One-year pacing dependency after pacemaker implantation in patients undergoing transcatheter aortic valve implantation: Systematic review and meta-analysis

Justine M. Ravaux, MD,[a] Michele Di Mauro, MD, PhD, MSc Biostat,[a] Kevin Vernooy, MD, PhD,[b,c,d] Arnoud W. Van't Hof, MD, PhD,[b,c] Leo Veenstra, MD,[b] Suzanne Kats, MD, PhD,[a] Jos G. Maessen, MD, PhD,[a,c] and Roberto Lorusso, MD, PhD[a,c]

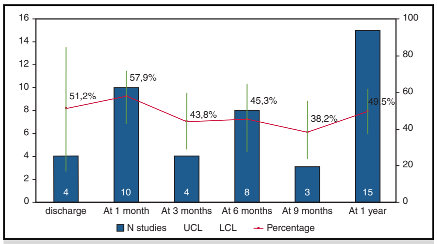
ABSTRACT

Objectives: Atrioventricular conductions disturbances, requiring permanent pacemaker implantation (PPI), represent a potential complication after transcatheter aortic valve implantation (TAVI), However, little is known about the pacemaker dependency after PPI in this patient setting. This systematic review analyses the incidence of PPI, the short-term (1-year) pacing dependency, and predictors for such a state after TAVI.

Methods: We performed a systematic search in PUBMED, EMBASE, and MEDLINE to identify potentially relevant literature investigating PPI requirement and dependency after TAVI. Study data, patients, and procedural characteristics were extracted. Odds ratio (OR) with 95% confidence intervals were extracted.

Results: Data from 23 studies were obtained that included 18,610 patients. The crude incidence of PPI after TAVI was 17% (range, 8.8%-32%). PPI occurred at a median time of 3.2 days (range, 0-30 days). Pacing dependency at 1-year was 47.5% (range, 7%-89%). Self-expandable prosthesis (pooled OR was 2.14 [1.15-3.96]) and baseline right bundle branch block (pooled OR was 2.01 [1.06-3.83]) showed 2-fold greater risk to maintain PPI dependency at 1 year after TAVI.

Conclusions: Although PPI represents a rather frequent event after TAVI, conduction disorders have a temporary nature in almost 50% of the cases with recovery and stabilization after discharge. Preoperative conduction abnormality and type of TAVI are associated with higher PPI dependency at short term. (JTCVS Open 2021;6:41-55)



Rate of pacemaker dependency across the time after TAVI.

CENTRAL MESSAGE

Up to 50% of the patients with permanent pacemaker implantation following TAVI exhibit no pacemaker dependency at 1-year follow-up.

PERSPECTIVE

Better understanding of pacemaker dependency after TAVI should allow better oriented guidelines with respect to indications and timing of pacemaker implantation, as well as postpermanent pacemaker implantation management, based on the high recovery rate of effective native atrio/ventricular conduction.

See Commentaries on pages 56 and 58.

Supplemental material is available online.

From the [a]Department of Cardio-Thoracic Surgery, Heart and Vascular Centre, [b]Department of Cardiology, and [c]Cardiovascular Research Institute Maastricht (CARIM), Maastricht University Medical Centre (MUMC+), Maastricht; and [d]Department of Cardiology, Radboud University Medical Center (Radboudumc), Nijmegen, The Netherlands.

Received for publication Feb 1, 2021; accepted for publication Feb 9, 2021; available ahead of print March 9, 2021.

Address for reprints: Justine M. Ravaux, MD, Department of Cardio-Thoracic Surgery, Heart & Vascular Centre, Maastricht University Medical Centre (MUMC+), Cardiovascular Research Institute Maastricht (CARIM), Maastricht University, P. Debyelaan, 25, 6202 AZ Maastricht, The Netherlands (E-mail: justine.ravaux@mumcl.nl or jmravaux@hotmail.com).

2666-2736

https://doi.org/10.1016/j.xjon.2021.02.002

Transcatheter aortic valve implantation (TAVI) was first introduced in 2002[1] as a less-invasive therapeutic option in patients with severe symptomatic aortic stenosis unfit for cardiac surgery.[2] Nowadays, there is a trend to extend these procedures even to intermediate- and low-risk patients, making the frequency of TAVI procedures grow exponentially.[3] However, complications, such as atrioventricular conduction disturbances requiring permanent pacemaker implantation (PPI), may diminish the benefit of these procedures: the incidence of PPI after TAVI, for instance, represents a rather frequent event after TAVI.[4] Indeed, an

Abbreviations and Acronyms

AF = atrial fibrillation
BE = balloon-expandable
CI = confidence interval
OR = odds ratio
PPI = permanent pacemaker implantation
RBBB = right bundle branch block
SE = self-expandable
STS = Society of Thoracic Surgeons
TAVI = transcatheter aortic valve implantation

association between PPI and all-cause deaths and heart failure rehospitalizations at 1 year from TAVI has been recently shown.[5] However, a certain percentage of atrioventricular conduction abnormalities after TAVI may resolve following PPI, even after a few days from implant.[6] Presently, the current literature available on pacing dependency after TAVI is limited and based on studies with small patient samples (evidence level B).[7,8] Therefore, we performed this systematic review to determine the incidence of PPI, the pacing dependency, and potential predictors for pacing-dependency at 1 year after TAVI procedures.

METHODS

Research Strategy

A broad, computerized literature search was performed to identify all relevant studies from PubMed, Embase, and MEDLINE databases. The PubMed database was searched entering the following key words: "Pacemaker, Artificial"[Mesh] OR pacemaker implantation AND "Transcatheter Aortic Valve Replacement"[Mesh] OR transcatheter aortic valve implantation. We restricted the research to English-language publications. Last access to the database was on April 25, 2020. The search was limited to studies in human recipients. A framework of the systematic review process is plotted in Figure 1, in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Because this study was a systematic review and meta-analysis based on published articles, ethical approval was waived by the institutional review board of the University Hospital of Maastricht.

Eligibility Criteria and Study Selection

Studies were included in the final analyses if patients were (1) >18 years; (2) >250 patients were included in the main analysis, to provide data interpretation of the most consistent clinical series; and (3) studies provided a definition of cardiac pacemaker dependency. Other studies following the same criteria, but having a smaller patient sample size (<250 patients), were included in a separated analysis (secondary analysis) and are provided in Appendix E1. Multiple publications from a single center were managed to include the last publication. If the same authors published more studies with the same series, the largest patient cohort was included. Studies were excluded if 1 of the following criteria was present: (1) presence of congenital pathology; (2) patients undergoing noncardiac surgery procedures or transcatheter procedure or heart transplantation; (3) no information provided about PPI; (4), publication before year 2002; or (5) outcomes not clearly reported or impossible to extract or calculate from the available results. Review, clinical update, and case reports were not taken into account. All potentially relevant studies were reviewed in detail to check their adhesion to the inclusion criteria. Title and abstracts of all retrieved paper were independently reviewed by 2 researchers (J.R. and M.D.M.) to identify studies fulfilling the inclusion criteria. Controversial findings were solved by the intervention of a third reviewer (R.L.). The quality of included studies was assessed using the Newcastle–Ottawa Scale for observational studies by 2 investigators independently (J.R. and M.D.M.).

Data Extraction

Microsoft Office Excel 2016 (Microsoft, Redmond, Wash) was used for data extraction that was performed independently by 2 researchers (K.V., L.V.). Year of publication, study design, sample size, age, Society of Thoracic Surgeons (STS) score, inclusion period, left ventricular ejection fraction, peripheral vascular disease, diabetes mellitus, valve type, follow-up, approach for TAVI, indications for PPI, timing of PPI (days), PPI rate, dependency definition, dependency follow-up (months), multivariable predictors of PPI, and PPI-related complications were extracted.

Statistical Analysis

The primary end point was 1-year pacing dependency, defined in different ways. Calculation of proportions of PM dependency at different time points was obtained using a meta-analytic approach by means of *metaprop* function of *meta package* in R (Foundation for Statistical Computing, Vienna, Austria). Odds ratio (OR) with 95% confidence intervals (CIs) were extracted. We calculated the I^2 statistics (0% ~ 100%) to explain the between-study heterogeneity, with $I^2 \leq 25\%$ suggesting more homogeneity, $25\% < I^2 \leq 75\%$ suggesting moderate heterogeneity, and $I^2 > 75\%$ suggesting high heterogeneity. If the null hypothesis was rejected, a random effects model was used to calculate pooled effect estimates. If the null hypothesis was not rejected, a fixed-effects model was used to calculate pooled effect estimates; 95% CI was also reported. Forest plots were used to plot the effect size, either for each study or overall.

Publication bias was evaluated by graphical inspection of funnel plot; estimation of publication bias was performed with trim-and-fill method and quantified by means of Egger's linear regression test. On-leave out study analysis was performed as sensitivity analysis in case of moderate or high heterogeneity. Meta-regression was performed to test the influence of age, time of pacemaker implantation, and sample size. The software used for the analyses was R-studio (meta package), version 1.1.463 (2009-2018).

RESULTS

Study Selection

A total of 877 records were initially screened at the title and abstract level, with 801 papers fully reviewed for eligibility. There were no duplicate data. Ultimately, 23 studies were identified and provided data for the research analysis.[9-31] An additional 30 studies are considered in Appendix E1 because of their limited sample size (<250 patients). The flowsheet for selection of included studies is represented in Figure 1. The Newcastle-Ottawa Scale confirmed a high-quality level for all studies included in the main analysis (Table E1).

