



Outcomes associated with pacemaker implantation following transcatheter aortic valve replacement: A nationwide cohort study

Nicolas Clementy, Arnaud Bisson, Alexandre Bodin, Julien Herbert, Thibaud Lacour, Christophe Saint Etienne, Bertrand Pierre, Pierre Deharo, Dominique Babuty, Laurent Fauchier

► To cite this version:

Nicolas Clementy, Arnaud Bisson, Alexandre Bodin, Julien Herbert, Thibaud Lacour, et al.. Outcomes associated with pacemaker implantation following transcatheter aortic valve replacement: A nationwide cohort study. Heart Rhythm, 2021, 18 (12), pp.2027-2032. 10.1016/j.hrthm.2021.06.1175 . hal-03654595

HAL Id: hal-03654595

<https://amu.hal.science/hal-03654595>

Submitted on 5 Jan 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

Title: Outcomes associated with pacemaker implantation following transcatheter aortic valve replacement. A nationwide cohort study.

Short title: Pacemaker following TAVR

Authors: Nicolas CLEMENTY, M.D., Ph.D.,¹ Arnaud BISSON, M.D.,¹ Alexandre BODIN, M.D.,¹ Julien HERBERT,^{1, 2} Thibaud LACOUR, M.D.,¹ Christophe SAINT ETIENNE, M.D.,¹ Bertrand PIERRE, M.D.,¹ Pierre DEHARO, M.D.,³ Dominique BABUTY, M.D., Ph.D.,¹ and Laurent FAUCHIER, M.D., Ph.D.¹

Affiliations:

¹ Service de Cardiologie, Centre Hospitalier Universitaire Trousseau et Faculté de Médecine, EA7505, Université de Tours, France.

² Service d'information médicale, d'épidémiologie et d'économie de la santé, Centre Hospitalier Universitaire et Faculté de Médecine, EA7505, Université de Tours, France.

³ Département de Cardiologie, Centre Hospitalier Universitaire Timone, Marseille, France, Inserm, Inra, C2VN, Marseille, France et Faculté de Médecine, Université Aix-Marseille, France.

Contributions: NC has drafted the manuscript; ABi, ABo, JH and LF have acquired and analyzed the data; TL, CSE, BP, PD and DB have contributed to significant revision of the manuscript.

Corresponding Author:

Dr Nicolas CLEMENTY

Address: Service de Cardiologie, Hôpital Trousseau, 37044 Tours, France

E-mail: nclementy@yahoo.fr

Word count (text, references, figure legends): 2,545

DECLARATIONS**Conflicts of interest and disclosures**

BP reports personal fees from Abbott, Biotronik, Boston Scientific and Microport. CSE reports honoraria from Abbott and Biotronik. LF reports consultant or speaker activities for Bayer, BMS/Pfizer, Boehringer Ingelheim, Medtronic, and Novartis. NC reports consultant activities for Medtronic and Boston Scientific. AB reports speaker activities for Medtronic. All other authors declare no competing interests.

Funding

None.

Acknowledgements

None.

CONDENSED ABSTRACT

In this retrospective analysis of 49,201 patients who underwent transcatheter aortic valvular replacement, using a 10-year nationwide administrative database, implantation of a pacemaker before or after the procedure was independently associated with a higher risk of death and hospitalization for heart failure.

ABSTRACT

Background: Conduction abnormalities following transcatheter aortic valve replacement (TAVR) may often require permanent pacemaker implantation (PPM).

Objective: We sought to evaluate outcomes associated with PPM after a TAVR procedure in a large nationwide level population.

Methods: Based on the administrative hospital-discharge database, incidence of all-cause death, cardiovascular death and hospitalization for heart failure (HF) were retrospectively collected, according to the presence or absence of PPM, in the first 30 days following all TAVR in France from 2010 to 2019.

Results: Among 520,662 patients hospitalized for aortic stenosis, 49,201 were treated with TAVR. A total of 29,422 patients had a follow-up ≥ 6 months (median 1.7 years), 22% already had PPM at baseline and 22% underwent PPM within the first 30 days post-TAVR procedure. Adjusted hazard ratios for the combined risk of all-cause death and hospitalization for HF, during the whole follow-up, were higher in both patients with a previous PPM and those implanted within 30 days [HR 1.12 [1.07-1.17] and 1.11 [1.06-1.16], respectively.

Conclusion: PPM at baseline and within 30 days post-TAVR are independently associated with higher mortality and HF hospitalization during follow-up.

KEYWORDS

Aortic stenosis; transcatheter aortic valve replacement; pacemaker; outcome; heart failure; pacing-induced cardiomyopathy.

