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Predictors of Permanent Pacemaker Implantation in Patients With Severe Aortic Stenosis Undergoing TAVR

A Meta-Analysis

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ABSTRACT

BACKGROUND Atrioventricular (AV) conduction disturbances requiring permanent pacemaker (PPM) implantation may complicate transcatheter aortic valve replacement (TAVR). Available evidence on predictors of PPM is sparse and derived from small studies.

OBJECTIVES The objective of this study was to provide summary effect estimates for clinically useful predictors of PPM implantation after TAVR.

METHODS We performed a systematic search for studies that reported the incidence of PPM implantation after TAVR and that provided raw data for the predictors of interest. Data on study, patient, and procedural characteristics were abstracted. Crude risk ratios (RRs) and 95% confidence intervals for each predictor were calculated by use of random effects models. Stratified analyses by type of implanted valve were performed.

RESULTS We obtained data from 41 studies that included 11,210 TAVR patients, of whom 17% required PPM implantation after intervention. The rate of PPM ranged from 2% to 51% in individual studies (with a median of 28% for the Medtronic CoreValve Revalving System [MCRS] and 6% for the Edwards SAPIEN valve [ESV]). The summary estimates indicated increased risk of PPM after TAVR for men (RR: 1.23; $p < 0.01$); for patients with first-degree AV block (RR: 1.52; $p < 0.01$), left anterior hemiblock (RR: 1.62; $p < 0.01$), or right bundle branch block (RR: 2.89; $p < 0.01$) at baseline; and for patients with intraprocedural AV block (RR: 3.49; $p < 0.01$). These variables remained significant predictors when only patients treated with the MCRS bioprosthesis were considered. The data for ESV were limited. Unadjusted estimates indicated a 2.5-fold higher risk for PPM implantation for patients who received the MCRS than for those who received the ESV.

CONCLUSIONS Male sex, baseline conduction disturbances, and intraprocedural AV block emerged as predictors of PPM implantation after TAVR. This study provides useful tools to identify high-risk patients and to guide clinical decision making before and after intervention. (J Am Coll Cardiol 2014;64:129–40) © 2014 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

AV = atrioventricular

CI = confidence interval

ESV = Edwards SAPIEN valve

EuroSCORE = European System for Cardiac Operative Risk Evaluation

LBBB = left bundle branch block

MCRS = Medtronic CoreValve Revalving System

PPM = permanent pacemaker

RBBB = right bundle branch block

RR = risk ratio

STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality

TAVR = transcatheter aortic valve replacement

Transcatheter aortic valve replacement (TAVR) has emerged as the treatment of choice among patients with symptomatic severe aortic stenosis deemed inoperable and a valuable treatment alternative to surgical aortic valve replacement for high-risk surgical patients (1–3). As a result, the number of patients undergoing TAVR worldwide has increased steadily, and the complications related to valve implantation have been well recognized. Atrioventricular (AV) conduction disturbances requiring permanent pacemaker (PPM) implantation are common and clinically important adverse events (4). Because of the close proximity of the AV conduction system to the aortic valvular complex, any intervention (percutaneous or surgical) at the valve level may result in conduction disturbances (5,6).

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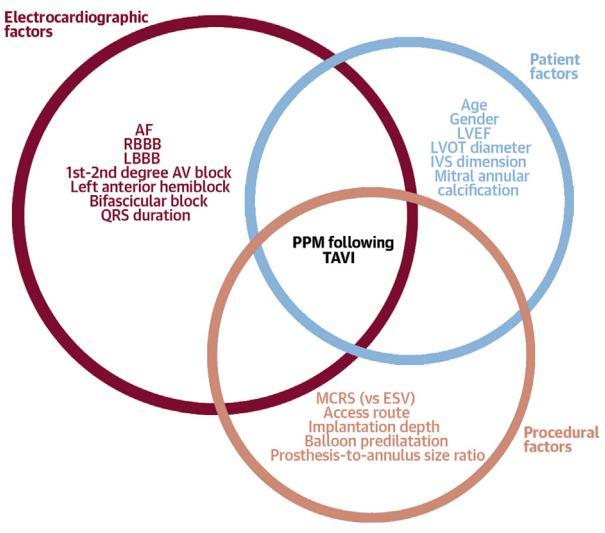
The incidence of AV conduction disturbances as a result of TAVR and the subsequent requirement for permanent pacing differs between the two most widely used bioprostheses, the balloon-expandable Edwards SAPIEN valve (ESV) (Edwards Lifesciences, Irvine, California) and the self-expandable Medtronic CoreValve Revalving System (MCRS) (Medtronic, Minneapolis, Minnesota). PPM implantation in patients receiving the ESV has been reported at a rate of between 5% and 12% (7–10), whereas the need for PPM has been higher with the use of the MCRS (up to 24% in the FRANCE-2 [French Aortic National CoreValve and Edwards] registry and 33% in the UK CoreValve registry) (11,12). Identification of high-risk patients for such complications is of great clinical importance. For that reason, several patient- and procedure-related characteristics have been evaluated and proposed as potential predictors; however, available evidence is limited and inconsistent, mainly derived from studies of relatively small patient populations that examined different variables without providing robust conclusions for their predictive performance. Therefore, this study sought to provide summary effect estimates for clinically useful risk predictors of PPM implantation after TAVR intervention.



CENTRAL ILLUSTRATION Previously Identified Factors Associated With Conduction Abnormalities After TAVR

Previously identified factors associated with conduction abnormalities after transcatheter aortic valve replacement (TAVR) fall into 3 broad but often overlapping categories: electrocardiographic, patient, and procedural factors. AF = atrial fibrillation; AV = atrioventricular; ESV = Edwards SAPIEN Valve; IVS = interventricular septal; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; LVOT = left ventricular outflow track; MCRS = Medtronic CoreValve Revalving system; PPM = permanent pacemaker; RBBB = right bundle branch block.

METHODS

SEARCH STRATEGY. We performed a broad, computerized literature search of certain text and key words in PubMed and EMBASE through October 2013. For our purposes, we focused only on published data. Our search was limited to studies in humans, but no language or year of publication restrictions were applied.

ELIGIBILITY CRITERIA AND STUDY SELECTION. We deemed eligible any study of original design that assessed the incidence of AV conduction or cardiac rhythm disturbances and the subsequent need for PPM implantation after TAVR. We included studies in which quantitative raw data that enabled the calculation of crude risk ratios (RRs) for the incidence of PPM implantation for the predictors of interest were available. When overlapping study populations (according to participating institutions and period of patient recruitment) were documented in different reports, we included the one with the most recent results and available data of interest; however, when different predictors were identified in reports of overlapping populations, each predictor was considered eligible and included separately. Finally, studies that reported outcomes only for patients with valve-in-valve interventions and studies of nonoriginal design were not included.

Two investigators independently conducted the literature searches, the study eligibility assessment,

and the data extraction in duplicate. Any discrepancies were resolved by consensus and arbitration by a third investigator.

DATA ABSTRACTION. The following study- and patient-related information was extracted from the main paper and accompanying supplemental material: study design; single or multicenter study; region and period of patient recruitment; length of follow-up (given metric); number of participants; number of PPM implantations after TAVR; age (given metric); sex (male); baseline procedural risk assessment (by logistic EuroSCORE [European System for Cardiac Operative Risk Evaluation] or STS-PROM [Society of Thoracic Surgeons Predicted Risk of Mortality] score); and the number of patients with atrial fibrillation (AF), left bundle branch block (LBBB), or right bundle branch block (RBBB) at baseline.

