

Supplementary Appendix

**Sharobeem S et al. Prognostic impact of permanent pacemaker
implantation following transcatheter aortic valve replacement**

I) Full version of the methods

METHODS

Study population

Patients who underwent TAVR at a single center (Rennes University Hospital) from February 2009 to June 2018 were studied. Exclusion criteria were in-hospital death, surgical conversion or unsuccessful TAVR procedure. All patients gave written informed consent for the procedures and anonymous collection of their data, which were prospectively gathered in an electronic database as part of the national registries¹. The institutional review board waived specific consent for this study due to its retrospective and observational nature. The research reported in this paper adhered to the Helsinki Declaration as revised in 2013.

Details regarding pre-procedural workup were previously described². TAVR indication, valve type, and approach were decided by the local heart team in accordance with previous guidelines³. Procedures were performed according to standardized protocols as previously described^{4,5}. Post-procedural care consisted of heart rhythm monitoring for at least 48 hours after intervention, laboratory tests and 12-lead electrocardiogram on daily basis, and echocardiography performed by an experienced operator before discharge, and analyzed in accordance with current guidelines⁶. Clinical outcomes were defined according to Valve Academic Research Consortium 2 criteria⁷.

PPI status

Patients were separated in the following four groups according to the occurrence and timing PPI: no PPI, previous PPI (P-PPI), in-hospital PPI (i.e. during the index hospitalization, IH-PPI) and PPI during follow-up (FU-PPI).

Indications for PPI

In accordance with international guidelines^{8,9}, IH-PPI was indicated for persistent high degree atrioventricular block (HAVB), defined as type 2 second degree AVB or third degree AVB, not expected to resolve or symptomatic sinus node dysfunction. Among patients with milder conduction disturbances such as new-onset LBBB with or without PR interval prolongation, the final indication of PPI was at the discretion of the senior electrophysiologist responsible for the patient, taking into

account clinical data and the in-hospital ECG evolution. For such patients with conduction disturbances not representing absolute PPI indications, a local electrophysiological study-guided PPI strategy was implemented in our center in June 2017. Details regarding this strategy have been previously published¹⁰.

During follow-up, the indication of PPI was at the discretion of the physician responsible for the patient.

Follow-up

Follow-up was performed by on-site clinical visit and/or telephone at 1-month post-TAVR, at 1 year and yearly thereafter. Records from referring cardiologists, general practitioners, and other hospitals were retrieved for further information.

Outcomes

The primary objective of the present study was to assess the long-term clinical impact of PPI, according to its timing relative to TAVR, on the composite of all-cause death and HHF. As secondary objectives, we analyzed the impact of PPI status on the components of the primary outcome and left ventricular ejection fraction (LVEF) at follow-up.

Statistical Analysis

Continuous variables were presented as mean \pm standard deviation or median (interquartile range) depending on their distribution, which was assessed using the Kolmogorov-Smirnov test, and were compared using the Kruskal-Wallis test. Categorical variables were summarized as numbers (percentages), and compared using chi-square tests or the Fisher exact test as appropriate. Cumulative incidence of all-cause mortality was summarized using Kaplan-Meier estimates, and log-rank test was used to compare groups. Nelson-Aalen estimates were used to depict the cumulative hazard of PPI post-TAVR. HHF was evaluated using competing-risk models with all-cause mortality as a competing event. Cumulative incidence function plots were constructed to present the cumulative probability of HHF in the presence of competing events. Competing-risk models were used to determine the predictors of HHF by reporting adjusted sub-hazard ratios (sub HR) with their 95% confidence intervals (CI). All-cause mortality was analyzed using Cox proportional hazard models. Proportional hazard assumption was verified. For each model, all variables with a univariate p-value

<0.1 were included in the multivariable analysis. To evaluate its impact on mortality and HHF, PPI status was included in the models as a time-varying covariate to take into account FU-PPI. All univariate analyses were performed on complete cases. Overall, 2.5% of data were missing and 32.9% of patients had at least one missing value. For the purposes of multivariable analyses, missing data were assumed to be random and handled by multiple imputation using chained equations. Ten imputed datasets were created. Results were pooled according to Rubin's rule. Parametric multistate survival models, adjusted for the previously identified variables, were performed to predict the probability of transitioning from one state (post-TAVR status, post-TAVR PPI status, post-TAVR HHF status, death) to another over time. The Weibull distribution, minimizing the most the Akaike and Bayesian information criteria, was chosen for these models. Generalised linear model for repeated measures with interaction was used to compare the changes in LVEF at different time points between groups. Post-hoc comparisons were performed with the Bonferroni correction. All tests were 2-sided at the 0.05 significance level. Statistical analyses were conducted using Stata Statistical Software Release 13 (StataCorp, College Station, TX) and the Statistical Package for Social Sciences version 25 (SPSS Inc., IBM, Armonk, New York).