INTRODUCTION

Transcatheter aortic valve replacement (TAVR) procedure has become an indispensable treatment in selected symptomatic patients presenting with aortic stenosis [1]. Conduction abnormalities following TAVR are commonly reported and may often require permanent pacemaker implantation (PPM), but little is known on its potential consequences on outcomes in this population [2]. Cardiac pacing is likely to reduce the risk of cardiac death related to severe bradycardia but may have deleterious effects on hemodynamic status and may also increase the risk of atrial fibrillation on a mid-term follow-up. We sought to evaluate outcomes associated with PPM after a TAVR procedure in the systematic analysis of a large-scale population of such patients seen at a nationwide level.

METHODS

Data collection

All patients admitted with aortic stenosis in France from January 2010 to June 2019 were screened using the national administrative PMSI database, through The French Data Protection Authority, covering hospital care from the entire French population, and as previously described [3,4]. The study was conducted retrospectively, with no impact on patients care. Data collection and management were approved by the Commission Nationale de l'Informatique et des Libertés, which ensures that all information remains confidential and anonymous, in compliance with the Declaration of Helsinki (authorization number 1897139).

Study population

From January 2010 to June 2019, a total of 520,662 patients with an age of 18 years or more were hospitalized with an aortic stenosis (ICD-10 codes: I350, I352, I060, and I062) as the principal (i.e., the health problem that justified admission to hospital), the related (i.e.,

potential chronic disease or health state during the hospital stay), or a significantly associated (i.e., comorbidity or associated complication) diagnosis. In this population, TAVR procedures were identified through one single procedure (CCAM code: DBLF001). Information regarding demographics, medical history, and events during hospitalization or follow-up was collected. PPI was identified using its CCAM codes, and a cut off at 30 days was used to define post-operative PPM, as currently used in the literature [5,6].

Outcomes

Patients were followed until June 2019 for the occurrence of outcomes, starting from date of TAVR procedure. Patients with a follow-up <6 months were excluded. Main outcomes were: all-cause death, cardiovascular death, hospitalization for heart failure (HF), and a combined endpoint of all-cause death and HF hospitalization [7]. Hospitalization was considered to be related to HF when HF was recorded as the main diagnosis. Secondary outcomes, potentially related to PPM, were: rehospitalization for new-onset atrial fibrillation (AF), infective endocarditis, worsening mitral regurgitation, and worsening tricuspid regurgitation.

Statistical analyses

Qualitative variables are described as frequency and percentages and quantitative variable as means \pm standard deviation (SD). Comparisons between groups were performed using chi-square tests for categorical variables and the Student *t* test or non-parametric Kruskal–Wallis test, as appropriate, for continuous variables. Incidence rates for outcomes in each group were estimated, and cumulative incidences curves were obtained using Kaplan Meier method. A Cox regression model on all baseline parameters described in **Table 1** was used to obtain adjusted hazard ratios (HR). A *p* value <0.05 was considered statistically significant. All analyses were performed using Enterprise Guide 7.1 (SAS Institute Inc., SAS Campus Drive, Cary, NC, USA) and STATA version 12.0 (Stata Corp, College Station, TX, USA).

RESULTS

Population

Among 49,201 patients, PPM at the time of or after the procedure was reported in 13,218 patients (26.9%) (**Supplemental Table 1**).

A total of 29,422 patients had a follow-up ≥ 6 months, or died earlier. This population included 6,362 patients (21.6%) who already had a pacemaker at baseline, and 6,549 (22.3%) who underwent PPM within the first 30 days post-TAVR procedure (**Table 1**). The latter were older, more likely to be male, had overall more comorbidities, and were more likely to be implanted with auto-expandable valves than those treated without PPM.

Main outcomes

Mean follow-up was 2.0 ± 1.5 years (median 1.7, interquartile range 0.9-2.9). Events recorded during follow-up are displayed in **Table 2**. All-cause death was recorded in 8,454 patients. Risk of all-cause death was higher both in the group with previous >PPM and with PPM during the first 30 days (HR 1.23 and 1.16, respectively; **Figure 1**). Rehospitalization for HF was recorded in 8,107 patients and risk was also higher both in the group with previous >PPM and with PPM during the first 30 days (HR 1.59 and 1.22, respectively; **Figure 2**). The incidence of cardiovascular death and of combined endpoint (death or rehospitalization for HF) was also higher in patients with PPM (**Supplemental Figure 1**).

After adjustment on all baseline parameters, PPM within 30 days after TAVR procedure was independently associated with higher overall mortality and HF hospitalization (**Table 3**). Previous PPM, prior to TAVR procedure, was also independently associated with a higher risk of rehospitalization for HF, but not a higher mortality. In the subgroup of patients with a left bundle branch block, PPM, not CRT, was independently associated with a higher rate of cardiovascular death (**Supplemental Table 2**).

Secondary outcomes

Results are reported in **Table 4** and **Supplemental Figure 2**. After adjustment, PPM before and after TAVR was independently associated with higher rates of rehospitalization for infective endocarditis, and previous PPM with worsening tricuspid regurgitation.

Of note, cumulative incidence of PPM in TAVR patients was significantly lower during the first 5 years of the study period, as compared with the last 5 years (**Supplemental Figure 3**).

