaker (N=448) | New Pacemaker (N=240) | *P* value Prior vs No Pacemaker | *P* value Prior vs New Pacemaker | *P* value No vs New Pacemaker |
|---|---|---|---|---|---|---|
| 30 days | 52 ± 11 (119) | 55 ± 11 (344) | 54 ± 11 (194) | 0.03 | 0.15 | 0.42 |
| 6 months | 54 ± 11 (97) | 56 ± 11 (298) | 54 ± 11 (172) | 0.13 | 0.79 | 0.03 |
| 1 year | 52 ± 11 (91) | 57 ± 11 (288) | 54 ± 10 (167) | <0.0001 | 0.31 | 0.004 |

Includes patients with LVEF measurements. Patients with follow-up days less than 30 days were excluded from the analysis.

**Table S4. Multivariate predictors of pacemaker implantation at 30 days in Lotus patients.**

| | UNIVARIATE MODEL | | MULTIVARIATE MODEL | |
|---|---|---|---|---|
| **Variable** | **Odds Ratio [95% CI]** | **P-value** | **Odds Ratio [95% CI]** | **P-value** |
| RBBB at baseline | 14.40 [6.50, 31.90] | <0.0001 | 21.63 [8.27, 56.57] | <0.0001 |
| Mean depth of implantation (mm) | 1.13 [1.02, 1.25] | 0.02 | 1.17 [1.04, 1.32] | 0.008 |
| Depth NCS | 1.09 [1.01, 1.18] | 0.03 | | |
| Moderate or greater COPD | 1.67 [1.02, 2.73] | 0.04 | | |
| Lvef <40% | 0.46 [0.21, 1.01] | 0.05 | 0.42 [0.17, 1.05] | 0.06 |
| Medically-treated diabetes | 1.47 [0.98, 2.19] | 0.06 | 1.66 [1.03, 2.67] | 0.04 |
| Serum albumin (g/dl) | 1.13 [0.97, 1.32] | 0.11 | | |
| Depth LCS | 1.07 [0.98, 1.17] | 0.11 | | |
| LVOT (LCC) calcification grade greater than 2 | 0.61 [0.32, 1.15] | 0.13 | | |
| Baseline LAFB | 1.45 [0.89, 2.35] | 0.13 | | |
| History of hyperlipidemia requiring medication | 1.38 [0.90, 2.11] | 0.14 | | |
| Overstretch (valve area/LVOT area, %) | 1.01 [0.99, 1.02] | 0.25 | | |
| Left carotid artery stenosis (≥80%) | 0.32 [0.05, 2.18] | 0.25 | | |
| History of atrial fibrillation or flutter | 1.26 [0.85, 1.88] | 0.25 | | |
| STS score | 1.03 [0.98, 1.07] | 0.26 | | |
| LVOT (RCC) calcification grade >2 | 0.16 [0.01, 4.12] | 0.27 | | |
| First degree AV block | 1.47 [0.74, 2.90] | 0.27 | | |
| Overstretch (valve area/annulus area, %) | 1.01 [0.99, 1.03] | 0.31 | | |
| Valve area ($mm^2$) | 1.00 [1.00, 1.00] | 0.32 | | |
| EuroSCORE II | 1.02 [0.98, 1.05] | 0.36 | | |
| History of cerebrovascular accidents | 0.76 [0.42, 1.38] | 0.37 | | |
| Age at time of consent | 1.01 [0.99, 1.04] | 0.40 | | |
| History of percutaneous coronary intervention | 1.18 [0.80, 1.76] | 0.40 | | |
| Platelet count <150 ($10^9$/L) | 1.22 [0.76, 1.97] | 0.40 | | |
| History of myocardial infarction | 1.21 [0.74, 1.98] | 0.45 | | |
| Prior carotid endarterectomy/carotid artery stenting | 0.78 [0.41, 1.51] | 0.47 | | |
| BMI | 0.99 [0.98, 1.01] | 0.48 | | |
| Aortic valve area ($cm^2$) | 0.72 [0.26, 2.01] | 0.53 | | |
| Severe liver disease/cirrhosis | 1.45 [0.36, 5.89] | 0.60 | | |
| History of CABG | 0.89 [0.58, 1.37] | 0.60 | | |
| Male | 1.10 [0.76, 1.59] | 0.62 | | |
| History of hypertension | 1.18 [0.58, 2.41] | 0.64 | | |
| Baseline LBBB | 0.84 [0.41, 1.72] | 0.64 | | |