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II) Supplementary Table 1

Supplementary table 1 – Procedural characteristics and in-hospital outcomes of the study population according to the presence and timing of implantation of a permanent pacemaker					
	Patients without a permanent pacemaker (n=894)	Patients with a previous permanent pacemaker (n=130)	Patients with in-hospital permanent pacemaker implantation (n=116)	Patients with permanent pacemaker implantation during follow-up (n=59)	p-value
Procedural characteristics					
Urgent procedure	23 (2.6)	1 (0.8)	2 (1.7)	0 (0.0)	0.35
Local anesthesia	598 (67.6)	87 (66.9)	80 (69.0)	43 (72.9)	0.84
Approach					0.41
Transfemoral	726 (81.2)	104 (80.0)	98 (84.5)	43 (72.9)	
Sub-clavian	53 (5.9)	7 (5.4)	10 (8.6)	4 (6.8)	
Transaortic	30 (3.4)	7 (5.4)	2 (1.7)	4 (6.8)	
Transapical	49 (5.5)	8 (6.2)	2 (1.7)	3 (5.1)	
Transcarotid	36 (4.0)	4 (3.1)	4 (3.4)	5 (8.5)	
Valve Type					<0.001
Sapien	149 (16.7)	25 (19.2)	9 (7.8)	12 (20.3)	
Sapien XT	44 (4.9)	8 (6.2)	3 (2.6)	1 (1.7)	
Sapien 3	428 (47.9)	52 (40.0)	40 (34.5)	31 (52.5)	
CoreValve	136 (15.2)	23 (17.7)	37 (31.9)	6 (10.2)	
Evolut R/Pro	121 (13.5)	18 (13.8)	20 (17.2)	8 (13.6)	
Others (Centera, Portico, Direct Flow)	16 (1.8)	4 (3.1)	7 (6.0)	1 (1.7)	
Valve mechanism					<0.001
Balloon-expandable	621 (69.5)	85 (65.4)	52 (44.8)	44 (74.6)	
Self-expandable	264 (29.5)	43 (33.1)	64 (55.2)	14 (23.7)	
Other	9 (1.0)	2 (1.5)	1 (1.7)	12 (1.0)	
Valve diameter					<0.001
23 mm	286 (32.0)	25 (19.2)	22 (19.0)	16 (27.1)	
25 mm	4 (0.4)	1 (0.8)	3 (2.6)	1 (1.7)	
26 mm	378 (42.3)	54 (41.5)	41 (35.3)	29 (49.2)	
27 mm	1 (0.1)	0 (0.0)	2 (1.7)	0 (0.0)	
29 mm	203 (22.7)	45 (34.6)	44 (37.9)	13 (22.0)	
31 mm	17 (1.9)	4 (3.1)	3 (2.6)	0 (0.0)	
34 mm	4 (0.4)	1 (0.8)	1 (0.9)	0 (0.0)	

Need for a second valve	12 (1.3)	0 (0.0)	4 (3.4)	0 (0.0)	0.09
In-hospital outcomes					
Periprocedural myocardial infarction	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0.95
Tamponade	7 (0.8)	1 (0.8)	2 (1.8)	0 (0.0)	0.64
Cerebrovascular events					0.94
Stroke	20 (2.3)	2 (1.6)	2 (1.8)	2 (3.4)	
TIA	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	
Major bleeding (BARC 3 or 5)	45 (5.0)	8 (6.2)	5 (4.3)	2 (3.4)	0.85
Acute kidney injury stage 2 or 3	9 (1.0)	1 (0.8)	2 (1.7)	1 (1.7)	0.85
Major vascular complications	29 (3.3)	2 (1.6)	2 (1.8)	1 (1.7)	0.57
New-onset atrial fibrillation	51 (6.0)	2 (1.6)	6 (5.4)	2 (3.6)	0.23
New-onset persistent LBBB	147 (17.3)	8 (6.6)	17 (15.2)	14 (25.0)	0.007
Length of ICU stay, days	1.0 (0.0-3.0)	1.0 (0.0-2.8)	3.0 (1.0-6.0)	2.0 (0.0-4.0)	<0.001
Length of hospital stay, days	4.0 (3.0-7.0)	5.0 (3.0-6.0)	7.0 (5.3-10.0)	6.0 (4.0-7.0)	<0.001
Echocardiography at discharge					
LVEF (%)	60.0 (50.8-66.0)	56.0 (45.0-65.0)	60.0 (50.0-66.8)	60.0 (50.0-65.0)	0.009
LVEF < 50%	166 (18.6)	37 (28.5)	27 (23.3)	13 (22.0)	0.05
LVEDD, mm	46.6 (42.0-52.0)	48.0 (45.0-55.0)	48.0 (43.0-52.3)	48.0 (43.0-52.5)	0.002
Aortic valve area (cm ²)	1.79 (1.50-2.10)	1.76 (1.40-2.20)	1.76 (1.47-2.00)	1.70 (1.40-2.00)	0.81
Patient-prosthesis mismatch					0.73
Moderate	156 (18.8)	27 (22.0)	17 (16.3)	10 (17.9)	
Severe	28 (3.4)	5 (4.1)	5 (4.8)	4 (7.1)	
Mean aortic gradient (mmHg)	11.0 (8.0-14.0)	10.0 (7.0-13.0)	9.0 (7.0-12.5)	12.0 (9.0-14.0)	0.003
Aortic regurgitation grade III or IV	12 (1.4)	2 (1.7)	3 (2.7)	1 (1.8)	0.79
Mitral regurgitation grade III or IV	23 (2.6)	6 (4.7)	4 (3.5)	0 (0.0)	0.29
sPAP, mmHg	35.0 (30.0-45.0)	40.0 (30.0-50.0)	35.0 (30.0-50.0)	35.0 (29.0-43.0)	0.23
Pulmonary hypertension					0.02
Moderate (sPAP:31-60 mmHg)	394 (44.1)	71 (54.6)	57 (49.1)	29 (49.2)	
Severe (sPAP: >60 mmHg)	32 (3.6)	5 (3.8)	10 (8.6)	1 (1.7)	
Right ventricular dysfunction	92 (10.7)	23 (19.0)	14 (12.4)	5 (8.8)	0.06
Tricuspid regurgitation grade III or IV	21 (2.5)	4 (3.4)	4 (3.6)	3 (5.6)	0.56