DISCUSSION

Main results

Our study shows for the first time at a nationwide scale that: (1) PPM before or after TAVR procedure is associated with a higher rate of rehospitalization for HF; (2) PPM in the post-operative period following TAVR procedure independently predicts a higher risk of death of any cause; (3) PPM in TAVR patients is independently associated with a higher risk of major complications, especially infective endocarditis.

We report a rather high rate of PPM of 22% in the post-operative period following TAVR, as previously published [8]. The impact of PPM following TAVR remains unclear in the literature. All-cause mortality at 1 year in newly pacemaker implanted patients ranges between 15.5 and 26.3%, in line with the 14.7% yearly rate found in our study [9-14]. None of these studies found a significant association between PPM and overall mortality, nor a metanalysis on this particular subject [15]. Only the PARTNER study found a significant impact of PPM on outcomes with an increased rate of rehospitalization [13].

Both patients with a previous PPM and with a new PPM following TAVR had a worse outcome. Patients with underlying conduction system disease may have a higher risk of poor

outcomes and higher mortality than those with normal myocardial conduction. This includes conduction disease at the atrioventricular junction or the His-Purkinje system [16-18]. Thus, conduction system disease requiring pacemaker implantation may be a marker of more severe myocardial disease, which may in part explain some of our results.

It is recognized that up to 20% of individuals with baseline normal left ventricular systolic function will develop a significant drop in left ventricular ejection fraction within the first years following high-burden right ventricular pacing, i.e. pacing-induced cardiomyopathy (PICM) [19]. In post-TAVR patients requiring permanent pacing, ventricular dyssynchrony may be seen both in patients requiring chronic RV pacing, and in those with a persistent left bundle branch block (LBBB) in case of atrioventricular block resumption. The specific risk of PICM in the TAVR population is unknown and it was not possible to precisely evaluate this issue in our analysis but it should not be underestimated in this high-risk population with a preexisting valvular cardiac disease. Chronic RV pacing and persistent underlying LBBB may have long-term detrimental effects in this population. Indeed, recognized risks factors for PICM include an older age (83 years in our study), a male gender (50%), atrial fibrillation (46%), and a longer intrinsic QRS duration (31% of bundle branch block at baseline). In the PACE study, patients had already a significant deterioration of LV function at 12 months of ventricular apical pacing, especially those with diabetes (31% of patients in our study) and large QRS complexes (25% of patients in our study) [20].

Interestingly, both CRT implantation before and after TAVR were not associated with a higher risk of HF hospitalization in our study. Biventricular pacing might have prevented the development of PICM in these patients. PPM may also induce or worsen a tricuspid valvular

disease, for which CRT is usually ineffective [21]. Finally, the fact that balloon-expandable valves are associated with better outcomes than self-expanding ones might be partly explained by the fact they are also associated with lower rates of PPM [4]. The presence of clinically significant tricuspid regurgitation concomitant with severe aortic stenosis has been shown to be associated with a poor long-term outcome, regardless of the initial treatment strategy [22]. Finally, long-term complications associated with PPM, especially infections, may also account for the excess of morbidity and mortality observed in the PPM group in our study [23,24].

We are in need for more accurate screening algorithms determining optimal indications for PPM in the post-TAVR population, and evaluation of alternative pacing approaches when PPM cannot be avoided [25]. The higher risk of PPM with TAVR as compared with conventional surgery will also have to be taken into account in lower-risk patients [26].

Limitations

Beside the retrospective, observational nature of the study and its potential biases, it was also based on administrative data obtained and manually filled by physicians and administrators. However, the large scale of the database, and the fact it underlies reimbursement, are likely to compensate some of these potential biases. Analyses were restricted to the variables coded in the database, excluding for instance echocardiographic measurements or use of medications. Comparisons between groups might not be fully appropriate, as the presence of other missing confounding factors cannot be ruled out. Data on lead placement, device programming, or percentage of ventricular pacing were not available. As ventricular pacing burden may be directly related to the development of PICM, it is difficult to assert the relation with worse outcomes.

Conclusions

In patients with aortic stenosis treated with TAVR, our systematic analysis at a nationwide level found high rates of PPM. Both PPM at baseline and during the first 30 days post TAVR was associated with higher risks of death and rehospitalization for HF. Further studies are needed to see whether a strategy aiming at reducing the rate of PPM can improve outcomes in patients treated with TAVR.