Study, Participants, and Procedural Characteristics

Baseline characteristics of selected studies are represented in Table 1. Studies were published between 2014 and 2019, and patient recruitment occurred between January 2005 and February 2018; 26% of them (n = 6) were prospective,[9,16,18,27,29,31] and the remaining studies

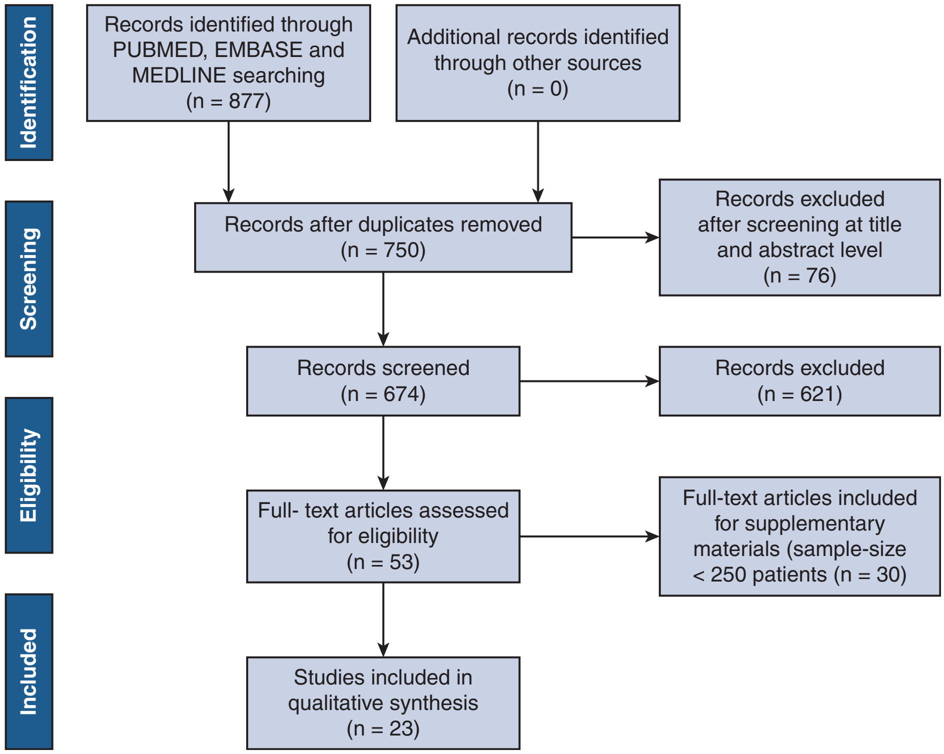


FIGURE 1. Study selection. Flow diagram of included studies based on the Preferred Reported Items for Systematic Reviews and Meta-Analysis (PRISMA).

were all retrospective observational. Mean duration of follow-up was 16 months.

In total, 18,610 patients were included in 23 studies from 79 centers. The crude incidence of PPI after TAVI procedure was 17%, ranging from 8.8%[11] to 32%.[14] Preprocedural risk was assessed by the STS score in the majority of the studies (11/23) and the mean STS score was 7.1 (0.74-34). Mean age was 81.8 years (range, 43-102 years). The implanted device was a self-expandable (SE) valve in 38% of patients, a mechanically expandable valve in 13.5%, and a balloon-expandable (BE) in 46% of the patient population. Others devices were used in 2.5% of the patients. Three studies used only BE valves,[11,21,28] and 3 studies implanted solely SE valve.[9,24,26] The transfemoral access route was preferred (88.2%) over the other approaches (transapical 2.3%; transsubclavian 0.9%, and other approach used in 8.7%). The mortality at 30 days was 9.6%. The baseline characteristics of the studies including <250 patients are provided in Table E2.

PPI Details

The PPI details in studies including >250 patients are reported in Table 2. Data regarding PPI details in studies including <250 patients are described in Table E3. All studies provided indications for PPI, except in 4 series.[20,24,25,30] The main indications for PPI were divided into 3 main categories of atrioventricular conduction disorders: atrioventricular block (second and third degree) in 82.7% of the patients, sick sinus syndrome in 2.7%, severe bradycardia in 2.8%, and others indications in 11.8% of the patients, respectively. The timing of PPI varied remarkably among studies, occurring at a median time of 3.2 days (range, 0-30 days) from TAVI procedure. Nine studies didn't provide information about the timing of PPI.[9,18-21,24,25,27,29] The overall incidence of PPI reached 17% of the TAVI patients, ranging from 8.8% to 32% of the cases.

Pacemaker Dependency

There was a large heterogeneity in the assessment and definition of the pacemaker dependency at follow-up. Indeed, 43% of the studies (10/23)[10-12,14,16,18-20,25,28] reported a right ventricular pacing rhythm as indicator of the pacemaker dependency at follow-up, whereas the remaining studies provided a wide range of pacemaker dependency definitions and evaluation.

Of the selected 23 articles, the majority (15 studies[10-15,19,20,24-28,30,31]) reported the 1-year pacemaker dependency (Figure 2). The pacemaker dependency rate varied across time (Figure 3); it was 51.2% (16.7%-84.6%, n = 4) already at discharge, 57.9% (43.1%-71.3%, n = 10) at 1 month, 45.3%% (27.5%-64.5%, n = 8) at 6 months, and 49.5% (37.1%-61.9%, n = 15) at 1 year.

TABLE 1. Baseline characteristics of studies including >250 patients (n = 23)

Study	Year	Study design (no. centers)	Sample size	Age, y	STS score, %	Inclusion period	Left ventricle ejection fraction, %	Peripheral vascular disease, %	Diabetes mellitus, %	Valve type	Follow-up, mo*	Approach for TAVI	Mortality at 30 d
Bjerre Thygesen et al[9]	2014	Prospective (1)	258	na	na	na	na	na	na	100% SE	na	na	na
Urena et al[10]	2014	Retrospective (8)	1556	80.5	7.5	January 2005 to February 2013	55.5	na	31.1	55.1% BE 44.9% SE	22	na	7%
Nazif et al[11]	2015	Retrospective (21)	1973	84.5	11.4	May 2007 to September 2011	53.7	42.4	36	100% BE	12	na	6.6%
Van Gils et al[12]	2017	Retrospective (4)	306	83	6.3	May 2008 to February 2016	na	22	30	38.2% SE 34.7% SE 27.1% ME	12	na	7%
Raelson et al[13]	2017	Retrospective (1)	578	85.5	na	March 2009 to December 2014	na	na	na	21% SE 79% BE	1	na	na
Dumonteil et al[14]	2017	Retrospective (14)	250	84	6.3	October 2012 to May 2014	58.3	na	22.5	100% ME	12	100% Transfemoral	4%
Kaplan et al[15]	2019	Retrospective (1)	594	81.6	na	January 2011 to December 2017	na	na	na	na	12	na	na
Chamandi et al[16]	2018	Prospective (9)	1692	81.5	10.9	May 2009 to February 2015	na	na	33.1	50.3% BE 49.7% SE	48	na	42.3%
Gaede et al[17]	2018	Retrospective (1)	1025	81.9	na	2010-2015	na	21.1	33.3	na	2.4	na	na
Gonska et al[18]	2018	Prospective (1)	612	80.4	6.5	February 2014 to September 2016	57.5	na	29.9	58.8% BE 36.7% ME 4.4% SE	12	na	1.3%
Marzahn et al[19]	2018	Retrospective (1)	856	80.5	na	July 2008 to May 2015	57.5	na	38	37.4% SE 57.8% BE 4.8% ME	12	100% Transfemoral	na
Nadeem et al[20]	2018	Retrospective (1)	672	81.4	7.4	2011-2017	53.8	21.5	41	na	12	na	na
Campelo-Parada et al[21]	2018	Retrospective (2)	347	na	na	May 2010 to December 2015	54.6	na	37.3	100% BE	1	77.8% Transfemoral	na
Mirolo et al[22]	2018	Retrospective (1)	936	na	na	October 2009 to January 2017	na	na	na	95% BE 5% SE	2.3	na	na
Van Gils et al[23]	2018	Retrospective (1)	291	79	na	January 2012 to December 2015	na	na	34	42% SE 51.5% BE 6.5% ME	12	94% transfemoral 6% transsubclavian	5%
Takahashi et al[24]	2018	Retrospective (4)	1621	84.3	na	January 2010 to December 2014	na	na	na	72.5% SE	13	na	na
Chan et al[25]	2018	Retrospective (2)	913	81.6	na	January 2012 to December 2017	na	na	na	na	12	na	na
Ghannam et al[26]	2019	Retrospective (1)	573	79.8	6.4	January 2012 to September 2017	57.2	45.8	37.8	100% SE	17.1	na	na
Costa et al[27]	2019	Prospective (1)	1116	82	4.4	June 2007 to February 2018	53.3	na	28.9	61.8% SE 27.2% BE 0.5% ME 10.5% Others	72	97% transfemoral 3% others	3.9%

(Continued)

TABLE 1. Continued

Study	Year	Study design (no. centers)	Sample size	Age, y	STS score, %	Inclusion period	Left ventricle ejection fraction, %	Peripheral vascular disease, %	Diabetes mellitus, %	Valve type	Follow-up, mo*	Approach for TAVI	Mortality at 30 d
Dolci et al[28]	2019	Retrospective (1)	266	80	na	February 2014 to February 2018	53	22	28	100% BE	12	84% transfemoral 16% transapical	na
Tovia-Brodie et al[29]	2019	Prospective (1)	795	82.5	na	April 2012 to December 2016	na	na	na	na	28.2	na	na
Junquera et al[30]	2019	Retrospective (2)	676	82	5	May 2007 to March 2017	57.4	na	31.2	60.5% BE 35.2% SE 0.7% ME 0.3% others	12	64.8% transfemoral	na
Meduri et al[31]	2019	Prospective (1)	704	82.5	6.6	na	na	28.2	30.9	34% SE 66% ME	12	na	na
Total	na	79	18,610	81.8 (43-102)	7.1 (0.74-34)	January 2005 to February 2018	55.6	29	32.6	SE 38% BE 46% ME 13.5% others 2.5%	16	88.2% transfemoral 2.3% transapical 0.9% transsubclavian Others 8.7%	9.6%

Values are n (%). *STS score*, Society of Thoracic Surgeons Risk Score; *TAVI*, transaortic valve implantation; *na*, not available; *SE*, self-expandable; *BE*, balloon-expandable; *ME*, mechanically expandable. *Follow-up is reported as mean or median as given by the authors.