Continuous variables are presented as mean \pm standard deviation or median (interquartile range). Categorical variables are presented as number (percentage). BARC: Bleeding academic research consortium; ICU: Intensive care unit; LBBB: Left bundle branch block; LVEDD: Left ventricular end-diastolic diameter; LVEF: Left ventricular ejection fraction; sPAP: Systolic pulmonary artery pressure; TIA: Transient ischemic attack; TAVR: Transcatheter aortic valve replacement.

III) Supplementary Table 2

Supplementary table 2 – Treatment at discharge according to the presence and timing of implantation of a permanent pacemaker					
	Patients without a permanent pacemaker (n=894)	Patients with a previous permanent pacemaker (n=130)	Patients with in-hospital permanent pacemaker implantation (n=116)	Patients with permanent pacemaker implantation during follow-up (n=59)	p-value
Aspirin	801 (90.0)	115 (88.5)	101 (87.1)	54 (91.5)	0.71
P2Y12 receptor inhibitor	533 (59.9)	61 (46.9)	66 (56.9)	36 (61.0)	0.04
Vitamin K antagonist	222 (24.9)	53 (40.8)	39 (33.6)	15 (25.4)	0.001
Direct-oral anticoagulant	68 (8.0)	7 (5.7)	12 (11.0)	2 (3.5)	0.29
RAS inhibitor	430 (50.5)	64 (52.5)	49 (45.0)	29 (50.9)	0.69
Percentage of optimal daily recommended dose of RAS inhibitor					0.92
0%	422 (49.7)	58 (48.3)	60 (55.6)	28 (49.1)	
1% - < 25%	40 (4.7)	8 (6.7)	6 (5.6)	1 (1.8)	
25% - < 50%	141 (16.6)	18 (15.0)	13 (12.0)	8 (14.0)	
50% - < 75%	148 (17.4)	22 (18.3)	19 (17.6)	11 (19.3)	
75% - 100%	98 (11.5)	14 (11.7)	10 (9.3)	9 (15.8)	
Beta-blocker	466 (54.8)	78 (63.9)	58 (53.2)	24 (42.1)	0.05
Percentage of optimal daily recommended dose of beta-blocker					0.04
0%	383 (45.2)	44 (36.1)	51 (46.8)	33 (57.9)	
1% - < 25%	84 (9.9)	11 (9.0)	9 (8.3)	5 (8.8)	
25% - < 50%	174 (20.5)	32 (26.2)	19 (17.4)	4 (7.0)	
50% - < 75%	138 (16.3)	19 (15.6)	13 (11.9)	8 (14.0)	
75% - 100%	69 (8.1)	16 (13.1)	17 (15.6)	7 (12.3)	
Mineralocorticoid receptor antagonist	69 (8.1)	19 (15.6)	7 (6.4)	5 (8.8)	0.04
Percentage of optimal daily recommended dose of MR antagonist					0.14
0%	783 (92.1)	103 (85.1)	102 (94.4)	52 (91.2)	
1% - < 25%	2 (0.2)	1 (1.8)	0 (0.0)	1 (1.8)	
25% - < 50%	36 (4.2)	10 (8.3)	5 (4.6)	1 (1.8)	
50% - < 75%	18 (2.1)	6 (5.0)	0 (0.0)	2 (3.5)	
75% - 100%	11 (1.3)	1 (0.8)	1 (0.9)	1 (1.8)	
Loop diuretics	447 (52.5)	89 (73.0)	66 (60.6)	35 (61.4)	<0.001