| | UNIVARIATE MODEL | | MULTIVARIATE MODEL | |
|---|---|---|---|---|
| **Variable** | **Odds Ratio [95% CI]** | **P-value** | **Odds Ratio [95% CI]** | **P-value** |
| Right carotid artery stenosis (≥80%) | 0.77 [0.19, 3.09] | 0.71 | | |
| History of dialysis dependent renal failure | 0.46 [0.00, 44.77] | 0.74 | | |
| Annulus area ($mm^2$) | 1.00 [1.00, 1.00] | 0.78 | | |
| Serum creatinine (mg/dl) | 1.06 [0.67, 1.67] | 0.81 | | |
| Currently taking immunosuppressive therapy | 0.93 [0.50, 1.73] | 0.81 | | |
| LVOT area ($mm^2$) | 1.00 [1.00, 1.00] | 0.82 | | |
| History of congestive heart failure | 1.05 [0.68, 1.62] | 0.84 | | |
| History of transient ischemic attacks | 1.06 [0.55, 2.04] | 0.87 | | |
| Mean aortic valve gradient (mmHg) | 1.00 [0.99, 1.01] | 0.89 | | |
| History of peripheral vascular disease | 0.99 [0.66, 1.47] | 0.95 | | |
| History of coronary artery disease | 1.01 [0.67, 1.51] | 0.98 | | |
| Prior balloon aortic valvuloplasty | 1.00 [0.46, 2.21] | 0.99 | | |

**Table S5. Multivariate predictors of pacemaker implantation at 30 days in CoreValve patients.**

| | UNIVARIATE MODEL | | MULTIVARIATE MODEL | |
|---|---|---|---|---|
| **Variable** | **Odds Ratio [95% CI]** | **P-value** | **Odds Ratio [95% CI]** | **P-value** |
| Baseline RBBB | 5.57 [2.28, 13.59] | 0.0002 | 5.42 [1.89, 15.58] | 0.002 |
| Mean depth of implantation (mm) | 1.16 [1.03, 1.32] | 0.02 | 1.15 [1.01, 1.32] | 0.04 |
| Depth LCS | 1.14 [1.02, 1.28] | 0.02 | | |
| Depth NCS | 1.13 [1.01, 1.26] | 0.03 | | |
| BMI | 1.04 [1.00, 1.08] | 0.05 | | |
| History of hyperlipidemia requiring medication | 2.19 [0.94, 5.09] | 0.07 | | |
| First degree AV block | 2.06 [0.78, 5.44] | 0.14 | | |
| History of hypertension | 3.63 [0.64, 20.73] | 0.15 | | |
| Baseline LBBB | 1.91 [0.73, 4.98] | 0.19 | 2.74 [0.92, 8.12] | 0.07 |
| Aortic valve area | 3.04 [0.58, 15.91] | 0.19 | | |
| Prior balloon aortic valvuloplasty | 1.98 [0.71, 5.54] | 0.19 | 3.01 [0.90, 10.13] | 0.07 |
| Baseline LAFB | 1.60 [0.75, 3.39] | 0.22 | | |
| LVOT (LCC) calcification grade >2 | 0.48 [0.15, 1.57] | 0.22 | | |
| History of transient ischemic attacks | 1.93 [0.63, 5.86] | 0.25 | | |
| EuroSCORE II | 1.04 [0.97, 1.11] | 0.25 | | |
| Evolut R | 0.71 [0.39, 1.32] | 0.28 | | |
| Overstretch (Valve area/Annulus area, %) | 0.99 [0.96, 1.01] | 0.29 | | |
| History of CABG | 1.41 [0.70, 2.84] | 0.34 | | |
| Platelet count <150 ($10^9$/L) | 0.68 [0.29, 1.62] | 0.39 | | |
| History of coronary artery disease | 1.34 [0.67, 2.69] | 0.41 | | |
| History of atrial fibrillation or flutter | 1.32 [0.68, 2.56] | 0.41 | | |
| History of congestive heart failure | 0.75 [0.37, 1.51] | 0.42 | | |
| Prior carotid endarterectomy/carotid artery stenting | 0.48 [0.08, 2.95] | 0.43 | | |
| Annulus area ($mm^2$) | 1.00 [1.00, 1.01] | 0.46 | | |
| History of cerebrovascular accidents | 1.34 [0.58, 3.05] | 0.49 | | |
| Right carotid artery stenosis (≥80%) | 0.33 [0.01, 7.98] | 0.49 | | |
| LVEF <40% | 0.62 [0.15, 2.59] | 0.51 | | |
| History of dialysis dependent renal failure | 0.38 [0.01, 10.03] | 0.56 | | |
| Medically-treated diabetes | 0.83 [0.43, 1.60] | 0.58 | | |
| Currently taking immunosuppressive therapy | 0.75 [0.25, 2.23] | 0.60 | | |
| Beta-blockers at baseline | 1.17 [0.63, 2.16] | 0.63 | | |
| Left carotid artery stenosis (≥80%) | 1.65 [0.19, 14.45] | 0.65 | | |
| LVOT (RCC) calcification grade >2 | 0.49 [0.02, 15.13] | 0.68 | | |