Influence of Baseline Right Bundle Branch Block (RBBB) and Atrial Fibrillation (AF) on 1-Year Pacemaker Dependency

In 6 studies,[13,15,20,25,27,31] among 531 patients undergoing pacemaker interrogation at 1 year, pacemaker dependency was present from 22% to 54% of the patients, and the difference between patients with and without baseline RBBB could be analyzed. The pooled OR was 1.76 (95% CI, 1.06-2.93). There was low heterogeneity ($I^2 = 14\%$) among the studies (Figure 4), nor was there publication bias (Figure E1). The Egger's test was not significant ($P = .90$). Leave-one-out study analysis (Table E4), as shown in the paper by Chan and colleagues[25] influenced the pooled analysis, since leaving it in, the pooled estimates was not significant anymore. The association between preimplant RBBB and 1-year pacemaker dependency was not influenced by age ($r = 0.0917$, $P = .6050$), time of PPI ($r = 0.0918$, $P = .9222$), or sample size ($r = 0.0920$, $P = .9245$).

The impact of baseline AF could be investigated in 4 studies[13,15,20,25] and revealed no effect on 1-year pacemaker dependency (pooled OR, 1.71; 95% CI, 0.83-3.53) (Figure 5). Again, there was neither heterogeneity among the studies nor publication bias (Figure E2) The Egger's test was not significant ($P = .79$). On-leave out study analysis (Table E4) confirmed as AF had no impact on pooled analysis.

Type of Implanted Prosthesis on 1-Year Pacemaker Dependency

The comparison between SE and BE protheses in terms of 1-year pacemaker dependency could be evaluated in 6studies (796 patients).[10,12,13,15,20,24] Patients who received SE prostheses had 2-fold greater risk for pacemaker dependency 1 year after TAVI (Figure 6). moderate heterogeneity was found ($I^2 = 43\%$). No publication bias was identified (Figure E3). The Egger's test was not significant ($P = .5658$). Leave-one-out study analysis (Table E4) showed as the paper by Urena and colleagues[10] influenced the pooled analysis, since leaving it, the pooled estimates was not significant anymore. The association between preimplant SE and 1-year pacemaker dependency was not influenced by age ($r = 0.1265$, $P = .5012$), time of PPI ($r = –1.1506$, $P = .0.6262$), or sample size ($r = 0.1123$, $P = .9812$). The pacemaker dependency rate was significantly greater in those studies including more than 50% of SE prostheses (Figure E4).

Third-Degree Atrioventricular Block and 1-Year Pacemaker Dependency

One-year pacemaker dependency rate was not significantly different between study where pacemaker was implanted due to third-degree atrioventricular block in a rate ranging from70%-79% (41.4%; 26.1%-58.5%),

TABLE 2. Pacemaker-related details in studies including >250 patients (n = 23)

Study	Indications for PPI	Timing of PPI, d*	PPI rate	Dependency definition	Dependency rate	Dependency follow-up, mo*	Multivariable predictors of PPI	Association	PPI-related complications
Bjerre Thygesen et al[9]	100% AVB	na	27.4%	Resolution of conduction abnormalities	50%	na	na	na	na
Urena et al[10]	75.3% AVB 7.1% SSS 7.9% bradycardia 9.6% others	3	15.4%	"paced rhythm" reported	66.9%	12	na	• PPI protective factor for the occurrence of unexpected (sudden or unknown) death • Negative effect on left ventricular function over time	na
Nazif et al[11]	79% AVB 17.3% SSS	3	8.8%	"ventricular pacing" reported	50.5%	12	• Pre-existing RBBB • Prosthesis to left ventricle outflow tract diameter ratio • Left ventricle -end diastolic diameter	• Longer duration of hospitalization • Greater rates of repeat hospitalization and mortality or repeat hospitalization at 1 y	na
Van Gils et al[12]	99% AVB 1% SSS	2	41%	% ventricular pacing rhythm reported	89%	12	• LOTUS valve • Greater BMI before TAVI	• RBBB at baseline associated with greater PPI	na
Raelson et al[13]	82% AVB	3	9%	No intrinsic ventricular activity during pacing at 30 bpm	39%	1	na	na	na
Dumonteil et al[14]	88.9% AVB 5.9% others	3	32%	"paced rhythm" reported	55.4%	12	• Baseline RBBB • Left ventricle outflow tract overstretch >10%	• Trend lower PPI rate at 30 d with shallower (≤5 mm) implant depth	na

(Continued)

TABLE 2. Continued

Study	Indications for PPI	Timing of PPI, d*	PPI rate	Dependency definition	Dependency rate	Dependency follow-up, mo*	Multivariable predictors of PPI	Association	PPI-related complications
Kaplan et al[15]	79% AVB 21% others	2,5	13.1%	High-grade AVB with a ventricular escape rate of less than 40 beats/min on device interrogation	21.9%	12	na	• Use of SE valves and postballoon dilatation associated with markedly increased risk of PPM dependency	na
Chamandi et al[16]	76.7% AVB 5.6% SSS 3.1% Bradycardia 14.6% others	2	19.8%	100% right ventricular pacing	27.4%	48	na	• PPI greater rates of rehospitalization due to heart failure and combined end point of mortality or heart failure rehospitalization • PPI lesser improvement in left ventricle ejection fraction over time, particularly if reduced before TAVI	na
Gaede et al[17]	90% AVB 8% SSS 2% Bradycardia	4	14.7%	Ventricular pacing >95%	29.5%	2.4	• Pre-existing RBBB • CoreValve prosthesis	Predictors of lack of recovery of AVB • Previous RBBB • Greater mean aortic valve gradient • Postdilatation of the prosthesis	na
Gonska et al[18]	85.% AVB 10.1% Bradycardia 4.8% others	na	24.4%	"ventricular pacing" reported	30.9%	1	na	• PPI without significant impact on survival or combined end point of major adverse events within 1 y	1.8% reoperation due to lead dislocation 2.4% hematomas/ bleeding at the site of the pacemaker

(Continued)

TABLE 2. Continued

Study	Indications for PPI	Timing of PPI, d*	PPI rate	Dependency definition	Dependency rate	Dependency follow-up, mo*	Multivariable predictors of PPI	Association	PPI-related complications
Marzahn et al[19]	89% AVB 5.5% Bradycardia 4.1% SSS 1.4% others	na	16.9%	"right ventricular pacing %" reported	55%	12	na	na	na
Nadeem et al[20]	na	na	21.7%	"right ventricular pacing %" reported	45.5%	12	na	• PPI more likely to have heart failure admissions • PPI trend toward increased mortality	na
Campelo-Parada et al[21]	84.3% AVB 9.3% Bradycardia Others 6.2%	na	9.2%	Ventricular pacing >1% at 1 mo = AVB resolution	67.2%	1	na	• BAV associated with increased risk of conduction abnormalities persistence	na
Mirolo et al[22]	68.8% AVB 30% others	2,5	9.3%	Ventricular pacing $\geq$ 1% = significant	75%	2.9	na	na	1.25% endocarditis lead leading to pacemaker explanation 2.5% partial left pneumothorax secondary to subclavian vein puncture 1.25% ventricular lead deplacement
Van Gils et al[23]	96% AVB 5% SSS	5	9.3%	Less than 20% ventricular pacing over 6 mo' follow-up	25%	6	na	na	na

(Continued)

TABLE 2. Continued

Study	Indications for PPI	Timing of PPI, d*	PPI rate	Dependency definition	Dependency rate	Dependency follow-up, mo*	Multivariable predictors of PPI	Association	PPI-related complications
Takahashi et al[24]	na	na	16.4%	Absence, inadequate intrinsic ventricular rhythm, or ventricular pacing >95% in pacemaker interrogation during follow-up (PPM on VVI 30/min)	52.8%	13	na	• DDD mode and SE valves use associated with pacemaker dependency	na
Chan et al[25]	na	na	13.1%	Ventricular pacing reported	59%	12	na	na	1.6% atrial lead dislodgement 6% ventricular lead dislodgement
Ghannam et al[26]	100% AVB	2,4	14%	No recovery of AV nodal conduction if CHB, high-grade AVB, or native ventricular rate <50 beats/min in absence of normal AV conduction	50%	12	na	• Larger aortic annulus less likely to recover conduction	1.2% (1 patient with right ventricular lead fracture)
Costa et al[27]	84.8% AVB 4.1%SSS 11% Others	na	13%	Absence of an escape or intrinsic rhythm for 30 s during temporary back-up pacing at a rate of 30 bpm	33.3%	12	na	• PPI associated with increased 6 y mortality • Baseline RBBB greater chance of being dependent at follow-up	na

(Continued)

TABLE 2. Continued

Study	Indications for PPI	Timing of PPI, d*	PPI rate	Dependency definition	Dependency rate	Dependency follow-up, mo*	Multivariable predictors of PPI	Association	PPI-related complications
Dolci et al[28]	80%AVB 11% Bradycardia 9% others	4	13%	"paced rhythm" reported	7%	12	• Baseline RBBB • QRS width immediately after TAVI	na	na
Tovia-Brodie et al[29]	92% AVB 8% others	na	8.8%	No need for ventricular pacing defined as <1% ventricular pacing and intrinsic 1:1 AV conduction with the device programmed to VVI 30 beats per minute	39%	28,2	• Baseline long PR interval • Use of newer generation valves	na	3.7% tamponade
Junquera et al[30]	na	6	12.7%	AVB/CHB recovery = ventricular pacing rate <1%	33.4%	12	na	na	na
Meduri et al[31]	90% AVB 6% Bradycardia 4% others	2	28.4%	Patients who were symptomatic or did not have a native rhythm + capture of the percentage of paced ventricular beats	50%	12	• Baseline RBBB • Mean depth of valve implantation	• Medically treated diabetes mellitus in LOTUS valve patients	na
Total	82.7% AVB 2.7% SSS 2.8% bradycardia 11.8% Others	3.2	17%	na	na	11.8	na	na	na

Values are n (%). *PPI*, Pacemaker implantation; *AVB*, atrioventricular block, *na*, not available; *SSS*, sick sinus syndrome; *RBBB*, right bundle branch block; *BMI*, body mass index; *TAVI*, transcatheter aortic valve implantation; *SE*, self-expandable; *BAV*, bicuspid aortic valve; *PPM*, permanent pacemaker; *VVI*, single-chamber device; *DDD*, dual-chamber device; *AV*, atrioventricular; *CHB*, complete heart block. *Follow-up is reported as mean or median as given by the authors.