Dose of loop diuretics equivalent to >40 mg/d of furosemide	152 (17.9)	34 (28.3)	17 (15.9)	10 (17.9)	0.001
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Continuous variables are presented as mean \pm standard deviation or median (interquartile range). Categorical variables are presented as number (percentage). MR: Mineralocorticoid receptor; RAS: Renin-angiotensin system.

IV) **Supplementary Table 3**

Supplementary table 3 – Details regarding in-hospital permanent pacemaker implantation	
Indication	
HAVB	100 (86.2%)
Others	
- All	16 (13.8%)
- Isolated LBBB	4 (3.4%)
- 1 st degree AVB + LBBB	11 (9.5%)
- Sinus node dysfunction	1 (0.9%)
Proportion of others indications in which an EPS was performed	
All	5 (31.3%) – 4.3% of all IH-PPI
Isolated LBBB	2 (50%) – 1.7% of all IH-PPI
1 st degree AVB + LBBB	3 (27.3%) – 2.6% of all IH-PPI
Devices	
Single chamber	35 (30.2)
Dual chamber	79 (68.1)
CRT-P	1 (0.9)
CRT-D	1 (0.9)
Time from TAVR to implantation (days)	3 (2-6)

Data are presented as number (percentage). CRT-D: cardiac resynchronization therapy-defibrillator; CRT-P: cardiac resynchronization therapy-pacemaker; EPS : Electrophysiological study ; HAVB: high atrioventricular block ; TAVR: Transcatheter Aortic Valve Replacement

V) Supplementary Table 4

Supplementary table 4 – Details regarding permanent pacemaker implantation and upgrading procedures during follow-up	
Delay	
Time from TAVR to implantation, years	1.7 (0.5-2.8)
Estimates of the rate of FU-PPI after TAVR	
1 year	2.5% (95% CI : 1.7%-3.8%)
2 year	3.8% (95% CI : 2.7%-5.4%)
3 year	6.6% (95% CI : 5.0%-8.8%)
4 year	8.2% (95% CI : 6.2% - 10.7%)
5 year	10.5% (95% CI : 7.9%-13.8%)
Devices	
All	59/953 (6.2%)
Single chamber	15 (25.4)
Dual chamber	34 (57.6)
CRT-P	6 (10.2)
- Within 1 year post-TAVR	2 (3.4)
- From 1 to 2 years post-TAVR	0 (0.0)
- From 2 to 3 years post-TAVR	3 (5.1)
- From 3 to 4 years post-TAVR	1 (1.7)
CRT-D	4 (6.8)
- Within 1 year post-TAVR	0 (0.0)
- From 1 to 2 years post-TAVR	2 (3.4)
- From 2 to 3 years post-TAVR	2 (3.4)
Time to an upgrading procedure	
From an IH-PPI to an ICD	1 during the 7th year of follow-up
From a P-PPI to a CRT-P	1 during the 6th year of follow-up
From a P-PPI to a CRT-D	3:1 in the first month and 2 during the first year of follow-up

Data are presented as number (percentage). CRT-D: cardiac resynchronization therapy-defibrillator; CRT-P: cardiac resynchronization therapy-pacemaker; HAVB: high atrioventricular block; FU-PPI: permanent pacemaker implantation during follow-up; TAVR: Transcatheter Aortic Valve Replacement