| | UNIVARIATE MODEL | | MULTIVARIATE MODEL | |
|---|---|---|---|---|
| **Variable** | **Odds Ratio [95% CI]** | **P-value** | **Odds Ratio [95% CI]** | **P-value** |
| History of peripheral vascular disease | 1.15 [0.57, 2.35] | 0.70 | | |
| Serum creatinine (mg/dl) | 1.15 [0.55, 2.42] | 0.71 | | |
| Moderate or greater COPD | 1.12 [0.51, 2.44] | 0.78 | | |
| LVOT area ($mm^2$) | 1.00 [1.00, 1.00] | 0.78 | | |
| Male | 0.92 [0.50, 1.70] | 0.80 | | |
| History of myocardial infarction | 1.10 [0.50, 2.39] | 0.81 | | |
| Overstretch (valve area/LVOT area, %) | 1.00 [0.99, 1.02] | 0.81 | | |
| Valve area ($mm^2$) | 1.00 [1.00, 1.00] | 0.82 | | |
| Severe liver disease/cirrhosis | 0.69 [0.02, 28.62] | 0.84 | | |
| History of percutaneous coronary intervention | 0.96 [0.50, 1.86] | 0.90 | | |
| Mean aortic valve gradient (mmHg) | 1.00 [0.98, 1.03] | 0.91 | | |
| Serum albumin (g/dl) | 1.03 [0.50, 2.11] | 0.94 | | |
| STS score | 1.00 [0.93, 1.08] | 0.95 | | |
| Age at time of consent | 1.00 [0.96, 1.04] | 0.99 | | |

**Table S6. Outcomes between 31 days and 1 year stratified by pacemaker dependency at 30 days.**

| | No Pacemaker (N=448) | New Pacemaker: Not Dependent at 30 days (N=113) | New Pacemaker: Dependent at 30 days (N=86) | *P* value No Pacemaker vs Not Dependent | *P* value No Pacemaker vs Dependent | *P* value Not Dependent vs Dependent |
|---|---|---|---|---|---|---|
| All-cause mortality | 39 (8.7) | 8 (7.1) | 3 (3.5) | 0.58 | 0.10 | 0.36 |
| Cardiovascular | 22 (4.9) | 6 (5.3) | 2 (2.3) | 0.86 | 0.40 | 0.47 |
| Non-cardiovascular | 17 (3.8) | 2 (1.8) | 1 (1.2) | 0.39 | 0.33 | >0.99 |
| Stroke | 10 (2.2) | 4 (3.5) | 1 (1.2) | 0.50 | >0.99 | 0.39 |
| Disabling | 8 (1.8) | 4 (3.5) | 0 (0) | 0.28 | 0.36 | 0.14 |
| Non-disabling | 3 (0.7) | 0 (0) | 1 (1.2) | >0.99 | 0.51 | 0.43 |
| All-cause mortality or disabling stroke | 43 (9.6) | 9 (8.0) | 3 (3.5) | 0.59 | 0.06 | 0.19 |
| Cardiac death or disabling stroke | 29 (6.5) | 7 (6.2) | 2 (2.3) | 0.91 | 0.20 | 0.30 |
| Major vascular complications | 1 (0.2) | 1 (0.9) | 0 (0) | 0.36 | >0.99 | >0.99 |
| Bleeding | 27 (6.0) | 1 (0.9) | 5 (5.8) | 0.03 | 0.94 | 0.09 |
| Life-threatening or Disabling | 15 (3.3) | 0 (0) | 2 (2.3) | 0.050 | >0.99 | 0.19 |
| Myocardial infarction | 12 (2.7) | 2 (1.8) | 3 (3.5) | 0.75 | 0.72 | 0.65 |
| Repeat TAVR | 0 (0) | 1 (0.9) | 0 (0) | 0.20 | Not evaluable | >0.99 |
| Rehospitalization | 36 (8.0) | 19 (16.8) | 5 (5.8) | 0.005 | 0.48 | 0.02 |
| TAV-in-TAV deployment | 0 (0) | 1 (0.9) | 0 (0) | 0.20 | Not evaluable | >0.99 |