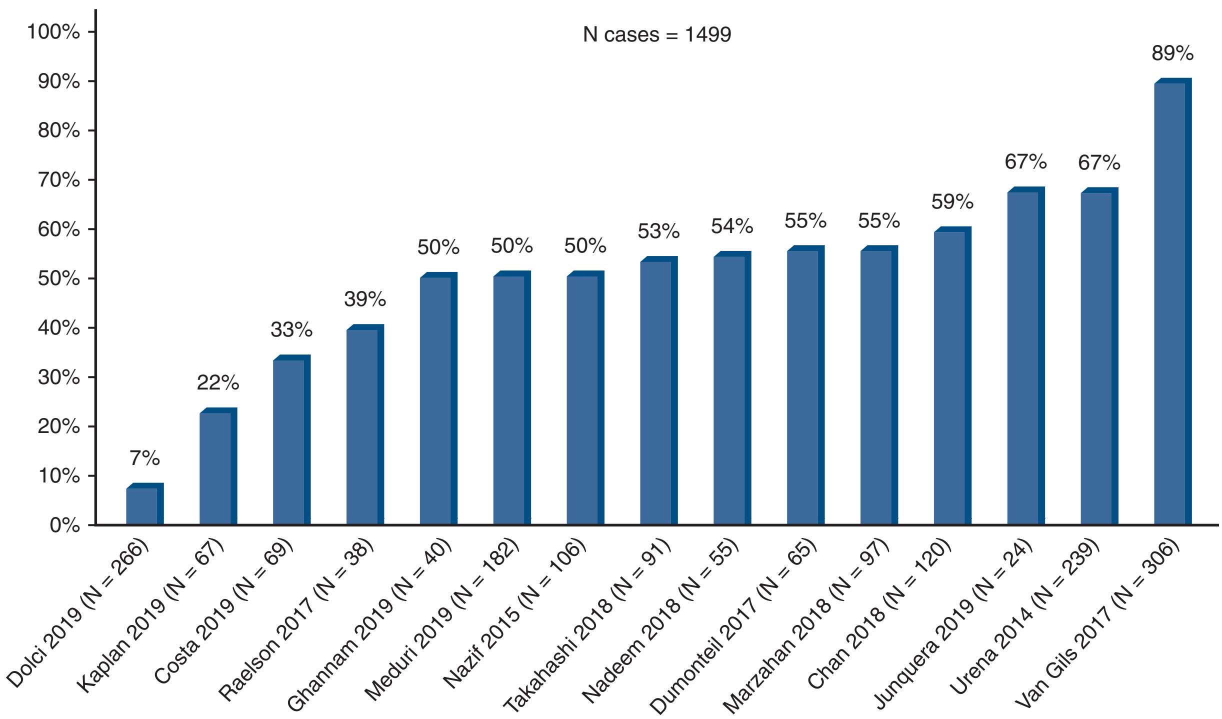


FIGURE 2. Pacemaker dependency at 1 year. *Bars* represent 1-year pacemaker dependency. The rate of pacemaker dependency ranged from 7% to 89% in individual studies.

80%-99% (48.3%; 21.3%-76.5%), and 100% (53.8%, 45.6%-61.7%), $P = .427$.

Complications and Multivariable Predictors of PPI

Only 5 studies[18,22,25,26,29] reported the PPI-related complications. The rate of PPI-related complications ranged from 1.2%[26] to 6%.[25] The list of various complications is reported in Table 2. Information about predictors of PPI were provided by 7 studies (5319 patients). Pre-existing RBBB was the most frequent determinant factor of PPI. Regarding pacemaker dependency after TAVI at follow-up, multivariable analysis to investigate the predictors was performed in 5 studies: early PPI after TAVI,[17] PPI on day 1,[27] and larger aortic annular size,[26] were found as independent predictor of persistent atrioventricular conduction disturbances. In contrast, 2 studies failed to

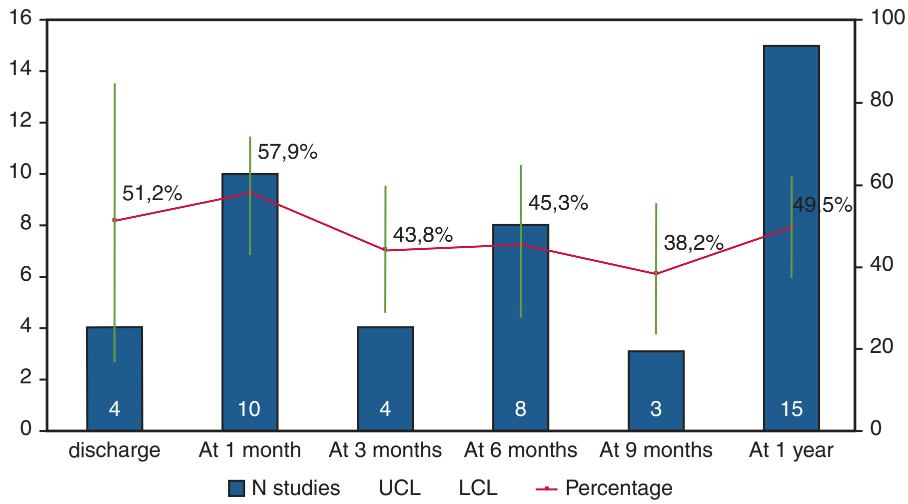


FIGURE 3. Rate of pacemaker dependency across the time after TAVI. Pooled percentage is reported with 95% confidence limits (*blue line*). *Light blue bars* represent number of studies. *Yellow line* is the interpolation line. *UCL*, Upper confidence limit; *LCL*, lower confidence limit.

Study	TE	SE	Weight	Odds Ratio IV, Random, 95% CI
Ghannam 2019	–0.190	0.6200	15.0%	0.827 [0.245; 2.788]
Kaplan 2019	–0.170	0.6700	13.1%	0.844 [0.227; 3.137]
Nadeem 2018	0.270	0.5400	18.9%	1.310 [0.455; 3.775]
Meduri 2019	1.240	0.9800	6.6%	3.456 [0.506; 23.589]
Chan 2018	1.550	0.5500	18.3%	4.711 [1.603; 13.846]
Costa 2019	0.890	0.6100	15.4%	2.435 [0.737; 8.049]
Raelson 2017	0.490	0.6800	12.8%	1.632 [0.431; 6.189]
Total (95% CI)			**100.0%**	**1.760 [1.058; 2.927]**

Heterogeneity: $Tau^2 = 0.0653$; $Chi^2 = 6.96$, df = 6 (P = .32); $I^2 = 14\%$

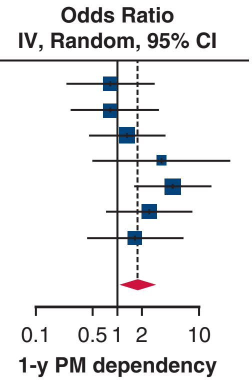


FIGURE 4. Impact of baseline RBBB on 1-year rate of pacemaker dependency Forest plot. Patients with baseline RBBB have 2-fold greater risk to develop pacemaker dependency 1 year after TAVI. *TE*, Log odds ratio; *SE*, standard error; *IV*, weighted mean difference; *CI*, confidence limits; *PM*, pacemaker.

demonstrate significant predictors for atrioventricular conduction recovery or pacemaker dependency.[13,22]

DISCUSSION

The main findings of this systematic review regarding PPI and subsequent recovery of atrioventricular conduction or persistent pacemaker dependency in TAVI are as follows (Figure 7): (1) up to 50% of the patients with PPI after TAVI exhibit no pacemaker dependency at 1 year follow-up; (2) patients with baseline RBBB and (3) SE prosthesis have 2-fold greater risk to develop pacemaker dependency 1 year after TAVI; and (4) baseline AF does not influence the risk of pacemaker dependency at 1 year.

Several recent reports show that atrioventricular conduction defects requiring PPI post-TAVI may involve as much as 30% of the treated patients, therefore representing the most frequent complication in such a setting.[16] However, nearly 50% of such patients are not pacemaker-dependent at 1-year follow-up, with recovery of atrioventricular conduction occurring even at a very early stage after implant, like before hospital discharge.[28] Nonetheless, the range of postimplant pacemaker dependency or effective atrioventricular conduction restoration varies largely, ranging from 7%[28] to 89%.[12] This wide interval could be explained by heterogeneity and lack of consensus on pacemaker dependency definition. This limitation negatively influenced the study data interpretation in our analysis. Furthermore, pacemaker dependency may intermittently occur, thereby characterizing a different pattern of pacing dependency. This peculiar aspect was not available but might represent an additional factor to be investigated.