Moreover, we extracted information related to procedural characteristics, including access site (transfemoral, transapical, transaortic, trans-subclavian, or transcarotid) and type of valve prosthesis (MCRS, ESV, or any other device), in each study. Both devices have received European CE Mark approval, although only the ESV had received approval from the U.S. Food and Drug Administration at the time of our search. When the authors did not clarify the access route used for MCRS implantation, we assumed that all implantations had been performed by the transfemoral approach. Finally, the indications for PPM implantation in each study were recorded.

ASSESSED PREDICTORS OF PPM IMPLANTATION. According to a recently published review (6), we focused on the following previously proposed predictors that could be plausibly related to the intervention owing to direct injury to the aortic root: age; sex (male); baseline (pre-intervention) atrial fibrillation (any type), first-degree AV block, left anterior or posterior hemiblock, intraprocedural AV block, LBBB, RBBB, PR interval (>200 ms), QRS duration, and preserved left ventricular ejection fraction; increased interventricular septal dimension; smaller left ventricular outflow tract diameter (<21 mm); access route (femoral vs. subclavian access for MCRS, arterial vs. apical access for ESV); implantation depth; MCRS versus ESV; MCRS (vs. ESV) balloon pre-dilation; larger MCRS prosthesis (>29 mm); and increased prosthesis-to-annulus size ratio (**Central Illustration**).

DATA ANALYSIS. Crude RRs were directly calculated for each predictor and entered into the primary analysis. We combined the given data across the studies using DerSimonian and Laird random effects models (13). Heterogeneity across the studies was quantified with the I^2 index, which takes values between 0% and 100%, with values of 25% typically suggesting low, 50% moderate, and 75% large heterogeneity (14). Stratified analyses were performed according to the type of implanted valve, whereas sensitivity analyses were performed after exclusion of small studies with fewer than 200 patients. Descriptive characteristics are presented as mean ± standard deviation or median (interquartile range) as appropriate for continuous variables, whereas categorical variables are presented as frequencies and percentages. Patients with prior PPM implantation unrelated to TAVR were excluded from our analysis, and each predictor was considered separately. All reported p values are 2-sided. Statistical analyses were performed in STATA software (version 12.0, STATA Corp., College Station, Texas).

RESULTS

INCLUSION OF STUDIES. A total of 2,996 reports were initially screened in title and abstract level, of which 536 were retrieved in full text and examined

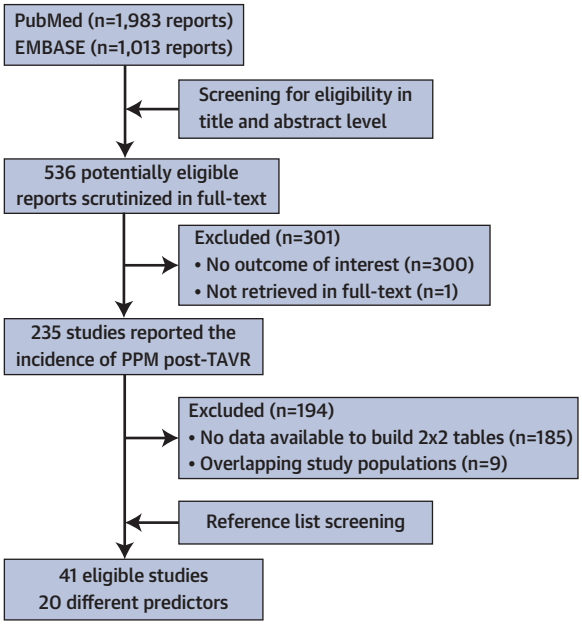


FIGURE 1 Study Selection

Flow chart demonstrating the results in each step of the systematic search to identify studies with available data to calculate crude risk ratios for the predictors of interest. PPM = permanent pacemaker implantation; TAVR = transcatheter aortic valve replacement.

TABLE 1 Characteristics of the Included Studies

First Author (Ref. #)	Year	Study Design (Centers)	Region(s)	Recruitment Period	Follow-Up (Months)*	Sample Size	Post-TAVR PPM	Baseline Characteristics						
								Age (yrs)	Male	Log EuroSCORE	STS-PROM	AF	LBBB	RBBB
Himbert et al. (15)	2009	Obs. (single)	France	Oct. 2006–Nov. 2008	10	75	4 (5)	82 ± 8	41 (55)	26 ± 13	16 ± 7	ND	ND	ND
Thielmann et al. (16)	2009	Obs. (single)	Germany	May 2005–Nov. 2008	12	39	4 (10)	81 ± 5	15 (38)	44 ± 13	18 ± 6	ND	ND	ND
Attias et al. (17)	2010	Obs. (single)	France	Oct. 2006–June 2009	1	83	7 (8)	81 ± 9	44 (53)	26 ± 14	15 ± 8	ND	ND	ND
Bleiziffer et al. (18)	2010	Obs. (single)	Germany	June 2007–Jan. 2009	0.5	159	44 (28)	81 ± 6	68 (43)	22 ± 13	ND	41 (26)	27 (17)	6 (4)
Eltchaninoff et al. (9)	2010	Obs. (multi.)	France	Feb. 2009–June 2009	1	244	9 (4)	82 ± 7	138 (57)	26 ± 11	19 ± 13	ND	ND	ND
Baan et al. (19)	2010	Obs. (single)	Netherlands	ND	1	29	7 (24)	80 ± 8	14 (52)	ND	5 ± 3	10 (34)	2 (7)	2 (7)
Erkapic et al. (20)	2010	Obs. (single)	Germany	Oct. 2008–Dec. 2009	0.4	50	17 (34)	80 ± 6	23 (46)	ND	ND	17 (34)	5 (10)	7 (14)
Ewe et al. (21)	2010	Obs. (multi.)	Netherlands, Singapore, Italy	ND	9	147	7 (5)	81 ± 7	63 (43)	22 ± 11	ND	33 (22)	ND	ND
Ferreira et al. (22)	2010	Obs. (single)	Portugal	Aug. 2007–Oct. 2009	ND	32	8 (25)	81 (76-85)	11 (34)	24 (17-31)	ND	9 (28)	ND	ND
Godino et al. (23)	2010	Obs. (single)	Italy	Nov. 2007–Feb. 2010	6	137	19 (14)	82 ± 6	73 (53)	28 ± 12	7 ± 5	ND	ND	ND
Haworth et al. (24)	2010	Obs. (single)	UK	2007–2008	5	33	8 (24)	82 ± 7	20 (57)	24 ± 15	ND	6 (18)	3 (9)	7 (21)
Petronio et al. (25)	2010	Obs. (multi.)	Italy	June 2007–July 2009	6	514	84 (16)	83 (78-86)	226 (44)	20 (13-31)	ND	ND	60 (12)	40 (8)
Piazza et al. (26)	2010	Obs. (single)	Netherlands	Nov. 2005–April 2009	6	91	17 (19)	81 ± 7	39 (43)	16 ± 9	ND	25 (28)	13 (15)	5 (6)
Rodés-Cabau et al. (27)	2010	Obs. (multi.)	Canada	Jan. 2005–June 2009	8	339	17 (5)	81 ± 8	152 (45)	ND	10 ± 6	115 (34)	ND	ND
Roten et al. (28)	2010	Obs. (single)	Switzerland	Aug. 2007–Dec. 2008	2.6	67	23 (34)	83 (80-85)	31 (46)	23 (13-34)	6 (4-9)	8 (12)	11 (16)	13 (19)
Thomas et al. (29)	2010	Obs. (multi.)	Europe	Nov. 2007–Jan. 2009	1	1,038	73 (7)	81 ± 9	463 (45)	27 ± 22	ND	ND	ND	ND
Bosmans et al. (30)	2011	Obs. (multi.)	Belgium	Until April 2010	1	328	40 (12)	83 ± 6	151 (46)	28 ± 16	ND	30 (9)	ND	ND
D'Ancona et al. (31)	2011	Obs. (single)	Germany	April 2008–March 2011	12	322	20 (6)	79 ± 8	107 (33)	37 ± 20	18 ± 10	93 (29)	ND	ND
Ewe et al. (32)	2011	Obs. (single)	Netherlands	ND	ND	104	4 (4)	81 ± 8	52 (50)	21 ± 12	9 ± 4	22 (21)	ND	ND
Fraccaro et al. (33)	2011	Obs. (single)	Italy	May 2007–April 2009	6	64	25 (39)	81 ± 7	29 (45)	24 ± 15	ND	10 (16)	9 (14)	8 (13)
Guetta et al. (34)	2011	Obs. (multi.)	Israel	2008–2010	3	70	28 (40)	83 ± 5	26 (37)	ND	ND	19 (27)	17 (24)	11 (16)
Khawaja et al. (12)	2011	Obs. (multi.)	UK	April 2007–June 2009	ND	243	81 (33)	81 ± 7	123 (51)	ND	ND	46 (19)	32 (13)	23 (10)