Rehospitalization for valve-related symptoms or worsening congestive heart failure (NYHA class III or IV). Abbreviations: TAV=transcatheter aortic valve; TAVR= transcatheter aortic valve replacement

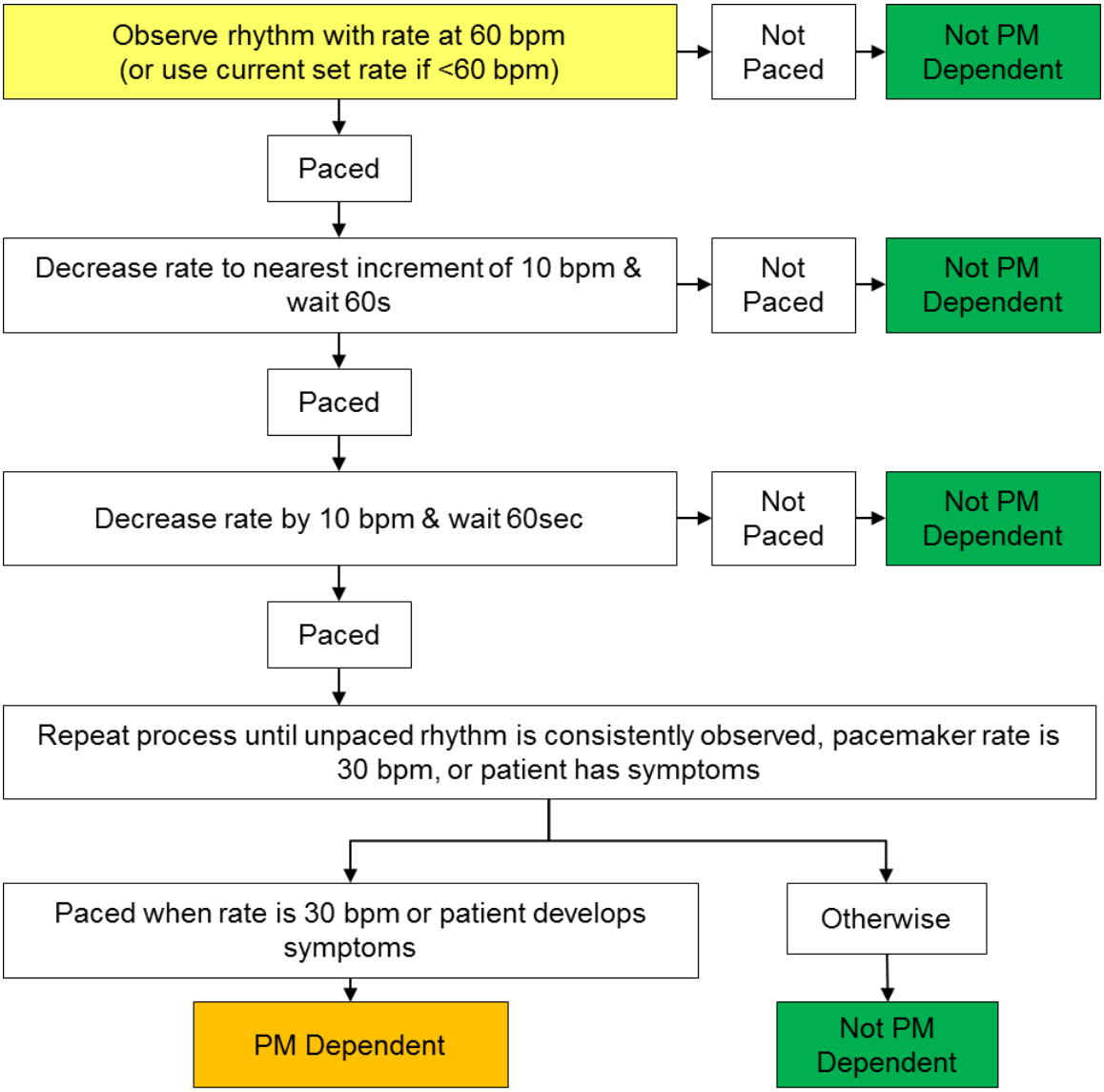
**Table S7. Multivariate predictors of pacemaker dependency at 30 days.**