REFERENCES

1. Nishimura RA, Otto CM, Bonow RO, et al. 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2017;70:252-89.
2. Auffret V, Puri R, Urena M, et al. Conduction Disturbances After Transcatheter Aortic Valve Replacement: Current Status and Future Perspectives. *Circulation*. 2017;136:1049-69.
3. Nguyen V, Michel M, Eltchaninoff H, et al. Implementation of Transcatheter Aortic Valve Replacement in France. *J Am Coll Cardiol*. 2018;71:1614-27.
4. Deharo P, Bisson A, Herbert J, et al. Impact of Sapien 3 Balloon-Expandable Versus Evolut R Self-Expandable Transcatheter Aortic Valve Implantation in Patients With Aortic Stenosis: Data From a Nationwide Analysis. *Circulation*. 2020;141:260-8.
5. Leon MB, Smith CR, Mack MJ, et al. Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients. *N Engl J Med*. 2016;374:1609-20.
6. Mack MJ, Leon MB, Thourani VH, et al. Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients. *N Engl J Med*. 2019;380:1695-705.
7. Kiani S, Kamioka N, Black GB, et al. Development of a Risk Score to Predict New Pacemaker Implantation After Transcatheter Aortic Valve Replacement. *JACC Cardiovasc Interv*. 2019;12:2133-42.
8. Bisson A, Bodin A, Herbert J, et al. Pacemaker Implantation After Balloon- or Self-Expandable Transcatheter Aortic Valve Replacement in Patients With Aortic Stenosis. *J Am Heart Assoc*. 2020;9:e015896.
9. Houthuizen P, Van Garsse LA, Poels TT, et al. Left bundle-branch block induced by transcatheter aortic valve implantation increases risk of death. *Circulation*. 2012;126:720-8.

10. Buellesfeld L, Stortecky S, Heg D, et al. Impact of permanent pacemaker implantation on clinical outcome among patients undergoing transcatheter aortic valve implantation. *J Am Coll Cardiol*. 2012;60:493-501.
11. Linke A, Wenaweser P, Gerckens U, et al. Treatment of aortic stenosis with a self-expanding transcatheter valve: the International Multi-centre ADVANCE Study. *Eur Heart J*. 2014;35:2672-84.
12. Urena M, Webb JG, Tamburino C, et al. Permanent pacemaker implantation after transcatheter aortic valve implantation: impact on late clinical outcomes and left ventricular function. *Circulation*. 2014;129:1233-43.
13. Nazif TM, Dizon JM, Hahn RT, et al. Predictors and clinical outcomes of permanent pacemaker implantation after transcatheter aortic valve replacement: the PARTNER (Placement of AoRtic TraNscathetER Valves) trial and registry. *JACC Cardiovasc Interv*. 2015;8:60-9.
14. Mouillet G, Lellouche N, Yamamoto M, et al. Outcomes following pacemaker implantation after transcatheter aortic valve implantation with CoreValve(®) devices: Results from the FRANCE 2 Registry. *Catheter Cardiovasc Interv*. 2015;86:E158-66.
15. Regueiro A, Abdul-Jawad Altisent O, Del Trigo M, et al. Impact of New-Onset Left Bundle Branch Block and Periprocedural Permanent Pacemaker Implantation on Clinical Outcomes in Patients Undergoing Transcatheter Aortic Valve Replacement: A Systematic Review and Meta-Analysis. *Circ Cardiovasc Interv*. 2016;9:e003635.
16. Shaw DB, Kekwick CA, Veale D, Gowers J, Whistance T. Survival in second degree atrioventricular block. *Br Heart J*. 1985;53:587-93.
17. Coumbe AG, Naksuk N, Newell MC, Somasundaram PE, Benditt DG, Adabag S. Long-term follow-up of older patients with Mobitz type I second degree atrioventricular block. *Heart*. 2013;99:334-8.

18. Kusumoto FM, Schoenfeld MH, Barrett C, et al. 2018 ACC/AHA/HRS guideline on the evaluation and management of patients with bradycardia and cardiac conduction delay: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *Heart Rhythm*. 2019;16:e128-e226.
19. Kiehl EL, Makki T, Kumar R, et al. Incidence and predictors of right ventricular pacing-induced cardiomyopathy in patients with complete atrioventricular block and preserved left ventricular systolic function. *Heart Rhythm*. 2016;13:2272-8.
20. Yu CM, Chan JY, Zhang Q, et al. Biventricular pacing in patients with bradycardia and normal ejection fraction. *N Engl J Med*. 2009;361:2123-34.
21. Chang JD, Manning WJ, Ebrille E, Zimetbaum PJ. Tricuspid Valve Dysfunction Following Pacemaker or Cardioverter-Defibrillator Implantation. *J Am Coll Cardiol*. 2017;69:2331-41.
22. Amano M, Izumi C, Taniguchi T, et al. Impact of concomitant tricuspid regurgitation on long-term outcomes in severe aortic stenosis. *Eur Heart J Cardiovasc Imaging*. 2019;20:353-60.
23. Sohail MR, Eby EL, Ryan MP, Gunnarsson C, Wright LA, Greenspon AJ. Incidence, Treatment Intensity, and Incremental Annual Expenditures for Patients Experiencing a Cardiac Implantable Electronic Device Infection: Evidence From a Large US Payer Database 1-Year Post Implantation. *Circ Arrhythm Electrophysiol*. 2016;9:e003929.
24. Clémenty N, Fernandes J, Carion PL, et al. Pacemaker complications and costs: a nationwide economic study. *J Med Econ*. 2019;22:1171-8.
25. Rodés-Cabau J, Ellenbogen KA, Krahn AD, et al. Management of Conduction Disturbances Associated With Transcatheter Aortic Valve Replacement: JACC Scientific Expert Panel. *J Am Coll Cardiol*. 2019;74:1086-106.