Continued on the next page

TABLE 1 Continued

First Author (Ref. #)	Year	Study Design (Centers)	Region(s)	Recruitment Period	Follow-Up (Months)*	Sample Size	Post-TAVR PPM	Baseline Characteristics						
								Age (yrs)	Male	Log EuroSCORE	STS-PROM	AF	LBBB	RBBB
Lefèvre et al. (35)	2011	Obs. (multi.)	Europe	April 2007–Jan. 2008	12	130	3 (2)	82 ± 6	58 (45)	30 ± 14	12 ± 7	32 (25)	ND	ND
Akin et al. (36)	2012	Obs. (single)	Germany	Jan. 2007–Jan. 2008	0.2	45	23 (51)	81 ± 6	18 (40)	21 ± 16	ND	7 (16)	1 (2)	2 (4)
Bagur et al. (37)	2012	Obs. (multi.)	Canada	Jan. 2005–Aug. 2010	1	411	30 (7)	81 ± 11	176 (43)	26 ± 17	9 ± 6	96 (23)	33 (8)	20 (5)
Calvi et al. (38)	2012	Obs. (single)	Italy	June 2007–April 2011	12	162	52 (32)	81 ± 5	60 (40)	28 ± 15	ND	27 (17)	5 (3)	ND
Chorianopoulos et al. (39)	2012	Obs. (single)	Germany	Jan. 2009–April 2011	1	130	46 (35)	81 ± 6	54 (42)	24 ± 13	ND	28 (22)	9 (7)	18 (14)
De Carlo et al. (40)	2012	Obs. (multi.)	Italy	Sept. 2007–July 2010	12	275	66 (24)	82 ± 6	128 (47)	23 ± 14	ND	ND	37 (14)	32 (12)
Fraccaro et al. (41)	2012	Obs. (multi.)	Italy	June 2007–Dec. 2010	9	384	63 (16)	80 ± 7	185 (48)	24 ± 16	10 ± 9	ND	ND	ND
Gilard et al. (42)	2012	Obs. (multi.)	France	Jan. 2010–Oct. 2011	3.8	3,107	495 (16)	83 ± 7	1,630 (51)	22 ± 14	14 ± 12	820 (31)	ND	ND
Hayashida et al. (11)	2012	Obs. (single)	France	Oct. 2006–Dec. 2010	7	260	17 (7)	83 ± 6	129 (50)	24 ± 11	ND	ND	ND	ND
Liang et al. (43)	2012	Obs. (single)	New Zealand	Aug. 2008–July 2011	21	53	5 (9)	80 ± 7	30 (57)	26 ± 16	6 ± 3	17 (32)	8 (15)	5 (9)
Muñoz-García et al. (44)	2012	Obs. (single)	Spain	April 2008–May 2011	ND	174	48 (28)	79 ± 7	65 (37)	19 ± 10	7 ± 5	56 (32)	30 (17)	29 (17)
Saia et al. (45)	2012	Obs. (multi.)	Italy	Feb. 2008–Oct. 2010	1	60	17 (28)	82 ± 6	26 (43)	23 ± 13	9 ± 7	ND	9 (15)	11 (18)
Salinas et al. (46)	2012	Obs. (single)	Spain	ND	1	130	3 (2)	84 ± ND	13 (38)	23 ± ND	ND	17 (50)	ND	ND
Schroeter et al. (47)	2012	Obs. (single)	Germany	2008–2009	ND	88	32 (36)	80 ± 6	ND	23 ± 12	ND	28 (32)	7 (8)	6 (7)
Stangl et al. (48)	2012	Obs. (single)	Germany	July 2009–July 2011	3	100	20 (20)	79 ± 8	42 (42)	20 ± 15	ND	19 (19)	ND	ND
Ledwoch et al. (49)	2013	Obs. (multi.)	Germany	Jan. 2009–June 2010	1	1,147	386 (34)	82 ± 6	468 (41)	20 ± 13	ND	277 (24)	ND	ND
Mouillet et al. (50)	2013	Obs. (single)	France	Dec. 2007–Jan. 2011	10	79	21 (27)	82 ± 17	24 (31)	23 ± 10	ND	20 (25)	16 (20)	7 (9)
Simms et al. (51)	2013	Obs. (single)	UK	May 2008–Dec. 2010	ND	100	17 (17)	81 ± 6	48 (48)	ND	ND	29 (29)	ND	ND
van der Boon et al. (52)	2013	Obs. (single)	Netherlands	Nov. 2005–Feb. 2011	12	167	36 (22)	81 ± 7	77 (46)	13 (8-19)	ND	41 (25)	14 (8)	17 (10)

Values are n (%), mean ± SD, or median (interquartile range) as appropriate. *Follow-up is reported as mean or median as given by the authors.

AF = atrial fibrillation; EuroSCORE = European System for Cardiac Operative Risk Evaluation; LBBB = left bundle branch block; multi. = multicenter; ND = no data; Obs. = observational; PPM = permanent pacemaker; RBBB = right bundle branch block; STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality; TAVR = transcatheter aortic valve replacement; UK = United Kingdom.

for eligibility (Fig. 1). Finally, we identified 235 studies that reported the incidence of PPM implantation after TAVR, whereas 41 studies (9,11,12,15-52) fulfilled our pre-specified inclusion criteria to be considered in our analysis (Table 1).

STUDY, PARTICIPANTS, AND PROCEDURAL CHARACTERISTICS. All of the studies were observational, and most included patients who had undergone TAVR in a single center (26 of 41 studies; 63%) (Table 1). Three studies were conducted in non-European countries (34,37,43). Studies were published between 2009 and 2013, and patient recruitment occurred between 2005 and 2011. Follow-up varied from 0.2 to 12 months, although 1 study of limited sample size reported mid-term follow-up to 21 months.

Overall, 11,210 patients were evaluated in 41 studies, and 1,917 (17%) received a PPM after TAVR. The incidence of PPM implantation after the intervention ranged from 2% to 51% in individual studies (for MCRS, median 28% [interquartile range: 24% to 35%]; for ESV, 6% [interquartile range: 5% to 7%]). The mean age ranged between 79 and 84 years, and men and women were enrolled equally (46% and 54%, respectively). Pre-procedural risk was assessed by the logistic EuroSCORE or the STS-PROM score in the majority of studies, although in 4 studies, the authors did not report any relevant information. Information on rhythm and conductance disturbances at baseline, such as AF, LBBB, or RBBB, was incompletely recorded in 25% (1,998 of 8,101), 12% (348 of 2,964), and 10% (269 of 2,802) of the patients, respectively.