| | UNIVARIATE MODEL | | MULTIVARIATE MODEL | |
|---|---|---|---|---|
| **Variable** | **Odds Ratio [95% CI]** | **P-value** | **Odds Ratio [95% CI]** | **P-value** |
| Baseline RBBB | 3.71 [1.96, 7.05] | <0.0001 | 4.87 [2.26, 10.48] | <0.0001 |
| Extreme surgical risk | 2.80 [1.35, 5.79] | 0.005 | | |
| History of CABG | 0.45 [0.23, 0.90] | 0.02 | 0.37 [0.13, 1.01] | 0.053 |
| Mean depth of implantation (mm) | 1.17 [1.02, 1.34] | 0.03 | 1.20 [1.03, 1.41] | 0.02 |
| New Interval Prolongation | 1.88 [1.07, 3.33] | 0.03 | | |
| BMI | 0.96 [0.93, 1.00] | 0.04 | | |
| Male | 0.56 [0.32, 0.98] | 0.04 | 0.49 [0.24, 1.02] | 0.057 |
| EuroSCORE II | 1.05 [1.00, 1.11] | 0.05 | 1.10 [1.03, 1.18] | 0.005 |
| Age at time of consent | 1.04 [1.00, 1.08] | 0.06 | | |
| LVOT (LCC) calcification grade >2 | 2.39 [0.78, 7.36] | 0.13 | | |
| History of peripheral vascular disease | 1.58 [0.85, 2.93] | 0.15 | | |
| History of percutaneous coronary intervention | 0.66 [0.36, 1.22] | 0.19 | | |
| History of hyperlipidemia requiring medication | 0.68 [0.34, 1.35] | 0.27 | | |
| History of myocardial infarction | 0.68 [0.33, 1.40] | 0.29 | | |
| Platelet count <150 ($10^9$/L) | 0.67 [0.31, 1.45] | 0.31 | | |
| EvolutR | 1.23 [0.81, 1.89] | 0.33 | | |
| STS Score | 1.04 [0.96, 1.13] | 0.36 | | |
| Currently taking immunosuppressive therapy | 0.65 [0.25, 1.67] | 0.37 | | |
| History of atrial fibrillation or flutter | 0.76 [0.41, 1.39] | 0.37 | | |
| History of congestive heart failure | 0.76 [0.39, 1.46] | 0.41 | | |
| Prior balloon aortic valvuloplasty | 1.52 [0.53, 4.36] | 0.44 | | |
| Baseline LBBB | 0.66 [0.22, 1.98] | 0.46 | | |
| History of coronary artery disease | 0.80 [0.43, 1.49] | 0.49 | | |
| LVOT (RCC) calcification grade >1 | 2.19 [0.21, 23.11] | 0.51 | | |
| Right Carotid Artery Stenosis (≥80%) | 4.31 [0.05, 397.70] | 0.53 | | |
| Severe liver disease/cirrhosis | 3.98 [0.04, 366.20] | 0.55 | | |
| LVOT Area ($mm^2$) | 1.00 [1.00, 1.00] | 0.55 | | |
| LVEF <40% | 0.69 [0.17, 2.81] | 0.61 | | |
| Lotus | 1.19 [0.59, 2.40] | 0.63 | | |
| Mean aortic valve gradient (mmHg) | 1.00 [0.98, 1.03] | 0.66 | | |
| History of hypertension | 1.31 [0.37, 4.58] | 0.68 | | |
| Valve Area ($mm^2$) | 1.00 [1.00, 1.00] | 0.70 | | |
| Moderate or greater COPD | 1.14 [0.58, 2.23] | 0.71 | | |
| Serum albumin (g/dL) | 0.89 [0.48, 1.65] | 0.72 | | |
| Annulus area ($mm^2$) | 1.00 [1.00, 1.01] | 0.73 | | |
| Left carotid artery stenosis (≥80%) | 0.45 [0.00, 43.86] | 0.73 | | |
| Overstretch (Valve area/LVOT area, %) | 1.00 [0.98, 1.01] | 0.74 | | |
| Overstretch (Valve area/ Annulus area, %) | 1.00 [0.98, 1.02] | 0.86 | | |
| History of transient ischemic attacks | 1.08 [0.41, 2.87] | 0.88 | | |
| History of cerebrovascular accidents | 1.03 [0.44, 2.41] | 0.94 | | |
| Medically-treated diabetes | 0.98 [0.54, 1.77] | 0.94 | | |
| Serum creatinine (mg/dL) | 0.99 [0.51, 1.93] | 0.97 | | |