26. Koshy AN, Murphy A, Farouque O, Horrigan M, Yudi MB. Outcomes of Transcatheter Versus Surgical Aortic Valve Replacement in Low-Risk Patients. *Heart Lung Circ.* 2020;29:1527-33.

FIGURE LEGENDS

Figure 1. Cumulative incidence of all-cause death in patients treated with TAVR, according to the absence of pacemaker, previous PPM or PPM within 30 days post-TAVR.

Figure 2. Cumulative incidence of hospitalization for heart failure in patients treated with TAVR, according to the absence of pacemaker, previous PPM or PPM within 30 days post-TAVR.

TABLES

Table 1. Characteristics of patients treated without pacemaker implantation (No PPM) or already implanted with a pacemaker at baseline (PPM) or during the post-operative period (first 30 days) following a TAVR procedure.

	No PPM (n=16,511)	PPM at baseline (n=6,362)	p vs no PPM	PPM day 0-30 post TAVR (n=6,549)	p vs no PPM
Age, years	82.2±7.2	83.0±6.8	<0.0001	82.6±6.7	<0.0001
Sex (male)	7,671 (46.5)	3,783 (59.5)	<0.0001	3,291 (50.3)	<0.0001
EuroSCORE II	3.7±1.0	4.1±1.1	<0.0001	3.8±1.0	0.002
Charlson comorbidity index	4.7±2.9	5.3±2.8	<0.0001	4.8±2.9	0.18
Frailty index	11.3±9.4	12.5±9.7	<0.0001	11.4±9.4	0.4
Hypertension	14,384 (87.1)	5,735 (90.1)	<0.0001	5,815 (88.8)	0.001
Diabetes mellitus	5,370 (32.5)	2,278 (35.8)	<0.0001	2,212 (33.8)	0.07
Heart failure with congestion	9,312 (56.4)	4,503 (70.8)	<0.0001	3,817 (58.3)	0.01
Coronary artery disease	10,892 (66.0)	4,646 (73.0)	<0.0001	4,357 (66.5)	0.42
Previous myocardial infarction	2,302 (13.9)	1,175 (18.5)	<0.0001	961 (14.7)	0.15
Previous PCI	4,536 (27.5)	1,989 (31.3)	<0.0001	1,886 (28.8)	0.04
Previous CABG	1,415 (8.6)	781 (12.3)	<0.0001	557 (8.5)	0.87
Vascular disease	6,148 (37.2)	2,748 (43.2)	<0.0001	2,383 (36.4)	0.23
Mitral regurgitation	3,162 (19.2)	1,529 (24.0)	<0.0001	1,210 (18.5)	0.24
Aortic regurgitation	1,963 (11.9)	952 (15.0)	<0.0001	866 (13.2)	0.01
Tricuspid regurgitation	630 (3.8)	364 (5.7)	<0.0001	258 (3.9)	0.66
Atrial fibrillation	7,224 (43.8)	3,796 (59.7)	<0.0001	3,021 (46.1)	0.001
Left BBB	2,562 (15.5)	913 (14.4)	0.03	1,323 (20.2)	<0.0001
Right BBB	851 (5.2)	688 (10.8)	<0.0001	726 (11.1)	<0.0001
Previous ICD	0 (0.0)	262 (4.1)	<0.0001	0 (0.0)	-
Previous CRT	0 (0.0)	317 (5.0)	<0.0001	0 (0.0)	-
ICD in 30-day post TAVR	0 (0.0)	37 (0.6)	<0.0001	64 (1.0)	<0.0001
CRT in 30-day post TAVR	0 (0.0)	63 (1.0)	<0.0001	202 (3.1)	<0.0001
Ischemic stroke	928 (5.6)	358 (5.6)	0.98	371 (5.7)	0.89
Smoker	1,614 (9.8)	650 (10.2)	0.32	651 (9.9)	0.7
Dyslipidemia	8,492 (51.4)	3,607 (56.7)	<0.0001	3,558 (54.3)	0.0001
Obesity	4,798 (29.1)	2,006 (31.5)	0.0002	2,172 (33.2)	<0.0001
Alcohol related diagnoses	980 (5.9)	406 (6.4)	0.21	408 (6.2)	0.4
Abnormal renal function	2,914 (17.6)	1,562 (24.6)	<0.0001	1,292 (19.7)	0.0002
Lung disease	4,184 (25.3)	1,783 (28.0)	<0.0001	1,670 (25.5)	0.8
Sleep apnea syndrome	1,478 (9.0)	727 (11.4)	<0.0001	595 (9.1)	0.75
Liver disease	928 (5.6)	386 (6.1)	0.19	341 (5.2)	0.21
Thyroid diseases	2,290 (13.9)	998 (15.7)	0.0004	883 (13.5)	0.44
Anemia	4,828 (29.2)	2,106 (33.1)	<0.0001	1,919 (29.3)	0.93
Previous cancer	3,277 (19.8)	1,282 (20.2)	0.61	1,300 (19.9)	1
Edwards Sapien XT	2,213 (13.4)	747 (11.7)	0.001	826 (12.6)	0.11
Edwards Sapien 3	8,205 (49.7)	2,788 (43.8)	<0.0001	2,884 (44.0)	<0.0001
Medtronic Corevalve	2,238 (13.6)	1,244 (19.6)	<0.0001	1,159 (17.7)	<0.0001
Medtronic Evolut	3,855 (23.3)	1,583 (24.9)	0.01	1,680 (25.7)	0.0002