The implanted devices and preferred access routes that had been used in each study are summarized in Table 2. MCRS was used exclusively in 18 studies (n = 2,356) and ESV in 10 (n = 2,735), whereas both prostheses were available in 13 studies (n = 6,119). No other devices were used. The transfemoral (73%) or transapical (23%) approach was preferred over others (4% for direct aortic or subclavian access). Transcarotid valve implantation was not reported in any of the included studies.

INDICATIONS FOR PPM IMPLANTATION. Indications for PPM implantation varied across the studies (Online Table 1). Complete AV block after TAVR was the most commonly reported indication for permanent pacing, whereas the authors did not report the reason(s) for PPM implantation in 14 studies.

DATA SYNTHESIS. Fourteen different predictors were eligible for the analysis (Table 3), and 2 or more nonoverlapping datasets were available for 11 of them. The number of patients with PPM implantation after TAVR (n = 1,917) for each predictor of interest as given in each study and enabled the calculation of crude RRs is summarized in Online Table 2.

The aggregate risk of PPM implantation after intervention in the overall population irrespective of type of valve was increased in men compared with women (RR: 1.23; 95% CI: 1.10 to 1.38) (Fig. 2, Online Fig. 1). Baseline electrocardiographic changes, first-degree AV block (RR: 1.52; 95% CI: 1.15 to 2.01), left anterior hemiblock (RR: 1.62; 95% CI: 1.17 to 2.25), and RBBB (RR: 2.89; 95% CI: 2.36 to 3.54), as well as intraprocedural AV block (RR: 3.49; 95% CI: 2.49 to 4.89), were significantly associated with PPM implantation. Statistical heterogeneity was low to moderate, with I^2 estimates ranging between 0% and 44%. Based on data derived from 9 studies, implantation of MCRS was associated with a 2.5-fold increased risk of PPM implantation compared with ESV (RR: 2.54; 95% CI: 2.08 to 3.12) in the overall population, with low statistical heterogeneity across the studies (I^2 of 14%). No difference in risk of PPM implantation was identified for patients with AF, LBBB, and preserved left ventricular ejection fraction at baseline. Only single datasets were available for advanced age (>80 years), left posterior hemiblock, and prolonged PR interval (>200 ms), and no significant associations were found. In a sensitivity analysis restricted to large studies of ≥200 patients (n = 13 studies), results remained consistent with the main findings (Online Table 3).

Male sex (RR: 1.29; 95% CI: 1.07 to 1.56), first-degree AV block (RR: 1.65; 95% CI: 1.22 to 2.23), left anterior hemiblock (RR: 1.64; 95% CI: 1.13 to 2.40), and RBBB (RR: 2.72; 95% CI: 2.14 to 3.45) remained significant predictors of PPM implantation when only patients who received the MCRS bioprosthesis were considered (Fig. 3, Online Fig. 2). I^2 indicated moderate heterogeneity only for RBBB (I^2=50%). The summary point estimate suggested a lower risk of permanent pacing with the transfemoral access route (compared with trans-subclavian), but the difference was not nominally significant given the sparse data (RR: 0.54; 95% CI: 0.28 to 1.04; p = 0.07).

Among the subgroup of patients with ESV implantation, the available data for evaluation of the selected predictors were limited. Sex (male), AF (at baseline), and access route (transarterial vs. transapical) did not appear to significantly increase the risk of PPM implantation (Fig. 4, Online Fig. 3), but 95% CIs were wide. Findings were based on datasets from 2, 3, and 7 studies, respectively.

TABLE 2 Implanted Valves and Access Site Across Studies

First Author (Ref. #)	ESV				MCRS			
	Any	Femoral	Apical	Other*	Any	Femoral	Apical	Other*
Himbert et al. (15)	75 (100)	51 (68)	24 (32)	No	No	No	No	No
Thielmann et al. (16)	39 (100)	15 (38)	24 (62)	No	No	No	No	No
Attias et al. (17)	72 (87)	72 (87)	No	No	11 (13)	11 (13)	No	No
Bleiziffer et al. (18)	36 (23)	4 (3)	32 (20)	No	123 (77)	112 (70)	5 (3)†	6 (4)
Eltchaninoff et al. (9)	166 (68)	95 (39)	71 (29)	No	78 (32)	66 (27)	No	12 (5)
Baan et al. (19)	No	No	No	No	29 (100)	29 (100)	No	No
Erkapic et al. (20)	14 (28)	No	14 (28)	No	36 (72)	36 (72)	No	No
Ewe et al. (21)	147 (100)	75 (51)	72 (49)	No	No	No	No	No
Ferreira et al. (22)	No	No	No	No	32 (100)	32 (100)	No	No
Godino et al. (23)	79 (58)	61 (45)	15 (11)	3 (2)	28 (43)	16 (34)	No	12 (9)
Haworth et al. (24)	No	No	No	No	33 (100)	33 (100)	No	No
Petronio et al. (25)	No	No	No	No	514 (100)	460 (89)	No	54 (11)
Piazza et al. (26)	No	No	No	No	91 (100)	91 (100)	No	No
Rodés-Cabau et al. (27)	339 (100)	162 (48)	177 (52)	No	No	No	No	No
Roten et al. (28)	26 (39)	9 (14)	17 (25)	No	41 (61)	41 (61)	No	No
Thomas et al. (29)	1,038 (100)	463 (45)	575 (55)	No	No	No	No	No
Bosmans et al. (30)	187 (57)	99 (30)	88 (27)	No	141 (43)	133 (41)	No	8 (2)
D'Ancona et al. (31)	322 (100)	No	322 (100)	No	No	No	No	No
Ewe et al. (32)	104 (100)	45 (43)	59 (57)	No	No	No	No	No
Fraccaro et al. (33)	No	No	No	No	64 (100)	60 (94)	No	4 (6)
Guetta et al. (34)	No	No	No	No	70 (100)	70 (100)	No	No
Khawaja et al. (12)	No	No	No	No	243 (100)‡	ND	No	ND
Lefèvre et al. (35)	130 (100)	69 (53)	61 (47)	No	No	No	No	No
Akin et al. (36)	No	No	No	No	45 (100)	45 (100)	No	No
Bagur et al. (37)	411 (100)	223 (54)	188 (46)	No	No	No	No	No
Calvi et al. (38)	No	No	No	No	162 (100)	162 (100)	No	No
Chorianopoulos et al. (39)	No	No	No	No	130 (100)	130 (100)	No	No
De Carlo et al. (40)	No	No	No	No	275 (100)‡	ND	No	ND
Fraccaro et al. (41)	ND§	ND	ND	ND	ND§	ND	ND	ND
Gilard et al. (42)	2,107 (67)	ND	ND	ND	1,043 (33)	ND	ND	ND
Hayashida et al. (11)	222 (85)	138 (53)	83 (31)	1 (1)	38 (15)	31 (12)	No	7 (3)
Liang et al. (43)	15 (28)	9 (17)	6 (11)	No	38 (72)	38 (72)	No	No
Muñoz-García et al. (44)	No	No	No	No	174 (100)	156 (90)	No	18 (10)
Saia et al. (45)	No	No	No	No	60 (100)	49 (82)	No	11 (18)
Salinas et al. (46)	34 (100)	31 (91)	3 (9)	No	No	No	No	No
Schroeter et al. (47)	No	No	No	No	88 (100)	88 (100)	No	No
Stangl et al. (48)	17 (17)	17 (17)	No	No	83 (83)	83 (83)	No	No
Ledwoch et al. (49)	232 (20)	ND	ND	ND	915 (80)	ND	ND	ND
Mouillet et al. (50)	No	No	No	No	79 (100)	79 (100)	No	No
Simms et al. (51)	No	No	No	No	100 (100)	100 (100)	No	No
van der Boon et al. (52)	No	No	No	No	167 (100)	162 (97)	No	5 (3)

Values are n (%). *Including transaortic and/or trans-subclavian access. †Authors reported that transapical implantation of the MCRS was approved by the institutional ethics committee. ‡Transfemoral and subclavian access were used. §Both bioprostheses were implanted via an arterial retrograde (transfemoral, trans-subclavian, or transaortic) approach or via an antegrade transapical approach. The authors did not provide further details.