In our analysis, patients receiving SE valves and presenting with a preoperative RBBB had a 2-fold greater risk to have persistent pacing dependency at 1 year after TAVI. Ramazzina and colleagues (Table E2) showed that atrioventricular block as indication for PPI was always associated with pacemaker dependency at follow-up. In contrast, Gaede and colleagues[17] demonstrated a low rate of long-term persistence of atrioventricular block after TAVI procedure. A few studies address investigate predictors of pacemaker dependency after TAVI. Naveh and colleagues (Table E2) showed that baseline RBBB, long post-TAVI PR interval, and delayed PR interval from baseline were independent predictors for long-term pacemaker dependency. Sharma and colleagues (Table E2) showed that bifascicular block, RBBB, intraprocedural complete heart block, and QRS duration >120 milliseconds were associated with pacemaker dependency at 30-day follow-up. The impact

Study	TE	SE	Weight	Odds Ratio IV, Random, 95% CI
Chan 2018	–0.920	1.1700	9.9%	0.399 [0.040; 3.948]
Kaplan 2019	–0.120	0.9800	14.1%	0.887 [0.130; 6.054]
Nadeem 2018	0.570	0.9100	16.4%	1.768 [0.297; 10.523]
Raelson 2017	0.570	0.6700	30.2%	1.768 [0.476; 6.574]
Ghannam 2019	1.300	0.6800	29.3%	3.669 [0.968; 13.912]
Total (95% CI)			**100.0%**	**1.714 [0.833; 3.529]**

Heterogeneity: $Tau^2 = 0$; $Chi^2 = 3.26$, df = 4 (P = .51); $I^2 = 0\%$

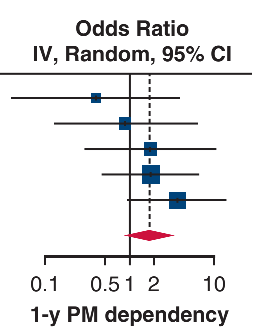


FIGURE 5. Impact of baseline AF on 1-year rate of pacemaker dependency. Forest plot. Patients with baseline AF have no greater risk to develop pacemaker dependency 1 year after TAVI. *TE*, Log odds ratio; *SE*, standard error; *IV*, weighted mean difference; *CI*, confidence limits; *PM*, pacemaker.

Study	TE	SE	Weight	Odds Ratio IV, Random, 95% CI
Raelson 2017	−0.190	0.6700	20.2%	0.827 [0.222; 3.075]
Nadeem 2018	0.260	0.5900	23.7%	1.297 [0.408; 4.122]
Urena 2014	1.160	0.3100	41.9%	3.190 [1.737; 5.857]
Kaplan 2019	1.630	0.8600	14.2%	5.104 [0.946; 27.538]
Total (95% CI)			**100.0%**	**2.096 [1.012; 4.341]**

Heterogeneity: $Tau^2 = 0.2334$; $Chi^2 = 5.23$, df = 3 ($P = .16$); $I^2 = 43\%$

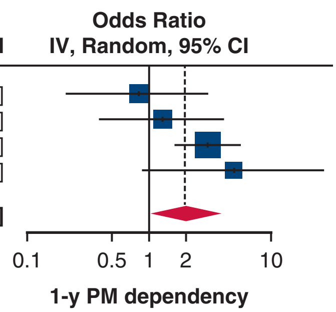


FIGURE 6. Impact of SE prosthesis (vs BE) on 1-year rate of pacemaker dependency. Forest plot. Patients with SE prosthesis have 2-fold greater risk to develop pacemaker dependency at 1 year after TAVI. *TE*, Log odds ratio; *SE*, standard error; *IV*, weighted mean difference; *CI*, confidence limits; *PM*, pacemaker.

of baseline AF on pacemaker dependency at follow-up is controversial. Early PPI after TAVI procedure was the strongest predictor regarding persistent atrioventricular block and pacemaker dependency, based on large sample-size studies.[17,27] According to these findings, we should emphasize that patients without baseline characteristics potentially leading to pacemaker dependency should benefit from other temporary leadless system as Micra AV (Medtronic, Minneapolis, Minn) to reduce the rate of permanent pacemaker implanted, as the Micra AV system is recently found to be safe; efficient and as performant as transvenous single-chamber pacemaker.[32,33]

Nowadays, guidelines regarding timing of PPI after TAVI are rather cloudy and not based on thorough clinical investigations.[8,34] Due to the lack of consistent data, the dilemma about the appropriate timing for pacemaker implantation after TAVI is left to the discretion of the attending cardiologist according to the different centers' policies and therefore is associated with extreme variability in clinical management. Erkapic and colleagues[35] showed that atrioventricular block occurs in more than 90% of the cases within the first post-TAVI week, which would allow to monitor carefully the patients at least seven days before considering PPI. However, some others studies support early PPI after TAVI procedure.[30] Actually, as the optimal timing for PPI after TAVI is not established, the variability of decision certainly influences the outcome of pacemaker dependency, making difficult to conclude about the best interval to proceed to a definitive PPI.

PPI after TAVI is associated with increased long-term mortality.[27] Faroux and colleagues[5] show the negative impact of PPI after TAVI on survival and heart failure hospitalization within the year following TAVI. Xi and colleagues[7] also show a greater all-cause mortality in TAVI patients receiving a PPI. In this systematic review, only 4 studies addressed the PPI-related complications and only 8 studies reported the 30-day mortality, making the overall appraisal of the impact of PPI on patient outcome likely underestimated, as emphasized by the Danish experience of Kirkfeldt and colleagues.[36] Report on PPI-related complications is also markedly variable[37] and the lack of a standardize international classification of these complications may further contribute to PPI-related complications and related outcome actually under-reported.

Limitations

This systematic review had several limitations that should be acknowledged. First, the follow-up varied remarkably among the included studies. The 1-year dependency was not available for all studies, limiting the conclusion to only 15 studies, whereas the others publications provided a follow-up mainly to 1 to 3 months. Only 3 studies presented a longer follow-up up to 4 years. Second, the heterogeneity about pacemaker dependency definition in the studies semantically limits our ability to compare the studies. Third, although several studies identified some risk-factors for PPI and only 1 study states multivariable predictors of pacemaker dependency, there was no agreement between studies. Finally, this is a systematic review of the literature; analysis of individual patients-data level may provide further understandings: in many of studies it was not specifically clear if the patient's native rhythm was assessed and thereby knowing for certain which patients truly required PPI.

CONCLUSIONS

This systematic review investigates the rate and predictors of pacing dependency after TAVI. Data from literature show that almost one half of the pacemakers are actively operating at 1-year follow-up. Baseline RBBB and SE valves are associated with a greater rate of pacemaker dependency at follow-up. These findings suggest that atrioventricular conduction disturbances after TAVI are reversible in a large percentage of patients. Such a condition may occur at variable time after the TAVI procedure, even within the TAVI-related hospitalization and, therefore, at a very early stage. These findings clearly indicate the need of thorough investigations regarding timing of pacemaker implantation, recovery of atrioventricular

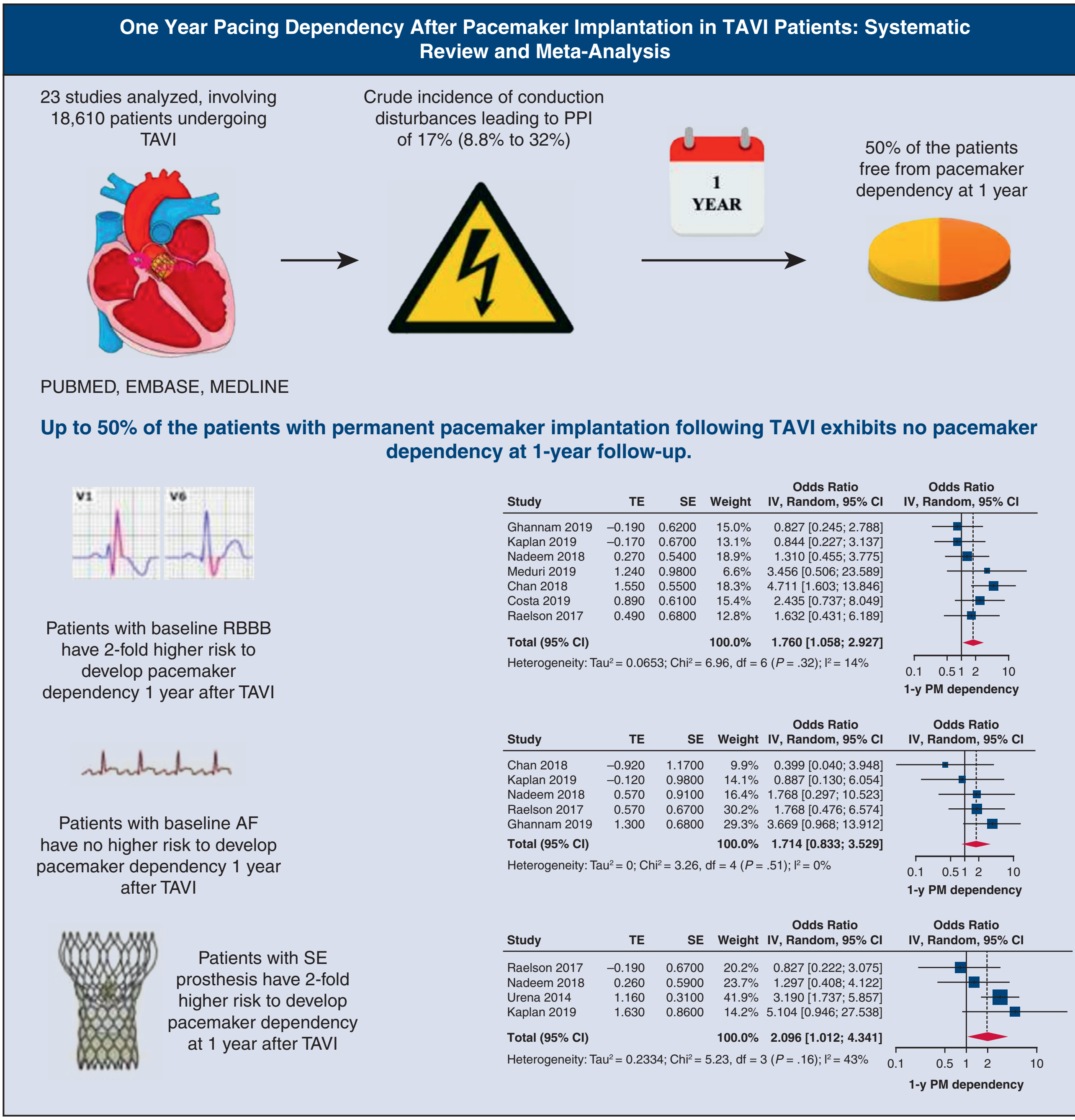


FIGURE 7. Up to 50% of the patients with permanent pacemaker implantation following TAVI exhibits no pacemaker dependency at 1-year follow-up. *TAVI*, Transcatheter aortic valve implantation; *PPI*, permanent pacemaker implantation; *RBBB*, right bundle branch block; *TE*, log odds ratio; *SE*, standard error; *IV*, weighted mean difference; *CI*, confidence limits; *PM*, pacemaker.

conduction, and predictors of pacemaker dependence as endpoints for further studies.