Values are mean ± standard deviation, or n (%).

BBB, bundle branch block; CABG, coronary artery bypass graft; CRT, cardiac resynchronization therapy device; ICD, implantable cardioverter-defibrillator; PCI, percutaneous coronary intervention; PM, pacemaker; PPM, permanent pacemaker implantation; SD, standard deviation; TAVR, transcatheter aortic valve replacement.

Table 2. Events during follow-up in patients treated with (PPM) or without (No PPM) pacemaker implantation during the post-operative period (first 30 days) following a TAVR procedure.

	No PPM (n=16,511)	Previous PPM (n=6,362)	Incidence rate ratio vs no PPM (95%CI)	p vs no PPM	PPM day 0-30 post TAVR (n=6,549)	Incidence rate ratio vs no PPM (95%CI)	p vs no PPM
Major bleeding events at day 30*	483 (2.9)	194 (3.1)	1.04 (0.88-1.24)	0.62	225 (3.4)	1.18 (1.01-1.39)	0.04
<i>Long-term follow-up</i>							
Death	4,452 (13.1)	2,031 (16.1)	1.23 (1.16-1.29)	<0.0001	1,971 (15.2)	1.16 (1.10-1.22)	<0.0001
Cardiovascular death	1,955 (5.8)	918 (7.3)	1.26 (1.17-1.37)	<0.0001	849 (6.5)	1.14 (1.05-1.23)	0.002
Rehospitalization for HF	4,045 (13.9)	2,198 (22.1)	1.59 (1.51-1.67)	<0.0001	1,864 (17.0)	1.22 (1.16-1.29)	<0.0001
Death or rehospitalization for HF	7,079 (24.4)	3,350 (33.7)	1.38 (1.33-1.44)	<0.0001	3,100 (28.3)	1.16 (1.11-1.21)	<0.0001
Mitral regurgitation	808 (2.4)	347 (2.8)	1.16 (1.02-1.32)	0.02	313 (2.5)	1.01 (0.89-1.15)	0.86
Tricuspid regurgitation	215 (0.6)	134 (1.1)	1.69 (1.35-2.11)	<0.0001	78 (0.6)	0.95 (0.72-1.24)	0.70
Infective endocarditis	573 (1.7)	267 (2.2)	1.26 (1.08-1.46)	0.002	261 (2.0)	1.20 (1.03-1.39)	0.02

Values are n (incidence rate, %/year). CI=confidence interval; TAVR=transcatheter aortic valve replacement. * values are n (%) and odds ratios for bleeding events at day 30.

Table 3. Independent predictors of main outcomes during the whole follow-up in patients treated with TAVR.

Multivariable Model	All-cause death		Cardiovascular death		HF hospitalization		HF and all-cause death	
	Adjusted HR (95%CI)	p	Adjusted HR (95%CI)	p	Adjusted HR (95%CI)	p	Adjusted HR (95%CI)	p
Previous PM or ICD (n=6,362)	1.014 (0.960-1.072)	0.62	0.988 (0.909-1.074)	0.78	1.250 (1.184-1.320)	<0.0001	1.116 (1.069-1.165)	<0.0001
Previous ICD (n=122)	1.444 (1.156-1.803)	0.001	1.526 (1.136-2.050)	0.005	1.264 (1.022-1.564)	0.03	1.219 (1.023-1.454)	0.03
Previous CRT (n=317)	0.746 (0.596-0.933)	0.01	0.846 (0.624-1.148)	0.28	0.881 (0.723-1.074)	0.21	0.846 (0.717-0.999)	0.05
PM/ICD in 30-day post TAVR (n=6,549)	1.120 (1.061-1.182)	<0.0001	1.084 (0.998-1.177)	0.06	1.155 (1.091-1.221)	<0.0001	1.109 (1.062-1.157)	<0.0001
ICD in 30-day post TAVR (n=64)	0.649 (0.386-1.092)	0.10	0.323 (0.102-1.017)	0.05	0.796 (0.505-1.254)	0.33	0.700 (0.475-1.032)	0.07
CRT in 30-day post TAVR (n=220)	1.119 (0.875-1.432)	0.37	1.048 (0.715-1.535)	0.81	1.236 (0.967-1.580)	0.09	1.145 (0.941-1.394)	0.18