ESV = Edwards SAPIEN Valve; MCRS = Medtronic CoreValve Revalving System; ND = no data.

DISCUSSION

Our findings suggest that male sex, pre-procedural evidence of abnormal AV conduction (including first-degree AV block, left anterior hemiblock, and RBBB), and intraprocedural AV block indicate an increased risk of PPM implantation after TAVR for patients receiving any type of prosthesis, although the risk of PPM implantation was 2.5-fold higher in patients receiving the MCRS than in those receiving the ESV in an unadjusted analysis. These variables remained significant predictors of permanent pacing among patients with MCRS bioprosthesis.

TABLE 3 Extracted Predictors Across Studies

Predictor (Ref. #)	Number of Studies
Age (>80 yrs) (49)	1
Sex (male) (11,18,19,28,31,33,36-38,40,44,45,48-52)	17
Atrial fibrillation (18-20,28,31,37-39,44,46,47,49-52)	15
First-degree AV block (9,18,37-40)	6
Left anterior hemiblock (20,37,38,40,52)	5
Left posterior hemiblock (52)	1
Intraprocedural AV block (18,44)	2
LBBB (9,12,18-20,24,28,37-40,44,45,47,50,52)	16
RBBB (12,18-20,22,24,26,28,34,37,39,40,44,45,47,50,52)	17
PR interval (>200 ms) (20)	1
MCRS (vs. ESV) (17,18,20,23,28,30,42,43,49)	9
Preserved LVEF (21,41,44,51)	4
Access route (arterial vs. apical): ESV (9,15,16,27-29,32,35,37)	9
Access route (femoral vs. subclavian): MCRS (25,33,45)	3

AV = atrioventricular; ESV = Edwards SAPIEN Valve; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; MCRS = Medtronic CoreValve Revalving system; RBBB = right bundle branch block.

Identification of patients at increased risk of PPM implantation after TAVR is of great clinical importance to prevent AV-block-related complications, including syncope, exercise intolerance, heart failure, and sudden death. As previously demonstrated, patients with AV conduction disturbances after TAVR are prone to prolonged hospitalization and use of in-hospital continuous telemetry, both of which result in a considerable increase of overall cost of the TAVR procedure (53). Moreover, there are concerns that patients who require PPM may not derive the same benefit as patients without PPM because of loss of AV synchrony, lack of physiological rate control, and right ventricular stimulation (54,55).

Evidence of sex-related differences in survival and common complications after TAVR intervention has been conflicted in recently published studies (56-58). In the present report, men had a higher risk for PPM implantation. Male patients undergoing TAVR tend to have more comorbidities and higher

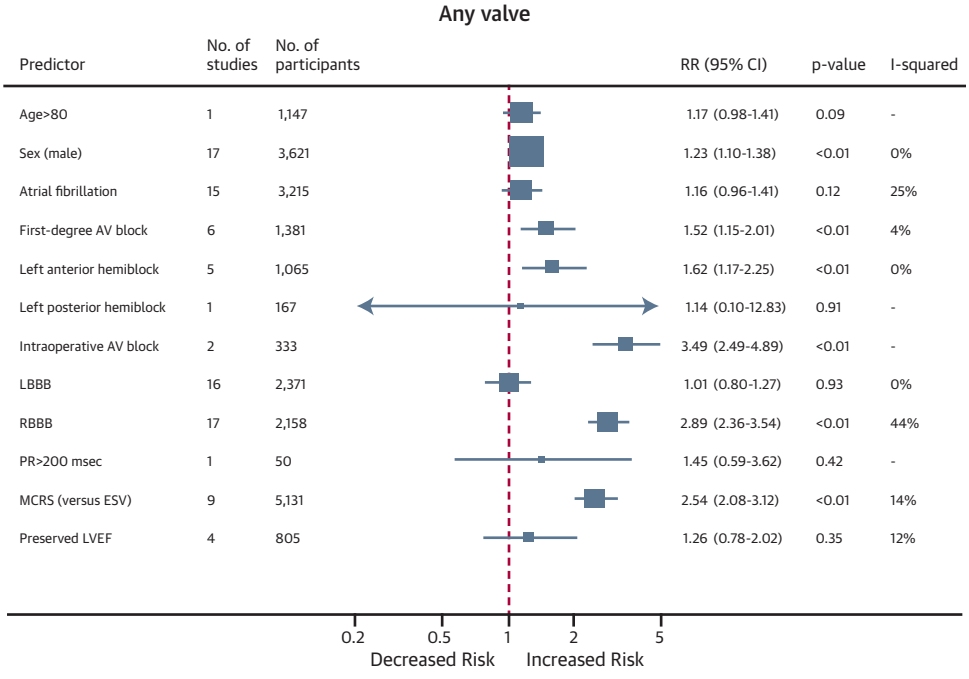


FIGURE 2 Summary RRs for Each Predictor of PPM Implantation After TAVR (Any Valve)

Forest plot of summary crude risk ratios (RRs) of each assessed predictor for patients receiving the Medtronic CoreValve Revalving System (MCRS) or Edwards SAPIEN valve (ESV) prosthesis. Heterogeneity estimates (I^2) are given for those predictors for which datasets from 2 or more studies were available. AV = atrioventricular; CI = confidence interval; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; PPM = permanent pacemaker; RBBB = right bundle branch block; TAVR = transcatheter aortic valve replacement.

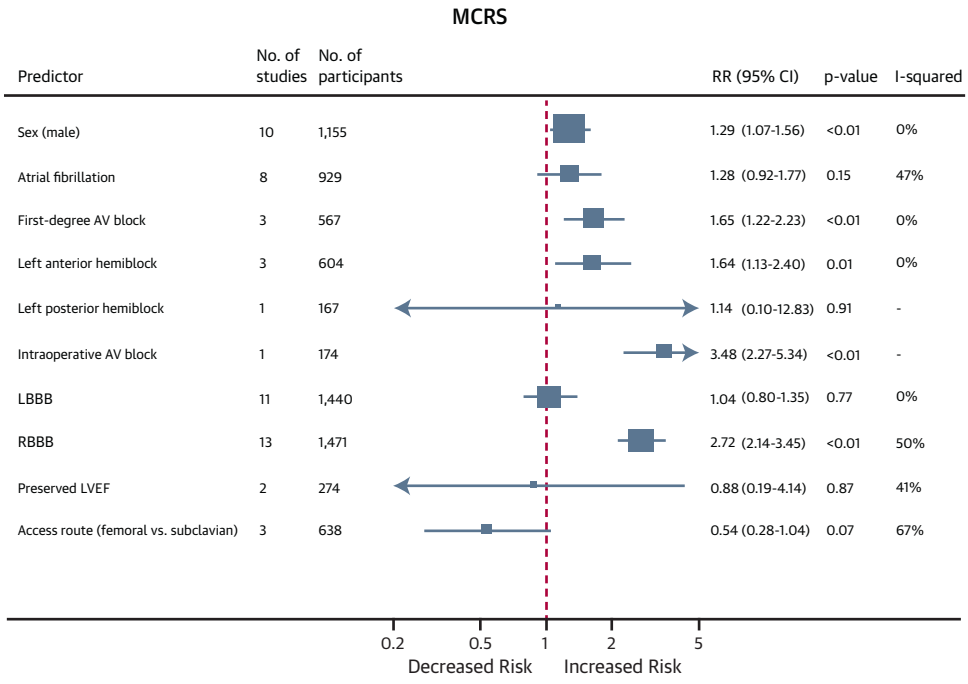


FIGURE 3 Summary RRs for Each Predictor of PPM Implantation After TAVR (MCRS Only)