VI) Supplementary Table 5

Supplementary Table 5 - Univariate and multivariable predictors of all-cause death				
Variable	Univariate HR (95% CI)	p-value	Multivariable HR (95% CI)	p-value
PPI				
Previous PPI	0.84 (0.60-1.16)	0.28	0.61 (0.43-0.87)	0.006
In-hospital PPI	1.18 (0.77-1.75)	0.49	0.95 (0.62-1.46)	0.82
PPI during follow-up	0.86 (0.46-1.62)	0.64	0.81 (0.43-1.53)	0.52
Age	1.02 (1.01-1.03)	0.001	1.01 (1.00-1.03)	0.06
Female sex	0.79 (0.65-0.95)	0.01	0.70 (0.56-0.87)	0.001
Previous CABG	0.74 (0.54-1.00)	0.05	0.75 (0.52-1.08)	0.12
Peripheral arterial disease	1.36 (1.06-1.76)	0.02	1.19 (0.89-1.58)	0.25
Previous cerebrovascular disease	1.34 (1.06-1.69)	0.01	1.36 (1.06-1.76)	0.016
Chest radiotherapy	0.63 (0.44-0.88)	0.007	0.76 (0.53-1.11)	0.16
Atrial fibrillation	1.72 (1.43-2.07)	<0.001	1.30 (1.05-1.61)	0.014
NTproBNP	1.00 (1.00-1.00)	<0.001	1.00 (1.00-1.00)	0.27
Previous acute heart failure	1.55 (1.29-1.87)	<0.001	1.13 (0.92-1.40)	0.25
Chronic lung disease	1.19 (0.99-1.44)	0.07	1.14 (0.94-1.40)	0.19
Previous Diabetes mellitus				
Oral antidiabetic drugs	1.31 (1.02-1.69)	0.04	1.19 (0.91-1.56)	0.21
Insulin-treated	1.25 (0.83-1.88)	0.28	1.12 (0.73-1.72)	0.60
Chronic kidney disease				
Moderate	1.45 (1.20-1.76)	<0.001	1.26 (1.01-1.57)	0.04
Severe	1.13 (0.66-1.94)	0.66	1.01 (0.57-1.77)	0.98
Dialysis	1.90 (0.61-5.93)	0.27	0.80 (0.23-2.74)	0.72
Logistic EuroScore II	1.04 (1.01-1.07)	0.003	1.02 (0.99-1.06)	0.23
Mean aortic gradient prior to TAVR	0.99 (0.99-1.00)	0.08	1.00 (0.99-1.00)	0.46
Aortic regurgitation grade III or IV prior to TAVR	0.51 (0.23-1.13)	0.097	0.52 (0.25-1.09)	0.08
Moderate or severe mitral stenosis prior to TAVR	1.53 (1.11-2.11)	0.009	1.27 (0.90-1.79)	0.17
Acute kidney injury stage 2 or 3	1.85 (0.91-3.74)	0.09	1.42 (0.67-3.02)	0.36
Percentage of optimal daily recommended dose of RAS inhibitor at discharge				
1% - < 25%	1.42 (0.92-2.18)	0.11	1.08 (0.69-1.67)	0.74
25% - < 50%	0.76 (0.57-1.00)	0.005	0.73 (0.54-0.97)	0.032
50% - < 75%	0.70 (0.53-0.92)	0.01	0.78 (0.59-1.04)	0.09
75% - 100%	0.65 (0.46-0.92)	0.01	0.77 (0.54-1.10)	0.14
Loop diuretics at discharge				
Dose < 40 mg/d	1.30 (1.05-1.62)	0.02	1.25 (0.98-1.59)	0.07
Dose > 40 mg/d	2.11 (1.64-2.71)	<0.001	1.58 (1.18-2.11)	0.002
LVEF at discharge	0.99 (0.983-0.997)	0.009	0.99 (0.99-1.00)	0.15
Aortic regurgitation grade III or IV at discharge	2.51 (1.33-4.71)	0.004	2.04 (0.95-4.35)	0.07
Tricuspid regurgitation grade III or IV at discharge	2.34 (1.42-3.87)	0.001	1.22 (0.67-2.23)	0.51
Pulmonary hypertension at discharge				
Moderate (sPAP:31-60 mmHg)	1.63 (1.34-1.98)	<0.001	1.45 (1.17-1.78)	0.001
Severe (sPAP: >60 mmHg)	3.52 (2.32-5.33)	<0.001	2.08 (1.30-3.33)	0.002

CABG: Coronary artery bypass graft; CI: confidence interval; EuroSCORE= European System for Cardiac Operative Risk Evaluation; HR: hazard-ratio; LVEF: Left ventricular ejection fraction; NT-proBNP: N-terminal pro B-type natriuretic peptide; PPI: permanent pacemaker implantation; RAS:

renin-angiotensin system; sPAP: Systolic pulmonary artery pressure; TAVR: Transcatheter aortic valve replacement.