Conflict of Interest Statement

Dr Vernooy reported research grant from Medtronic. Dr Van't Hof reported grants from Medtronic, Astra Zeneca, Boehringer Ingelheim, and Abbott. Dr Lorusso reported grants from Medtronic, LivaNova, and Eurosets. All other authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: conduction disturbances, pacemaker dependency, permanent pacemaker, transcatheter aortic valve implantation

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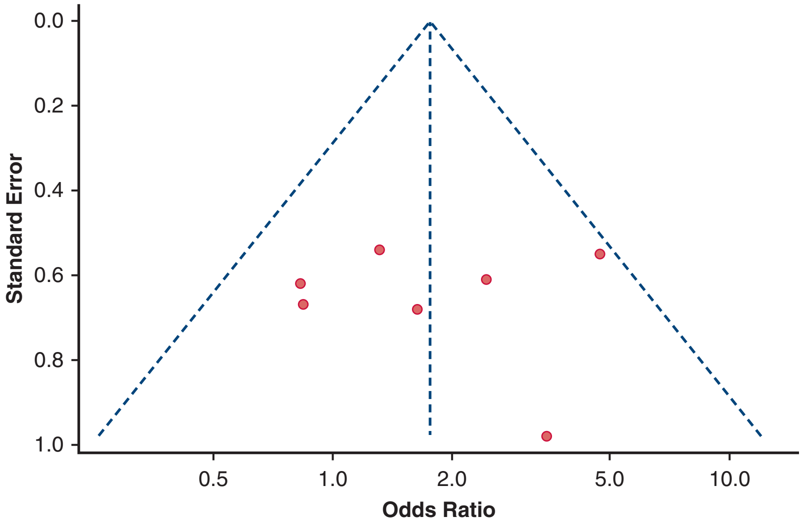

FIGURE E1. Funnel plot on the impact of baseline RBBB on 1-year rate of pacemaker dependency. No publication bias was found among studies reporting the influence of baseline RBBB on pacemaker dependency.

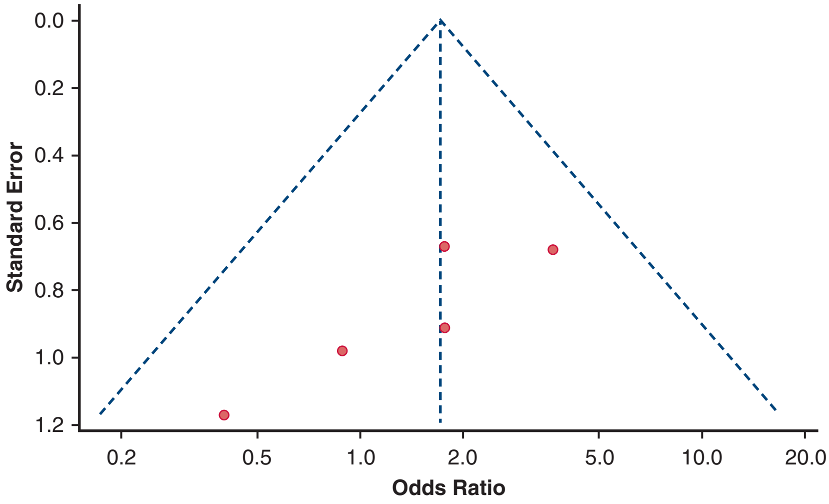

FIGURE E2. Funnel plot on the influence of baseline AF on pacemaker dependency. No publication bias was found among studies reporting the influence of baseline AF on pacemaker dependency.

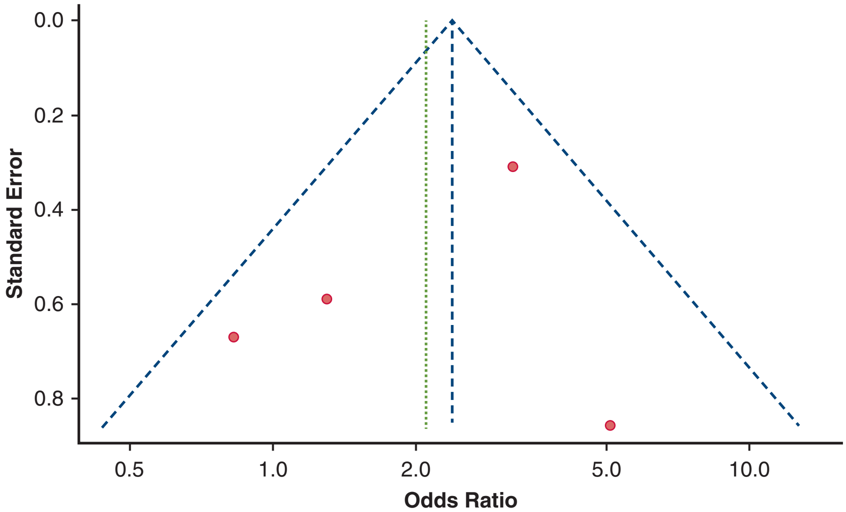

FIGURE E3. Funnel plot on the influence of SE versus BE valves on pacemaker dependency. No publication bias was found among studies reporting the influence of SE versus BE on pacemaker dependency.

Study or Subgroup	Events	Total	Weight	IV, Random, 95% CI
SE_. = > 50%				
Costa 2019	23	69	6.7%	0.333 [0.224; 0.457]
Nadeem 2018	30	55	6.6%	0.545 [0.406; 0.680]
Chan 2018	71	120	6.9%	0.592 [0.498; 0.680]
Takahashi 2018	48	91	6.8%	0.527 [0.420; 0.633]
Ghannam 2019	20	40	6.4%	0.500 [0.338; 0.662]
Kaplan 2019	15	67	6.5%	0.224 [0.131; 0.342]
Total (95% CI)		**442**	**39.9%**	**0.451 [0.338; 0.571]**
Heterogeneity: $Tau^2 = 0.2931$; $Chi^2 = 29.22$, df = 5 ($P < .01$); $I^2 = 83\%$				
SE_. = 0-25%				
Dolci 2019	19	266	6.7%	0.071 [0.044; 0.109]
Dumonteil 2017	36	65	6.7%	0.554 [0.425; 0.677]
Meduri 2019	91	182	6.9%	0.500 [0.425; 0.575]
Nazif 2015	53	106	6.8%	0.500 [0.401; 0.599]
Raelson 2017	15	38	6.4%	0.395 [0.240; 0.566]
Total (95% CI)		**657**	**33.5%**	**0.365 [0.181; 0.600]**
Heterogeneity: $Tau^2 = 1.1338$; $Chi^2 = 100.32$, df = 4 ($P < .01$); $I^2 = 96\%$				
SE_. = 25-50%				
Junquera 2019	16	24	5.9%	0.667 [0.447; 0.844]
Marzahan 2018	53	97	6.8%	0.546 [0.442; 0.648]
Van Gils 2017	272	306	6.9%	0.889 [0.848; 0.922]
Urena 2014	160	239	7.0%	0.669 [0.606; 0.729]
Total (95% CI)		**666**	**26.6%**	**0.716 [0.515; 0.857]**
Heterogeneity: $Tau^2 = 0.7161$; $Chi^2 = 56.07$, df = 3 ($P < .01$); $I^2 = 95\%$				
Total (95% CI)		**1765**	**100.0%**	**0.495 [0.370; 0.620]**
Heterogeneity: $Tau^2 = 0.9546$; $Chi^2 = 300.35$, df = 14 ($P < .01$); $I^2 = 95\%$				
Residual heterogeneity: Tau^2 = NA; $Chi^2 = 185.60$, df = 12 ($P < .01$); $I^2 = 94\%$				

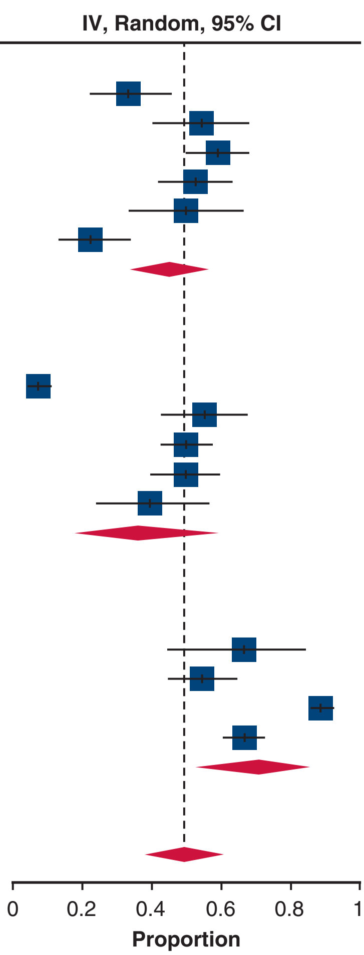

FIGURE E4. Forest plot pooling pacemaker dependency according to percentage of SE prosthesis included in the study. *IV*, Weighted mean difference; *CI*, confidence interval; *SE*, self-expandable.