Forest plot of summary crude RRs of each assessed predictor for patients receiving the MCRS prosthesis. Heterogeneity estimates (I^2) are given for those predictors for which datasets from 2 or more studies were available. Abbreviations as in Figure 2.

procedural risks, although they also receive larger bioprostheses, which may have an impact on AV conduction (11,58).

Previous studies have documented a significant increase in the frequency of LBBB after TAVR, which indicates direct injury of the intraventricular conduction system during valve implantation (59,60). As a result, any additional damage to the conduction system in patients with AV conduction abnormalities before intervention may lead to complete AV block. In our meta-analysis, patients with RBBB, first-degree AV block, or left anterior hemiblock at baseline were at higher risk for PPM implantation after the intervention. AV conduction disturbances and a subsequent requirement for PPM are more common after MCRS than ESV implantation (4,59), an observation from single studies that was validated in our meta-analysis. The increased risk of AV block with MCRS has been attributed to the valve design (self-expanding vs. balloon-expandable) and the potential of a deeper implantation into the left ventricular outflow tract. This may result in more injury to the AV node and left bundle branches, which may be delayed because of the self-expanding nature of the prosthesis and tissue edema (12).

The reported indications for permanent pacing were inconsistent across the studies, resulting in a lack of consensus for early PPM implantation after TAVR. Although PPM is indicated for asymptomatic patients with acquired third- or second-degree type 2 AV block (61), absolute and relative indications for TAVR patients have not been established. In patients with aortic stenosis and severe comorbidities undergoing TAVR, a somewhat more aggressive approach may have been adopted, although a proportion of AV conduction disturbances after the intervention have been shown to recover over time (10,34,62). Currently, consensus statements suggest continuous post-procedural monitoring in all patients early after TAVR, although high-risk patients (as defined by pre-existing or new AV conduction abnormalities) may require longer monitoring (2). As a consequence, a proportion of patients may have unnecessarily undergone “prophylactic”

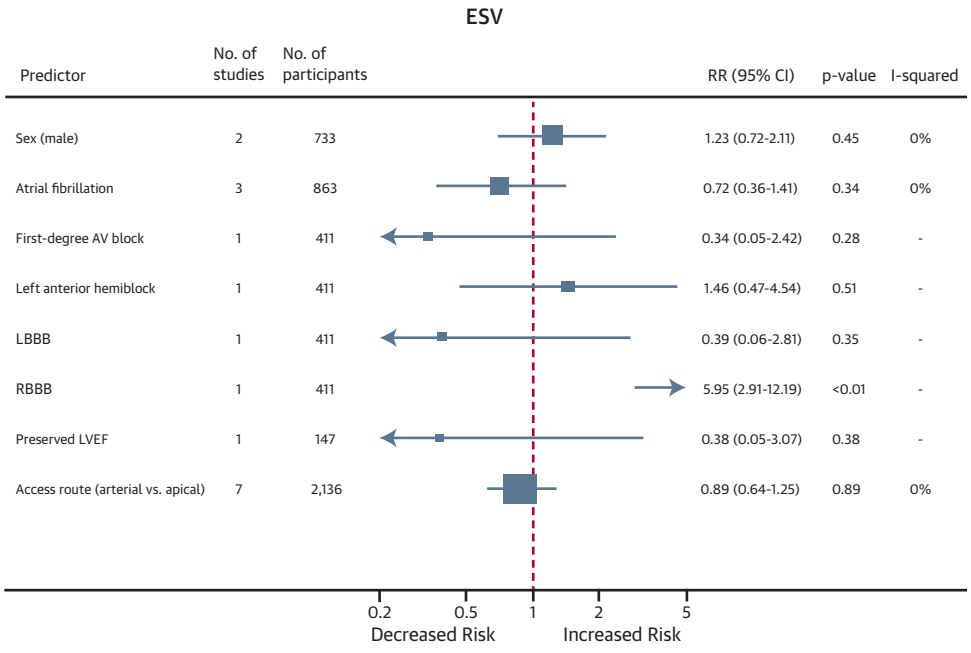


FIGURE 4 Summary RRs for Each Predictor of PPM Implantation After TAVR (ESV Only)

Forest plot of summary crude RRs of each assessed predictor for patients receiving the ESV prosthesis. Heterogeneity estimates (I^2) are given for those predictors for which datasets from 2 or more studies were available. Abbreviations as in Figure 2.

PPM implantation in the absence of an absolute indication.

STUDY LIMITATIONS. Several limitations should be acknowledged. We looked into a considerable number of clinically meaningful variables, but we did not aim to systematically examine all recently discussed predictors. However, even among the selected predictors, the available data were sparse. Long-term follow-up data were not reported in the majority of the studies, and clinical outcomes related to PPM also were missing. Thus, we could not address the clinical long-term effectiveness of PPM implantation in these high-risk patients. PPM implantation after TAVR does not represent a surrogate marker of AV conduction disturbances but may be influenced by several logistic and economic factors that were not addressed in our analysis. Finally, adjusted estimates were unavailable for most of the predictors, and we used crude RRs only. Confounding could therefore have influenced our results, and we were unable to determine the independent role of individual predictors after appropriate adjustment.

CONCLUSIONS

The present study provides evidence for a number of variables that serve as predictors of PPM implantation after TAVR in high-risk patients receiving 1 of the 2 most widely used devices. Future research should focus on collaborative efforts to validate previously identified predictors and to explore the role of others, and well-designed large-scale studies that include different devices should focus on long-term clinical outcomes. Given the clinical and economic impact of such interventions (53,63), clinicians should appropriately risk-stratify patients. Well-established predictors can be useful tools to guide clinical decision making before and after TAVR (appropriate device selection and decision for permanent pacing, respectively) and subsequently improve clinical outcomes.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE 1: Indications for permanent pacing in patients undergoing TAVR have not been clearly established, and criteria have varied across studies.

COMPETENCY IN MEDICAL KNOWLEDGE 2: Male sex, abnormal AV conduction before the procedure, and intraprocedural AV block identify patients more likely to require PPM implantation after TAVR with the Edwards SAPIEN or Medtronic CoreValve prosthesis.

COMPETENCY IN PATIENT CARE: Identification of patients at increased risk for PPM implantation after TAVR is of great clinical importance to reduce the length of hospitalization and to prevent complications related to AV-block conduction disturbances.

TRANSLATIONAL OUTLOOK: Better understanding of the factors that lead to development of complete heart block among patients undergoing TAVR could identify appropriate candidates for prophylactic permanent pacemaker implantation and improve clinical outcomes.