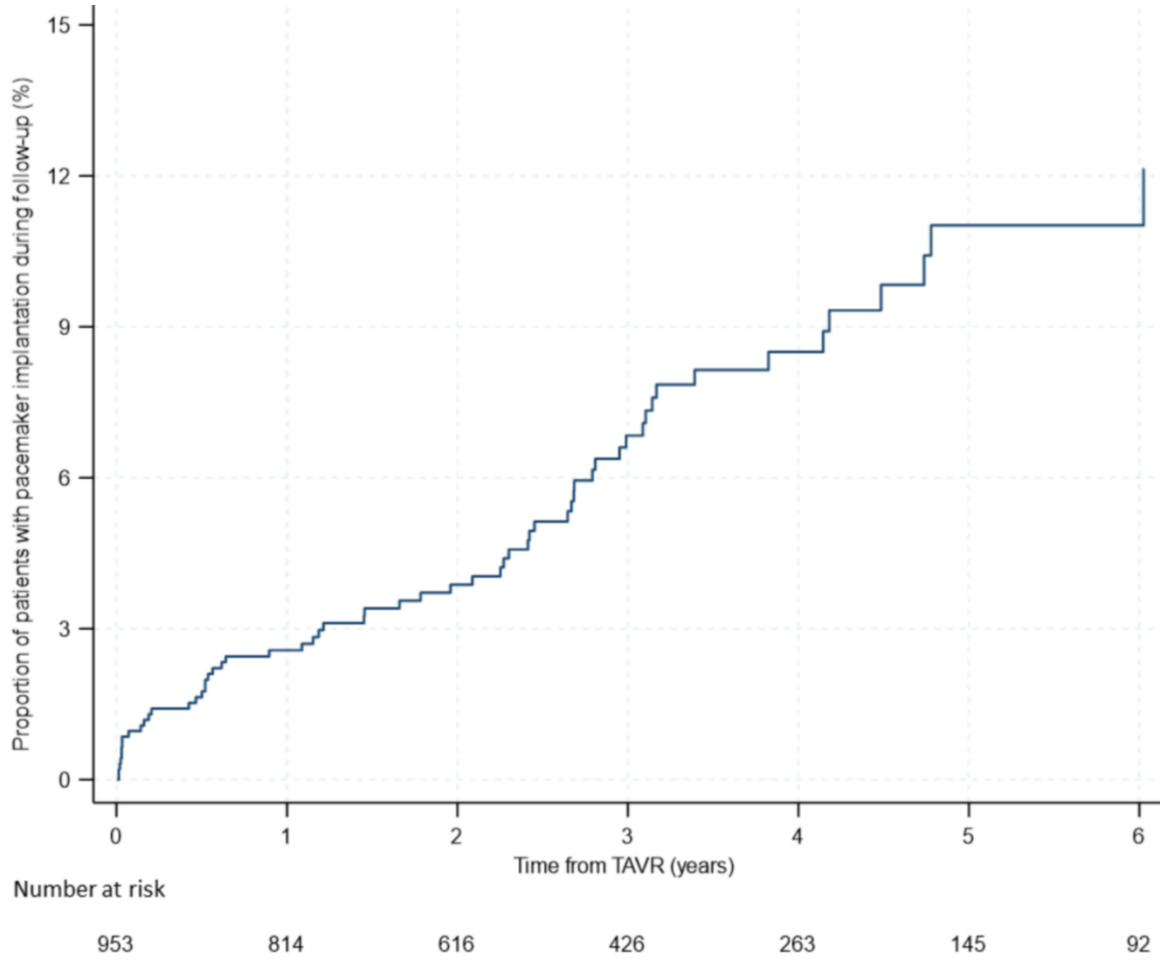
VII) Supplementary Table 6

Supplementary Table 6 - Univariate and multivariable predictors of heart failure hospitalization				
Variable	Univariate SHR (95% CI)	p-value	Multivariable SHR (95% CI)	p-value
PPI				
Previous PPI	1.91 (1.34-2.73)	<0.001	1.51 (0.99-2.29)	0.05
In-hospital PPI	1.48 (0.92-2.37)	0.11	1.27 (0.74-2.17)	0.39
PPI during follow-up	3.77 (2.43-5.85)	<0.001	3.21 (2.02-5.11)	<0.001
Body mass index	1.03 (1.01-1.06)	0.003	1.02 (0.98-1.06)	0.32
Body surface area	2.41 (1.42-4.07)	0.001	0.75 (0.29-1.95)	0.55
Previous aortic balloon valvuloplasty	1.43 (1.00-2.05)	0.05	1.14 (0.77-1.70)	0.50
Previous cerebrovascular disease	1.33 (0.99-1.77)	0.05	1.25 (0.90-1.75)	0.19
Hypertension	1.26 (0.97-1.64)	0.08	1.21 (0.89-1.64)	0.23
Atrial fibrillation	1.67 (1.32-2.11)	<0.001	1.27 (0.96-1.68)	0.095
NYHA III or IV	1.48 (1.17-1.88)	0.001	1.25 (0.95-1.63)	0.10
NTproBNP	1.00 (1.00-1.00)	0.02	1.00 (1.00-1.00)	0.76
Previous acute heart failure	1.94 (1.52-2.46)	<0.001	1.33 (0.99-1.78)	0.059
Chronic lung disease	1.59 (1.25-2.02)	<0.001	1.48 (1.12-1.96)	0.007
Previous Diabetes mellitus				
Oral antidiabetic drugs	1.39 (1.02-1.89)	0.04	1.12 (0.78-1.62)	0.54
Insulin-treated	2.08 (1.36-3.20)	0.001	1.60 (0.96-2.65)	0.071
Chronic kidney disease				
Moderate	1.54 (1.20-1.96)	0.001	1.25 (0.93-1.67)	0.15
Severe	1.51 (0.84-2.70)	0.17	0.99 (0.51-1.92)	0.97
Dialysis	1.52 (0.33-6.98)	0.59	0.57 (0.09-3.67)	0.55
Logistic EuroScore II	1.04 (1.01-1.07)	0.003	0.99 (0.95-1.04)	0.67
Mean aortic gradient prior to TAVR	0.99 (0.98-0.99)	<0.001	0.99 (0.98-1.00)	0.068
Approach				
Sub-clavian	1.64 (1.09-2.47)	0.02	1.34 (0.84-2.14)	0.22
Transaortic	1.09 (0.60-2.00)	0.77	0.91 (0.48-1.72)	0.77
Transapical	1.31 (0.79-2.17)	0.30	1.48 (0.85-2.58)	0.17