TABLE E1. Newcastle–Ottawa Scale for the assessment of the risk of bias in individual nonrandomized studies

Author	Score	Selection	Comparability	Outcome/exposure
Bjerre Thygesen et al[9]	8	****	**	**
Urena et al[10]	9	****	**	***
Nazif et al[11]	9	****	**	***
Van Gils et al[12]	9	****	**	***
Raelson et al[13]	8	****	**	**
Dumonteil et al[14]	9	****	**	***
Kaplan et al[15]	9	****	**	***
Chamandi et al[16]	8	****	**	**
Gaede et al[17]	8	****	**	**
Gonska et al[18]	7	****	*	**
Marzahn et al[19]	9	****	**	***
Nadeem et al[20]	9	****	**	***
Campelo-Parada et al[21]	8	****	**	**
Mirolo et al[22]	8	****	**	**
Van Gils et al[23]	8	****	**	**
Takahashi et al[24]	8	****	**	**
Chan et al[25]	9	****	**	***
Ghannam et al[26]	9	****	**	***
Costa et al[27]	9	****	**	***
Dolci et al[28]	9	****	**	***
Tovia-Brodie et al[29]	9	****	**	**
Junquera et al[30]	9	****	**	***
Meduri et al[31]	9	****	**	***

TABLE E2. Baseline characteristics of studies including <250 patients (n = 30)

Study	Year	Study design (no. centers)	Sample size	Age, y	STS score, %	Inclusion period	Left ventricle ejection fraction, %	Peripheral artery disease, %	Diabetes mellitus, %	Valve type	Follow-up, mo*	Approach for TAVI	Mortality at 30 d
Sinhal et al[E1]	2008	Prospective (1)	106	84.2	na	na	62.5	na	na	100% SAPIEN	1	na	na
Jilaihawi et al[E2]	2009	Retrospective (1)	30	84.4	8.3	January 2007 to March 2008	47.5	na	17.6	100% MCV	na	na	8.8%
Baan et al[E3]	2010	Retrospective (1)	34	80.4	5	na	na	na	32	100% MCV	1	na	20.5%
Fraccaro et al[E4]	2011	Retrospective (1)	64	81	na	May 2007 to April 2009	52.3	34.4	na	100% MCV	12	94% transfemoral 6% transsubclavian	5%
Van der boon et al[E5]	2013	Prospective (1)	167	81	na	November 2005 to February 2011	51	10.2	21.6	100% MCV	11,5	97% transfemoral 3% transsubclavian	na
Pereira et al[E6]	2013	Retrospective (1)	65	79.3	na	August 2007 to May 2011	na	47.7	38.5	100% MCV	6	78.5% transfemoral 20% transsubclavian 1.5% direct aortic	na
Goldenberg et al[E7]	2013	Retrospective (1)	191	na	na	February 2009 to July 2012	na	na	na	65% MCV 35% SAPIEN	17	na	na
Ramazzina et al[E8]	2014	Retrospective (1)	97	83	na	October 2010 to January 2013	55	na	26.4	61% MCV 39% SAPIEN	12	100% transfemoral	na
Boerlage-Van Dijk et al[E9]	2014	Retrospective (1)	121	80.5	4.5	October 2007 to June 2011	na	na	28	100% MCV	12	100% Transfemoral	na
Renilla et al[E10]	2015	Retrospective (1)	95	na	na	January 2007 to December 2011	na	na	na	100% MCV	35	86.9% transfemoral 13% transsubclavian	na
Petronio et al[E11]	2015	Prospective (9)	194	80.2	7.2	October 2011 to April 2013	na	27.6	31	100% MCV	1	89.7% transfemoral 6.2% transsubclavian 4.1% direct aortic	1.6%
Weber et al[E12]	2015	Retrospective (1)	212	80.8	9.4	2008 - 2012	52.8	na	25	100% MCV	9	100% transfemoral	6.1%
Schernthaner et al[E13]	2016	Retrospective (1)	153	81	6	na	na	na	31	82% MCV 18% SAPIEN	1,5	94% transfemoral 6% direct aortic	na
Kostopoulou et al[E14]	2016	Prospective (1)	45	81	na	January 2010 to February 2012	49	na	27	100% MCV	24	na	na
Sideris et al[E15]	2016	Prospective (1)	168	na	na	January 2009 to October 2015	na	na	na	100% MCV	na	100% transfemoral	na
Luke et al[E16]	2016	Retrospective (1)	140	81	na	July 2011 to May 2016	na	na	na	81% MCV 19% EVOLUT	na	100% transfemoral	na
Makki et al[E17]	2017	Retrospective (1)	172	83	na	November 2011 to January 2016	51	na	46	92% MCV 8% LOTUS	22	100% transfemoral	na

(Continued)

TABLE E2. Continued

Study	Year	Study design (no. centers)	Sample size	Age, y	STS score, %	Inclusion period	Left ventricle ejection fraction, %	Peripheral artery disease, %	Diabetes mellitus, %	Valve type	Follow-up, mo*	Approach for TAVI	Mortality at 30 d
Nijenhuis et al[E18]	2017	Retrospective (1)	155	80.5	6	June 2007 to June 2015	59	30.3	34.8	na	24	na	na
Naveh et al[E19]	2017	Prospective (1)	110	80.7	na	September 2008 to November 2013	57.6	23.6	30	75.5% MCV 24.5% SAPIEN	12	88.2% transfemoral 6.4% transsubclavian 5.5% direct aortic	na
Alasti et al[E20]	2018	Prospective (1)	152	83.6	na	April 2012 to October 2016	59.2	5.3	18.7	100% LOTUS	12	99.4% transfemoral 0.6% direct aortic	2.6%
Ortak et al[E21]	2018	Prospective (1)	66	80.4	3.7	2014 -2016	53.2	na	na	100% LOTUS	7	na	3.5%
Rodes-Cabau et al[E22]	2018	Prospective (11)	103	80	5	June 2014 to July 2016	56	na	43	14.5% MCV 37% EVOLUT R 51.5% SAPIEN	12	86% transfemoral 10% transapical 4% transsubclavian	na
Leong et al[E23]	2018	Retrospective (1)	67	80.5	na	January 2013 to December 2015	na	na	30	16.4% EVOLUT R 35.8% MCV 34.3% SAPIEN 13.4% Others	2,4	na	na
Sharma et al[E24]	2018	Prospective (1)	226	81.2	na	March 2012 to October 2016	na	na	na	100% BE	1	na	na
Bacik et al[E25]	2018	Prospective (1)	116	77.1	na	August 2013 to Mar 2017	50.5	na	40.5	100% SAPIEN	12	82.8% transfemoral 17.2% transapical	na
Megaly et al[E26]	2019	Prospective (1)	172	na	na	January 2010 to May 2017	na	na	50	na	12	na	na
Yazdchi et al[E27]	2019	Retrospective (1)	na	na	na	2013 - 2017	na	na	na	na	14	na	na
McCaffrey et al[E28]	2019	Retrospective (1)	98	79.6	5	May 2015 to March 2018	55.7	26	35	100% SAPIEN	1	93% transfemoral 6% transapical 1% direct aortic	4.8%
Miura et al[E29]	2019	Retrospective (1)	201	84.8	6.4	October 2013 to September 2016	60.6	9	26	100% SAPIEN	13.5	68% transfemoral l 27% transapical 5% transiliac	0.5%
Dhakal et al[E30]	2020	Retrospective (1)	176	80	5.7	Seprember 2012 to March 2017	53	31	43	na	18.9	na	na
Total	na	49 centers	3612	81.2	6	November 2005 to March 2018	54.4	24.5	32.1	65.6% MCV 23.1% SAPIEN 8% LOTUS 2.7% EVOLUT 0.5% Others	11.4	92.5% transfemoral 3% transsubclavian 1% direct aortic 3.2% transapical 0.3% transiliac	6%

Values are n (%). *STS score*, Society of Thoracic Surgeons Risk Score; *TAVI*, transaortic valve implantation; *na*, not available; *MCV*, Medtronic CoreValve. *Follow-up is reported as mean or median as given by the authors.