REFERENCES

1. Makkar RR, Fontana GP, Jilaihawi H, et al. Transcatheter aortic-valve replacement for inoperable severe aortic stenosis (published correction appears in N Engl J Med 2012;367:881). N Engl J Med 2012;366:1696–704.

2. Holmes DR Jr., Mack MJ, Kaul S, et al. 2012 ACCF/AATS/SCAI/STS expert consensus document on transcatheter aortic valve replacement: developed in collaboration with the American Heart Association, American Society of Echocardiography, European Association for Cardio-Thoracic Surgery, Heart Failure Society of America, Mended Hearts, Society of Cardiovascular Anesthesiologists, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular Magnetic Resonance. J Am Coll Cardiol 2012;59:1200–54.

3. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med 2011;364:2187–98.

4. Khatri PJ, Webb JG, Rodés-Cabau J, et al. Adverse effects associated with transcatheter aortic valve implantation: a meta-analysis of contemporary studies. Ann Intern Med 2013;158:35–46.

5. Calvi V, Puzzangara E, Pruiti GP, et al. Early conduction disorders following percutaneous aortic valve replacement. Pacing Clin Electrophysiol 2009;32 Suppl 1:S126–30.

6. Steinberg BA, Harrison JK, Frazier-Mills C, Hughes GC, Piccini JP. Cardiac conduction system disease after transcatheter aortic valve replacement. Am Heart J 2012;164:664–71.

7. Webb JG, Altwegg L, Boone RH, et al. Transcatheter aortic valve implantation: impact on clinical and valve-related outcomes. Circulation 2009;119:3009–16.

8. Laynez A, Ben-Dor I, Barbash IM, et al. Frequency of conduction disturbances after Edwards SAPIEN percutaneous valve implantation. Am J Cardiol 2012;110:1164–8.

9. Eltchaninoff H, Prat A, Gilard M, et al., and on behalf of the FRANCE Registry Investigators. Transcatheter aortic valve implantation: early results of the FRANCE (FRench Aortic National CoreValve and Edwards) registry. Eur Heart J 2011;32:191–7.

10. Leon MB, Smith CR, Mack M, et al., for the PARTNER Trial Investigators. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med 2010;363:1597–607.

11. Hayashida K, Morice MC, Chevalier B, et al. Sex-related differences in clinical presentation and outcome of transcatheter aortic valve implantation for severe aortic stenosis. J Am Coll Cardiol 2012;59:566–71.

12. Khawaja MZ, Rajani R, Cook A, et al. Permanent pacemaker insertion after CoreValve transcatheter aortic valve implantation: incidence and contributing factors (the UK CoreValve Collaborative). Circulation 2011;123:951–60.

13. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986;7:177–88.

14. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med 2002;21:1539–58.

15. Himbert D, Descoutures F, Al-Attar N, et al. Results of transfemoral or transapical aortic valve implantation following a uniform assessment in high-risk patients with aortic stenosis. J Am Coll Cardiol 2009;54:303–11.

16. Thielmann M, Wendt D, Eggebrecht H, et al. Transcatheter aortic valve implantation in patients with very high risk for conventional aortic valve replacement. Ann Thorac Surg 2009;88:1468–74.

17. Attias D, Himbert D, Ducrocq G, et al. Immediate and mid-term results of transfemoral aortic valve implantation using either the Edwards Sapien transcatheter heart valve or the Medtronic CoreValve System in high-risk patients with aortic stenosis. Arch Cardiovasc Dis 2010;103:236–45.

18. Bleiziffer S, Ruge H, Hörer J, et al. Predictors for new-onset complete heart block after transcatheter aortic valve implantation. J Am Coll Cardiol Intv 2010;3:524–30.

19. Baan J Jr., Yong ZY, Koch KT, et al. Factors associated with cardiac conduction disorders and permanent pacemaker implantation after percutaneous aortic valve implantation with the CoreValve prosthesis. Am Heart J 2010;159:497–503.

20. Erkapic D, Kim WK, Weber M, et al. Electrocardiographic and further predictors for permanent pacemaker requirement after transcatheter aortic valve implantation. Europace 2010;12:1188–90.

21. Ewe SH, Ajmone Marsan N, Pepi M, et al. Impact of left ventricular systolic function on clinical and echocardiographic outcomes following transcatheter aortic valve implantation for severe aortic stenosis. Am Heart J 2010;160:1113–20.

22. Ferreira ND, Caeiro D, Adão L, et al. Incidence and predictors of permanent pacemaker requirement after transcatheter aortic valve implantation with a self-expanding bioprosthesis. Pacing Clin Electrophysiol 2010;33:1364–72.

23. Godino C, Maisano F, Montorfano M, et al. Outcomes after transcatheter aortic valve implantation with both Edwards-SAPIEN and CoreValve devices in a single center: the Milan experience. J Am Coll Cardiol Intv 2010;3:1110–21.

24. Haworth P, Behan M, Khawaja M, et al. Predictors for permanent pacing after transcatheter aortic valve implantation. Catheter Cardiovasc Interv 2010;76:751–6.

25. Petronio AS, De Carlo M, Bedogni F, et al. Safety and efficacy of the subclavian approach for transcatheter aortic valve implantation with the CoreValve revalving system. Circ Cardiovasc Interv 2010;3:359–66.

26. Piazza N, Nuis RJ, Tzikas A, et al. Persistent conduction abnormalities and requirements for pacemaking six months after transcatheter aortic valve implantation. EuroIntervention 2010;6:475–84.

27. Rodés-Cabau J, Webb JG, Cheung A, et al. Transcatheter aortic valve implantation for the treatment of severe symptomatic aortic stenosis in patients at very high or prohibitive surgical risk: acute and late outcomes of the multicenter Canadian experience. J Am Coll Cardiol 2010;55:1080–90.

28. Roten L, Wenaweser P, Delacrétaz E, et al. Incidence and predictors of atrioventricular

conduction impairment after transcatheter aortic valve implantation. Am J Cardiol 2010;106:1473–80.

29. Thomas M, Schymik G, Walther T, et al. Thirty-day results of the SAPIEN aortic Bioprosthesis European Outcome (SOURCE) Registry: a European registry of transcatheter aortic valve implantation using the Edwards SAPIEN valve. Circulation 2010;122:62–9.

30. Bosmans JM, Kefer J, De Bruyne B, et al., for the Belgian TAVI Registry Participants. Procedural, 30-day and one year outcome following CoreValve or Edwards transcatheter aortic valve implantation: results of the Belgian national registry. Interact Cardiovasc Thorac Surg 2011;12:762–7.

31. D'Ancona G, Pasic M, Unbehaun A, Hetzer R. Permanent pacemaker implantation after transapical transcatheter aortic valve implantation. Interact Cardiovasc Thorac Surg 2011;13:373–6.

32. Ewe SH, Delgado V, Ng AC, et al. Outcomes after transcatheter aortic valve implantation: transfemoral versus transapical approach. Ann Thorac Surg 2011;92:1244–51.

33. Fraccaro C, Buja G, Tarantini G, et al. Incidence, predictors, and outcome of conduction disorders after transcatheter self-expandable aortic valve implantation. Am J Cardiol 2011;107:747–54.

34. Guetta V, Goldenberg G, Segev A, et al. Predictors and course of high-degree atrioventricular block after transcatheter aortic valve implantation using the CoreValve Revalving System. Am J Cardiol 2011;108:1600–5.