**Table S8. Multivariate predictors of pacemaker dependency at 1 year.**

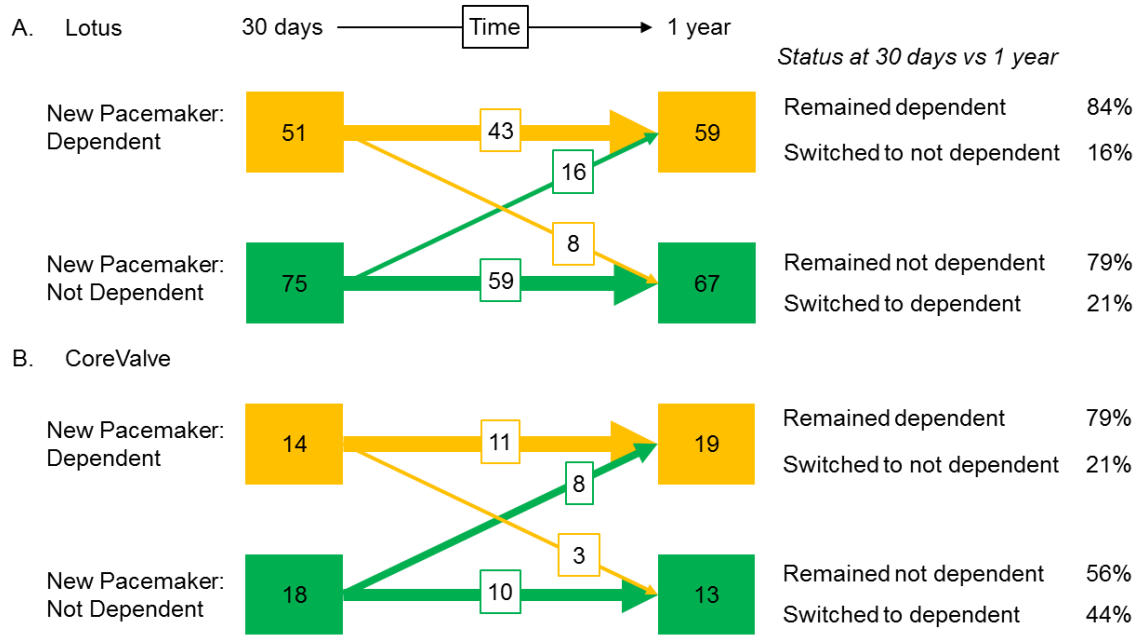
| | UNIVARIATE MODEL | | MULTIVARIATE MODEL | |
|---|---|---|---|---|
| **Variable** | **Odds Ratio [95% CI]** | **P-value** | **Odds Ratio [95% CI]** | **P-value** |
| Baseline RBBB | 3.15 [1.59, 6.22] | 0.001 | 3.46 [1.70, 7.06] | 0.0006 |
| Overstretch (Valve area/LVOT area, %) | 1.02 [1.00, 1.04] | 0.01 | 1.02 [1.01, 1.04] | 0.005 |
| Extreme Surgical Risk | 2.40 [1.10, 5.27] | 0.03 | 2.23 [0.98, 5.09] | 0.057 |
| Overstretch (Valve area/ Annulus area, %) | 1.02 [1.00, 1.04] | 0.04 | | |
| New interval prolongation | 1.78 [0.99, 3.21] | 0.06 | | |
| Age at time of consent | 1.04 [1.00, 1.08] | 0.08 | | |
| LVOT Area ($mm^2$) | 1.00 [0.99, 1.00] | 0.08 | | |
| Baseline LBBB | 0.40 [0.12, 1.30] | 0.13 | | |
| History of CABG | 0.63 [0.32, 1.25] | 0.19 | | |
| History of coronary artery disease | 0.65 [0.34, 1.25] | 0.20 | | |
| Mean depth of implantation (mm) | 1.10 [0.95, 1.29] | 0.20 | | |
| LVEF <40% | 0.37 [0.08, 1.80] | 0.22 | | |
| Male | 0.71 [0.39, 1.26] | 0.24 | | |
| History of hypertension | 2.25 [0.57, 8.78] | 0.25 | | |
| Valve Area ($mm^2$) | 1.00 [1.00, 1.01] | 0.25 | | |
| LVOT (RCC) calcification grade >1 | 0.14 [0.00, 4.28] | 0.26 | | |
| EvolutR | 0.77 [0.49, 1.22] | 0.27 | | |
| History of myocardial infarction | 0.68 [0.33, 1.43] | 0.31 | | |
| Serum creatinine (mg/dL) | 0.70 [0.35, 1.40] | 0.32 | | |
| Annulus area ($mm^2$) | 1.00 [0.99, 1.00] | 0.33 | | |
| Currently taking immunosuppressive therapy | 0.63 [0.23, 1.70] | 0.36 | | |
| History of cerebrovascular accidents | 1.48 [0.60, 3.64] | 0.40 | | |
| History of congestive heart failure | 1.28 [0.65, 2.50] | 0.47 | | |
| Serum albumin (g/dL) | 1.27 [0.65, 2.49] | 0.48 | | |