TABLE E3. Pacemaker details in studies including < 250 patients (n = 30)

Study	Indications PPI	Timing of PPI, d	PPI rate	Dependency definition	Dependency rate	Dependency follow-up, months*	Multivariable Predictors PPI	Association	PPI-related complications
Sinhal et al[E1]	na	2	5.6%	na	86%	6	na	na	na
Jilaihawi et al[E2]	90% AVB 10% SSS	na	33.3%	Description by case of the % ventricular pacing at follow-up	66.6%	1	• LBBB with left axis deviation • Diastolic interventricular septa dimension >17 mm • Noncoronary cuspid thickness >8 mm	na	na
Baan et al[E3]	100% AVB	3	26.9%	"ventricular pacing" reported	100%	1	na	• Smaller left ventricle outflow tract diameter • More left-sided heart axis • More mitral annular calcification • Smaller postimplantation indexed effective orifice area	na
Fraccaro et al[E4]	96% AVB 4% SSS	na	39%	With pacemaker to VVI at the lowest rate possible: continuous pacing or complete AVB or AF with inadequate ventricular response	23.5%	12	• Depth of the prosthesis implantation • Pre-existing RBBB	na	na

(Continued)

TABLE E3. Continued

Study	Indications PPI	Timing of PPI, d	PPI rate	Dependency definition	Dependency rate	Dependency follow-up, months*	Multivariable Predictors PPI	Association	PPI-related complications
Van der boon et al[E5]	83.3% AVB 13.8% bradycardia 2.7% others	8	21.6%	By temporarily turning off the PPM or programming to a VVI modus at 30 bpm to assess dependency → if high-degree AVB (second degree Mobitz II or third degree) or a slow (<30 bpm) or absent ventricular escape rhythm observed	44.4%	11.5	na	na	na
Pereira et al[E6]	100% AVB	3	33%	Absence of any intrinsic or escape rhythm during back-up pacing at 30 beats/min (VVI)	27%	12	na	• Porcelain aorta = independent predictors of pacing dependency at follow-up	na
Goldenberg et al[E7]	61.5% AVB 3% SSS 34% others	na	16.8%	High degree of AVB (second degree or complete) or intrinsic rhythm <30 beats/min during pacemaker inhibition	29%	12	na	na	na

(Continued)

TABLE E3. Continued

Study	Indications PPI	Timing of PPI, d	PPI rate	Dependency definition	Dependency rate	Dependency follow-up, months*	Multivariable Predictors PPI	Association	PPI-related complications
Ramazzina et al[E8]	46% AVB 55% others	na	36.1%	>99% ventricular pacing	29%	12	• Use of MCV	• Diabetes • Atrial fibrillation before TAVI • Associated with no need for PPI	na
Boerlage-Van Dijk et al[E9]	91.3% AVB	3	19%	Ventricular-paced rhythm (no other definition)	52%	11.3	• Mitral annular calcification • Pre-existing RBBB	• No factors found	4.3% atrial lead repositioning 4.3% pocket hematoma 4.3% cerebral vascular accident
Renilla et al[E10]	100% AVB	2	37.9%	Presence of a high-degree AVB (Mobitz II and III) or a slow <30 bpm or absent ventricular escape rhythm (pacemaker turned off or programmed to VVI modus at 30 bpm)	39.1%	35	na	na	3% pacemaker pocket infection
Petronio et al[E11]	na	na	24.4%	VVI programming 30 beats/min	40.7%	1	• Implantation depth	• Implantation depth <4 mm	na
Weber et al[E12]	90% AVB 2% bradycardy 2% SSS 5% others	na	23%	Pacemaker is partially or frequently needed to ensure heartbeat	35%	9	na	na	na

(Continued)

TABLE E3. Continued

Study	Indications PPI	Timing of PPI, d	PPI rate	Dependency definition	Dependency rate	Dependency follow-up, months*	Multivariable Predictors PPI	Association	PPI-related complications
Schernthaner et al[E13]	78% AVB 7% SSS 13% Others	7	20%	Absence of an escape or intrinsic rhythm for 30 s during temporary back-up pacing at a rate of 30 bpm	37%	1.5	na	na	na
Kostopoulou et al[E14]	100% AVB	na	22%	Asystole or CHB with or without escape rhythm after cessation of pacing	9%	12	• Prolonged HV interval prognostic for PPI	• Trend between ⊿ QRS and PPI at 6-mo analysis	na
Sideris et al[E15]	100% AVB	na	38.7%	High ventricular pacing rate >99%	100%	6	na	na	1.5% pneumothorax
Luke et al[E16]	100% AVB	na	39.3%	“Pacing"	0.7%	3	• Previous conduction system disease • History of atrial fibrillation	Trends with • history of atrial fibrillation • presence of RBBB • male sex • atrioventricular nodal blocking drugs	na
Makki et al[E17]	63% AVB 4% bradycardia 33% others	3	14%	Underlying ventricular asystole >5 s, CHB, >50% pacing, symptoms in the setting of bradycardia (rate <50 bpm)	33%	3	na	na	na

(Continued)

TABLE E3. Continued

Study	Indications PPI	Timing of PPI, d	PPI rate	Dependency definition	Dependency rate	Dependency follow-up, months*	Multivariable Predictors PPI	Association	PPI-related complications
Nijenhuis et al[E18]	87% AVB	8	24%	Ventricular pacing reported	68%	27	• Previous atrial fibrillation • Use of digoxin • MCV implantation • Left heart axis	na	na
Naveh et al[E19]	100% AVB	na	34.5%	Absent or inadequate intrinsic ventricular rhythm on pacemaker interrogation (intrinsic rhythm <30 bpm); >5% VP from the last follow-up on pacemaker interrogation; any evidence of VP on pacemaker interrogation in case where the programmed AV interval was >300 ms	68.4%	12	• Baseline RBBB • PR interval (each increment of 10 milliseconds in PR interval, risk for PPI 17% greater)	na	0%

(Continued)

TABLE E3. Continued

Study	Indications PPI	Timing of PPI, d	PPI rate	Dependency definition	Dependency rate	Dependency follow-up, months*	Multivariable Predictors PPI	Association	PPI-related complications
Alasti et al[E20]	89.2% AVB 2.6% SSS 7.8% Others	3	25%	The need for ventricular pacing when the pacing rate was lowered to 40 bpm for 10 s → dependent: slow (<40 bpm) or absent ventricular escape rhythm or AVB (Mobitz II or III)	38%	12	na	na	16% hematomas
Ortak et al[E21]	83% AVB 16% others	na	22%	na	64%	1	• Implantation depth • LOTUS implantation depth >4.8 mm = cut-off to predict PPI	na	na
Rodes-Cabau et al[E22]	81% AVB 9% bradycardia 9% others	42	11%	na	78%	12	na	na	na
Leong et al[E23]	74.6% AVB 20.8% bradycardia 13.5% others	2.3	44.8%	Ventricular pacing reported	73%	2.4	na	• Male sex • Increase in QRS duration post-TAVI • Associated with PPI	0%

(Continued)

TABLE E3. Continued

Study	Indications PPI	Timing of PPI, d	PPI rate	Dependency definition	Dependency rate	Dependency follow-up, months*	Multivariable Predictors PPI	Association	PPI-related complications
Sharma et al[E24]	na	na	11.1%	Spontaneous response ventricular rate less than 30 bpm during backup pacing set at 30 beats/ min for 30 s	32%	1	na	• RBBB • Intra-procedural CHB • Bifascicular block • QRS duration >120 ms • All associated with pacing dependence at 30 d	na
Bacik et al[E25]	49.8% AVB 6.3% SSS 43.9% others	5.5	13.8%	More than 95% pacing events	12%	12	• Weight • Absence of AF • Aortic peak gradient • Aortic valve area • Severity of pulmonary hypertension	na	na
Megaly et al[E26]	50.6% AVB 34.9% others	na	35%	CHB requiring ventricular pacing	3.5%	12	na	na	na
Yazdchi et al[E27]	78% AVB	2	8.7%	Ventricular pacing reported	87%	14	na	na	na

(Continued)

TABLE E3. Continued

Study	Indications PPI	Timing of PPI, d	PPI rate	Dependency definition	Dependency rate	Dependency follow-up, months*	Multivariable Predictors PPI	Association	PPI-related complications
McCaffrey et al[E28]	na	na	11.2%	Ventricular pacing reported	75%	1	na	• Predictive factors of acute conduction abnormalities (4) • Predictive factors of new conductions abnormalities after discharge (5)	na
Miura et al[E29]	90% AVB 10% SSS	6	5%	Ventricular pacing reported	40%	12	na	na	na
Dhakal et al[E30]	80% AVB 17% SSS 3% others	2	17%	Ventricular pacing rate	54%	2.7	RBBB	In univariate analysis: • Valve size • SE valve • RBBB • Prolonged PR interval	na
Total	72% AVB 1.7% SSS 3% bradycardia 23.2% others	6,5	23.8%	na	na	9	na	na	na

Values are n (%). *PPI*, Pacemaker implantation; *na*, not available; *AVB*, atrioventricular block; *SSS*, sick sinus syndrome; *LBBB*, left bundle branch block; *VVI*, single-chamber device; *AF*, atrial fibrillation; *RBBB*, right bundle branch block; *PPM*, permanent pacemaker; *MCV*, Medtronic CoreValve; *TAVI*, transcatheter aortic valve implantation; *CHB*, complete heart block; *SE*, self-expandable. *Follow-up is reported as mean or median as given by the authors.

TABLE E4. Leave-one-study out analysis

Left-out study	OR	95% CI	*P* value
RBBB			
Kaplan 2019[15]	2.3798	1.1797-4.8008	.0155
Nadeem 2018[20]	2.2425	1.0932-4.6002	.0276
Raelson 2017[13]	2.0960	1.0400-4.2241	.0385
Costa 2019[27]	1.9345	1.0126-3.9288	.0479
Meduri 2019[31]	1.8850	1.0136-3.7261	.0483
Chan 2018[25]	1.6386	0.8001-3.3559	.1770
AF			
Kaplan 2019[15]	1.2220	0.4251-3.5122	.7098
Nadeem 2018[20]	0.9829	0.3378-2.8599	.9748
Raelson 2017[13]	0.9094	0.2919-2.8336	.8699
Chan 2018[25]	1.4551	0.5188-4.0811	.4760
SE			
Kaplan 2019[15]	1.9233	1.0326-3.7266	.0426
Nadeem 2018[20]	2.3432	1.1402-4.8153	.0205
Raelson 2017[13]	2.5419	1.3676-4.7244	.0032
Van Gils 2017[12]	2.3947	1.1342-5.0562	.0220
Urena 2014[10]	1.8686	0.8743-3.9938	.1067
Takahashi 2018[24]	1.8711	1.0048-3.4844	.0483

OR, Odds ratio; *CI*, confidence interval; *RBBB*, right bundle branch block; *AF*, atrial fibrillation; *SE*, self-expandable.