35. Lefèvre T, Kappetein AP, Wolner E, et al., on behalf of the PARTNER EU Investigator Group. One year follow-up of the multi-centre European PARTNER transcatheter heart valve study. Eur Heart J 2011;32:148–57.

36. Akin I, Kische S, Paranskaya L, et al. Predictive factors for pacemaker requirement after transcatheter aortic valve implantation. BMC Cardiovasc Disord 2012;12:87.

37. Bagur R, Rodés-Cabau J, Gurvitch R, et al. Need for permanent pacemaker as a complication of transcatheter aortic valve implantation and surgical aortic valve replacement in elderly patients with severe aortic stenosis and similar baseline electrocardiographic findings. J Am Coll Cardiol Intv 2012;5:540–51.

38. Calvi V, Conti S, Pruiti GP, et al. Incidence rate and predictors of permanent pacemaker implantation after transcatheter aortic valve implantation with self-expanding CoreValve prosthesis. J Interv Card Electrophysiol 2012;34:189–95.

39. Chorianopoulos E, Krumsdorf U, Pleger ST, Katus HA, Bekeredjian R. Incidence of late occurring bradyarrhythmias after TAVI with the self-expanding CoreValve aortic bioprosthesis. Clin Res Cardiol 2012;101:349–55.

40. De Carlo M, Giannini C, Bedogni F, et al. Safety of a conservative strategy of permanent pacemaker implantation after transcatheter aortic CoreValve implantation. Am Heart J 2012;163:492–9.

41. Fraccaro C, Al-Lamee R, Tarantini G, et al. Transcatheter aortic valve implantation in patients with severe left ventricular dysfunction: immediate and mid-term results, a multicenter study. Circ Cardiovasc Interv 2012;5:253–60.

42. Gilard M, Eltchaninoff H, Iung B, et al., for the FRANCE 2 Investigators. Registry of transcatheter aortic-valve implantation in high-risk patients. N Engl J Med 2012;366:1705–15.

43. Liang M, Devlin G, Pasupati S. The incidence of transcatheter aortic valve implantation-related heart block in self-expandable Medtronic CoreValve and balloon-expandable Edwards valves. J Invasive Cardiol 2012;24:173–6.

44. Muñoz-García AJ, Hernández-García JM, Jiménez-Navarro MF, et al. Factors predicting and having an impact on the need for a permanent pacemaker after CoreValve prosthesis implantation using the new Accutrak delivery catheter system. J Am Coll Cardiol Intv 2012;5:533–9.

45. Saia F, Lemos PA, Bordoni B, et al. Transcatheter aortic valve implantation with a self-expanding nitinol bioprosthesis: prediction of the need for permanent pacemaker using simple baseline and procedural characteristics. Catheter Cardiovasc Interv 2012;79:712–9.

46. Salinas P, Moreno R, Calvo L, et al. Clinical and prognostic implications of atrial fibrillation in patients undergoing transcatheter aortic valve implantation. World J Cardiol 2012;4:8–14.

47. Schroeter T, Linke A, Haensig M, et al. Predictors of permanent pacemaker implantation after Medtronic CoreValve bioprosthesis implantation. Europace 2012;14:1759–63.

48. Stangl V, Baldenhofer G, Knebel F, et al. Impact of gender on three-month outcome and left ventricular remodeling after transfemoral transcatheter aortic valve implantation. Am J Cardiol 2012;110:884–90.

49. Ledwoch J, Franke J, Gerckens U, et al., on behalf of the German Transcatheter Aortic Valve Interventions Registry Investigators. Incidence and predictors of permanent pacemaker implantation following transcatheter aortic valve implantation: analysis from the German Transcatheter Aortic Valve Interventions Registry. Catheter Cardiovasc Interv 2013;82:E569–77.

50. Mouillet G, Lellouche N, Lim P, et al. Patients without prolonged QRS after TAVI with CoreValve device do not experience high-degree atrio-ventricular block. Catheter Cardiovasc Interv 2013;81:882–7.

51. Simms AD, Hogarth AJ, Hudson EA, et al. Ongoing requirement for pacing post-transcatheter aortic valve implantation and surgical aortic valve replacement. Interact Cardiovasc Thorac Surg 2013;17:328–33.

52. van der Boon RM, Van Mieghem NM, Theuns DA, et al. Pacemaker dependency after transcatheter aortic valve implantation with the self-expanding Medtronic CoreValve System. Int J Cardiol 2013;168:1269–73.

53. Chevreul K, Brunn M, Cadier B, et al., on behalf of the FRANCE Registry Investigators. Cost of transcatheter aortic valve implantation and factors associated with higher hospital stay cost in patients of the FRANCE (FRench Aortic National CoreValve and Edwards) registry. Arch Cardiovasc Dis 2013;106:209–19.

54. Curtis AB, Worley SJ, Adamson PB, et al., for the Biventricular versus Right Ventricular Pacing in Heart Failure Patients with Atrioventricular block (BLOCK HF) Trial Investigators. Biventricular pacing for atrioventricular block and systolic dysfunction. N Engl J Med 2013;368:1585–93.

55. Tops LF, Schalij MJ, Bax JJ. The effects of right ventricular apical pacing on ventricular function and dyssynchrony implications for therapy. J Am Coll Cardiol 2009;54:764–76.

56. D'Ascenzo F, Gonella A, Moretti C, et al. Gender differences in patients undergoing TAVI: a multicentre study. EuroIntervention 2013;9:367–72.

57. Onorati F, D'Errigo P, Barbanti M, et al., on behalf of the OBSERVANT Research Group. Different impact of sex on baseline characteristics and major periprocedural outcomes of transcatheter and surgical aortic valve interventions: results of the multicenter Italian OBSERVANT Registry. J Thorac Cardiovasc Surg 2013.

58. Buja P, Napodano M, Tamburino C, et al., Italian Multicenter CoreValve Registry Investigators. Comparison of variables in men versus women undergoing transcatheter aortic valve implantation for severe aortic stenosis (from Italian Multicenter CoreValve registry). Am J Cardiol 2013;111:88–93.

59. Franzoni I, Latib A, Maisano F, et al. Comparison of incidence and predictors of left bundle branch block after transcatheter aortic valve implantation using the CoreValve versus the Edwards valve. Am J Cardiol 2013;112:554–9.

60. Piazza N, Onuma Y, Jesserun E, et al. Early and persistent intraventricular conduction abnormalities and requirements for pacemaking after percutaneous replacement of the aortic valve. J Am Coll Cardiol Intv 2008;1:310–6.

61. Brignole M, Auricchio A, Baron-Esquivias G, et al. 2013 ESC guidelines on cardiac pacing and cardiac resynchronization therapy: the Task Force on cardiac pacing and resynchronization therapy of the European Society of Cardiology (ESC): developed in collaboration with the European Heart Rhythm Association (EHRA). Europace 2013;15:1070–118.

62. Gutiérrez M, Rodés-Cabau J, Bagur R, et al. Electrocardiographic changes and clinical outcomes after transapical aortic valve implantation. Am Heart J 2009;158:302–8.

63. Simons CT, Cipriano LE, Shah RU, Garber AM, Owens DK, Hlatky MA. Transcatheter aortic valve replacement in nonsurgical candidates with severe, symptomatic aortic stenosis: a cost-effectiveness analysis. Circ Cardiovasc Qual Outcomes 2013;6:419–28.

KEY WORDS aortic stenosis, conduction disturbances, permanent pacemaker, predictor, transcatheter aortic valve implantation, transcatheter aortic valve replacement

APPENDIX For supplemental figures and tables, please see the online version of this article.