CRT, cardiac resynchronization therapy device; HR, hazard ratio; ICD, implantable cardioverter-defibrillator; PM, pacemaker; TAVR, transcatheter aortic valve replacement. Adjustment was performed on the following baseline characteristics: age, sex, EuroSCORE II, Charlson comorbidity index, frailty index, hypertension, diabetes mellitus, heart failure with congestion, coronary artery disease, previous myocardial infarction, previous percutaneous coronary intervention, previous coronary artery bypass graft, vascular disease, aortic, mitral and tricuspid regurgitation, atrial fibrillation, left and right bundle branch blocks, ischemic stroke, smoking status, dyslipidemia, obesity, alcohol related diagnoses, abnormal renal function, lung disease, sleep apnea syndrome, liver disease, thyroid disease, anemia, previous cancer, and valve model.

Table 4. Independent predictors of secondary outcomes during the whole follow-up in patients treated with TAVR.

Multivariable Model	Major bleeding at day 30		Infective endocarditis		Atrial fibrillation		Mitral regurgitation		Tricuspid regurgitation	
	Adjusted OR (95%CI)	p	Adjusted HR (95%CI)	p	Adjusted HR (95%CI)	p	Adjusted HR (95%CI)	p	Adjusted HR (95%CI)	p
Previous PM or ICD (n=6,362)	0.912 (0.778-1.070)	0.26	1.202 (1.031-1.400)	0.02	1.088 (0.988-1.198)	0.09	1.110 (0.973-1.266)	0.12	1.369 (1.089-1.720)	0.007
Previous ICD (n=122)	0.724 (0.314-1.669)	0.45	1.246 (0.654-2.374)	0.51	0.937 (0.542-1.618)	0.82	1.072 (0.567-2.027)	0.83	0.805 (0.319-2.036)	0.65
Previous CRT (n=317)	1.144 (0.594-2.203)	0.69	0.925 (0.507-1.687)	0.80	0.911 (0.564-1.471)	0.70	0.956 (0.549-1.664)	0.87	1.472 (0.731-2.966)	0.28
PM/ICD in 30-day post TAVR (n=6,549)	1.145 (0.987-1.328)	0.07	1.224 (1.054-1.421)	0.008	0.985 (0.900-1.077)	0.74	0.988 (0.864-1.129)	0.86	0.906 (0.693-1.184)	0.47
ICD in 30-day post TAVR (n=64)	0.726 (0.169-3.112)	0.67	0.520 (0.123-2.196)	0.37	0.398 (0.126-1.251)	0.12	1.388 (0.541-3.561)	0.50	0.582 (0.072-4.696)	0.61
CRT in 30-day post TAVR (n=220)	1.222 (0.628-2.379)	0.56	1.097 (0.529-2.275)	0.80	1.698 (1.105-2.612)	0.02	1.222 (0.625-2.392)	0.56	2.172 (0.832-5.669)	0.11

CRT, cardiac resynchronization therapy device; HR, hazard ratio; ICD, implantable cardioverter-defibrillator; OR, odds ratio; PM, pacemaker; TAVR, transcatheter aortic valve replacement. Adjustment on all characteristics in Table 1.

Figure 1.