Transcarotid	2.13 (1.27-3.56)	0.004	1.27 (0.72-2.22)	0.41
Acute kidney injury stage 2 or 3	2.83 (1.17-6.82)	0.02	1.10 (0.35-3.43)	0.87
Percentage of optimal daily recommended dose of RAS inhibitor at discharge				
1% - < 25%	0.65 (0.31-1.36)	0.25	0.47 (0.21-1.06)	0.07
25% - < 50%	1.36 (0.99-1.87)	0.06	1.13 (0.80-1.61)	0.49
50% - < 75%	0.97 (0.69-1.35)	0.85	0.83 (0.58-1.19)	0.32
75% - 100%	0.92 (0.62-1.38)	0.70	0.89 (0.59-1.36)	0.60
Percentage of optimal daily recommended dose of betablockers at discharge				
1% - < 25%	0.95 (0.60-1.52)	0.85	0.83 (0.49-1.40)	0.48
25% - < 50%	1.18 (0.85-1.63)	0.33	1.26 (0.87-1.81)	0.22
50% - < 75%	1.32 (0.94-1.85)	0.11	1.13 (0.77-1.66)	0.53
75% - 100%	1.56 (1.06-2.29)	0.02	1.29 (0.86-1.94)	0.21
Loop diuretics at discharge				
Dose < 40 mg/d	1.17 (0.88-1.54)	0.28	0.88 (0.64-1.22)	0.45
Dose > 40 mg/d	1.85 (1.34-2.54)	<0.001	1.10 (0.74-1.62)	0.63
LVEF at discharge	0.99 (0.98-0.99)	0.002	1.00 (0.99-1.02)	0.24
LVEDD at discharge	1.04 (1.02-1.05)	<0.001	1.03 (1.00-1.05)	0.007
Indexed aortic valve area	0.54 (0.34-0.85)	0.007	0.93 (0.60-1.42)	0.73

Aortic regurgitation grade III or IV at discharge	2.08 (0.93-4.68)	0.08	1.69 (0.69-4.16)	0.24
Mitral regurgitation grade III or IV at discharge	1.74 (0.91-3.32)	0.09	1.09 (0.47-2.51)	0.85
Tricuspid regurgitation grade III or IV at discharge	2.26 (1.20-4.24)	0.01	1.10 (0.50-2.44)	0.81
Right ventricle dysfunction at discharge	1.40 (0.99-1.99)	0.06	1.04 (0.66-1.63)	0.86
Pulmonary hypertension at discharge				
Moderate (sPAP:31-60 mmHg)	1.55 (1.21-1.99)	<0.001	1.39 (1.06-1.82)	0.017
Severe (sPAP: >60 mmHg)	3.84 (2.32-6.35)	<0.001	3.39 (1.79-6.40)	<0.001

LVEDD: Left ventricular end-diastolic diameter; NYHA: New-York Heart Association. Other abbreviations as in Table 1 and 2.