| History of transient ischemic attacks | 0.70 [0.25, 1.92] | 0.48 | | |
| History of percutaneous coronary intervention | 0.82 [0.44, 1.53] | 0.53 | | |
| EuroSCORE II | 1.02 [0.96, 1.07] | 0.54 | | |
| Prior balloon aortic valvuloplasty | 1.41 [0.43, 4.62] | 0.57 | | |
| History of hyperlipidemia requiring medication | 1.21 [0.60, 2.46] | 0.60 | | |
| LVOT (LCC) calcification grade >2 | 1.34 [0.45, 4.02] | 0.60 | | |
| Moderate or greater COPD | 1.14 [0.56, 2.33] | 0.72 | | |
| Mean aortic valve gradient (mmHg) | 1.00 [0.98, 1.03] | 0.80 | | |
| Platelet count <150 ($10^9$/L) | 1.07 [0.51, 2.29] | 0.85 | | |
| History of atrial fibrillation or flutter | 1.05 [0.57, 1.94] | 0.88 | | |
| Medically-treated diabetes | 1.05 [0.57, 1.93] | 0.88 | | |
| Left carotid artery stenosis (≥80%) | 1.17 [0.07, 19.13] | 0.91 | | |
| Right carotid artery stenosis (≥80%) | 1.15 [0.07, 18.83] | 0.92 | | |
| BMI | 1.00 [0.96, 1.04] | 0.94 | | |
| STS Score | 1.00 [0.92, 1.09] | 0.95 | | |
| History of peripheral vascular disease | 1.00 [0.53, 1.88] | 1.00 | | |
| Severe liver disease/cirrhosis | 1.00 [0.06, 16.23] | 1.00 | | |

**Figure S1. Pre-specified pacemaker dependency algorithm.**




At 30 days and 1 year, patients with new permanent pacemaker after TAVR had pacemaker dependence and % of paced beats evaluated by pacemaker interrogation using this algorithm.

**Figure S2. Pacemaker dependency at 30 days and 1 year.**




Pacemaker dependency at 30 days and 1 year in Lotus (A) and CoreValve (B) patients with data at both timepoints. Number of patients shown in each box and line thickness indicates number of patients. Pacemaker dependent patients are shown in orange and patients who are not pacemaker dependent are shown in green.

**Figure S3. Quality of life outcomes in patients with a new pacemaker.**