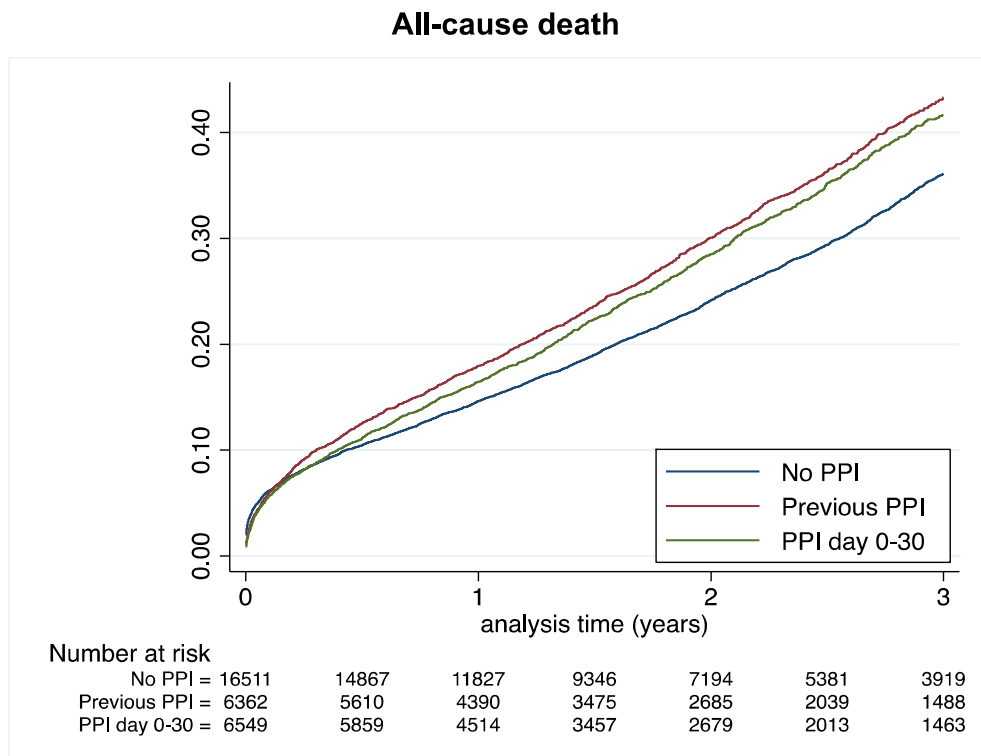
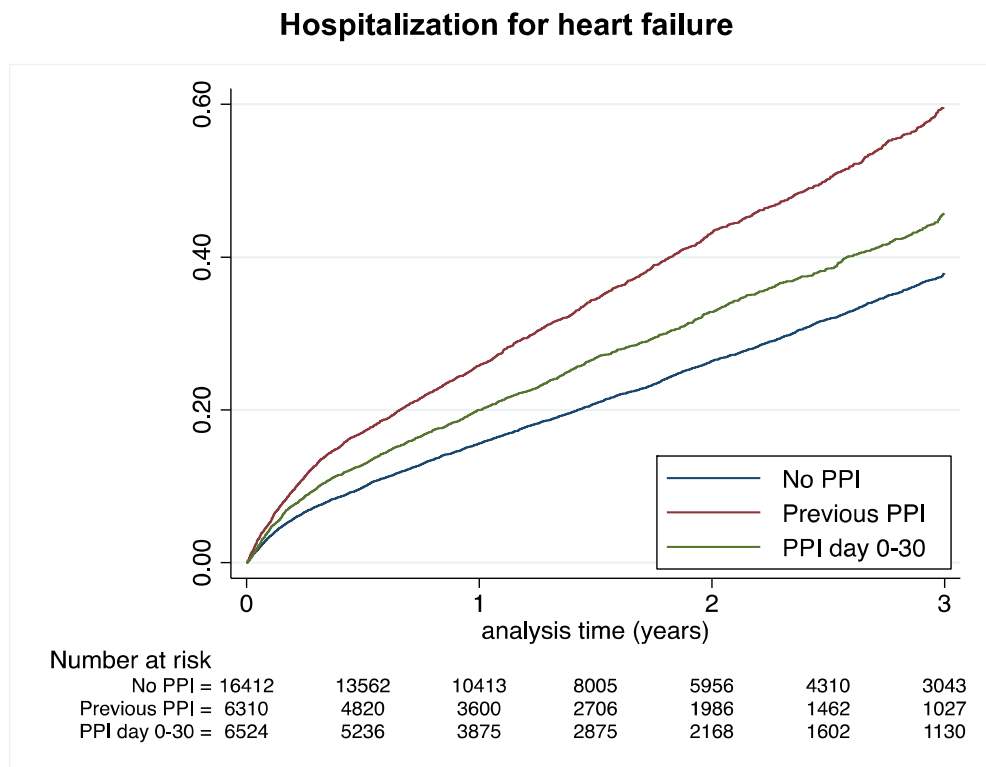
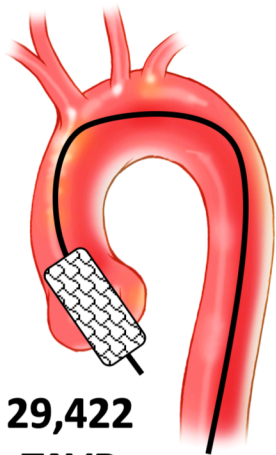


Figure 2.

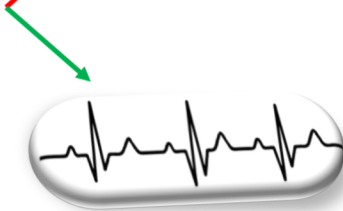




29,422
TAVR

with follow-up ≥ 6 months
(France, 2010-2019)

12,911
PACEMAKER
- 6,362 before TAVR
- 6,549 post-TAVR (30 days)



16,511
NO PACEMAKER

1.7 years median follow-up

ALL CAUSE DEATH

- NS before TAVR
- aHR 1.12 post-TAVR

HF HOSPITALIZATION

- aHR 1.25 before TAVR
- aHR 1.16 post-TAVR