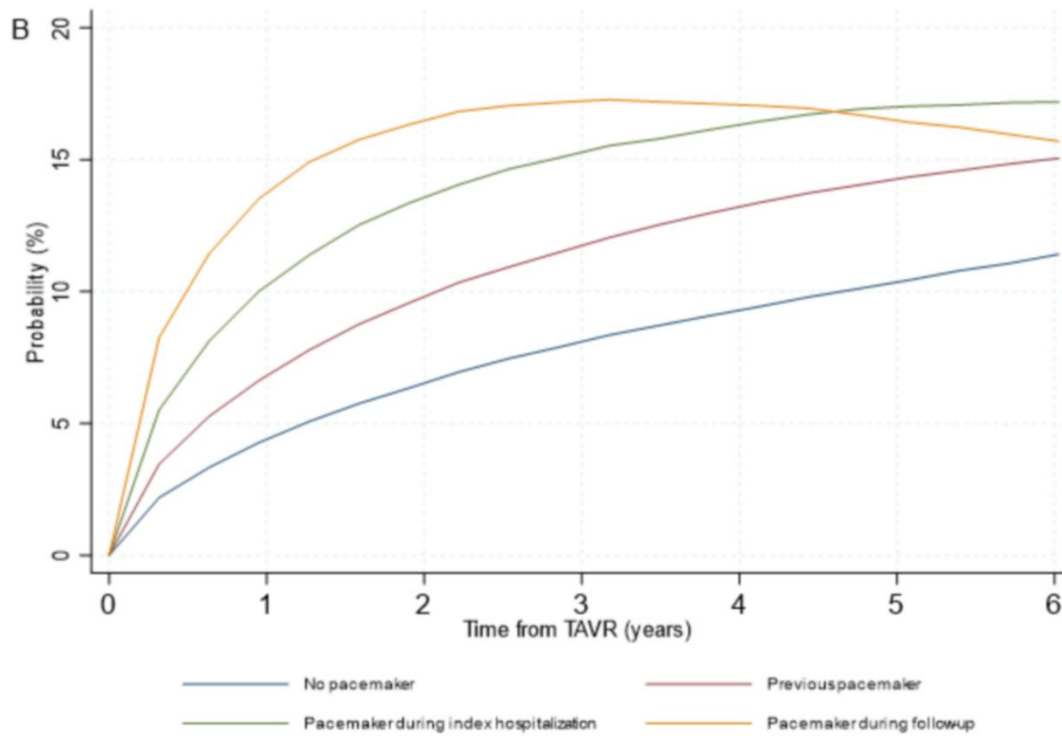
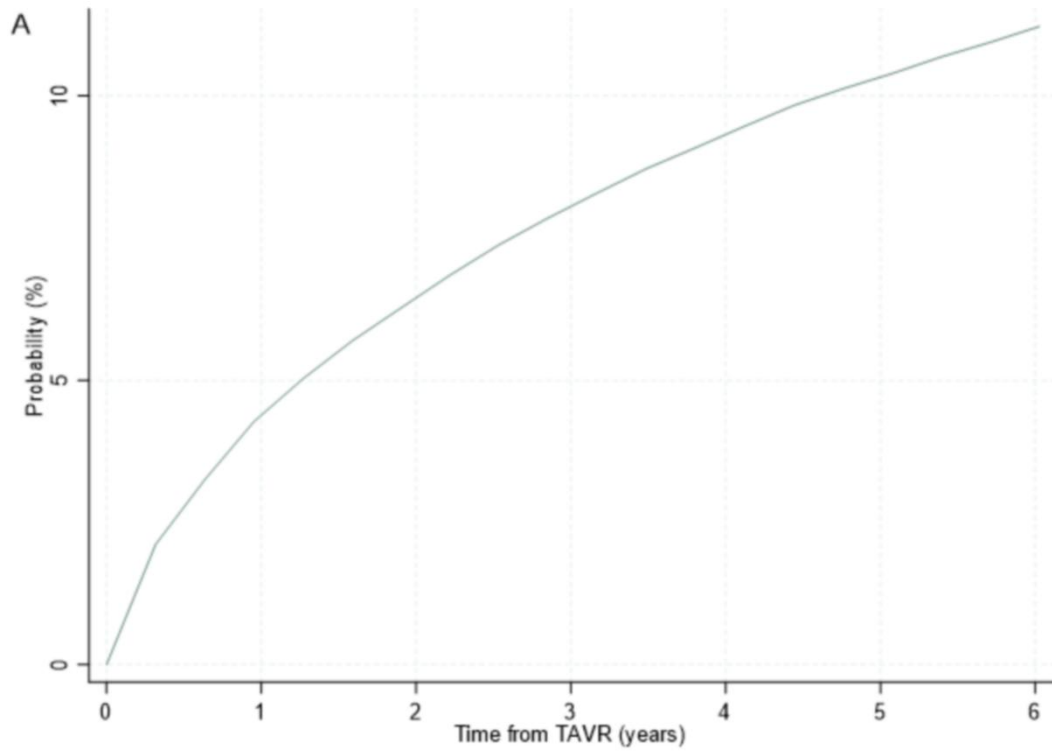
VIII) Supplementary Figure 1 – Nelson-Aalen estimates of the rate of permanent pacemaker implantation during follow up



IX) Supplementary Figure 2 – Adjusted probabilities of transitioning from post-TAVR status to post-TAVR heart failure hospitalization

Panel A: Probability over time in the overall population

Panel B: Probability over time according to PPI status

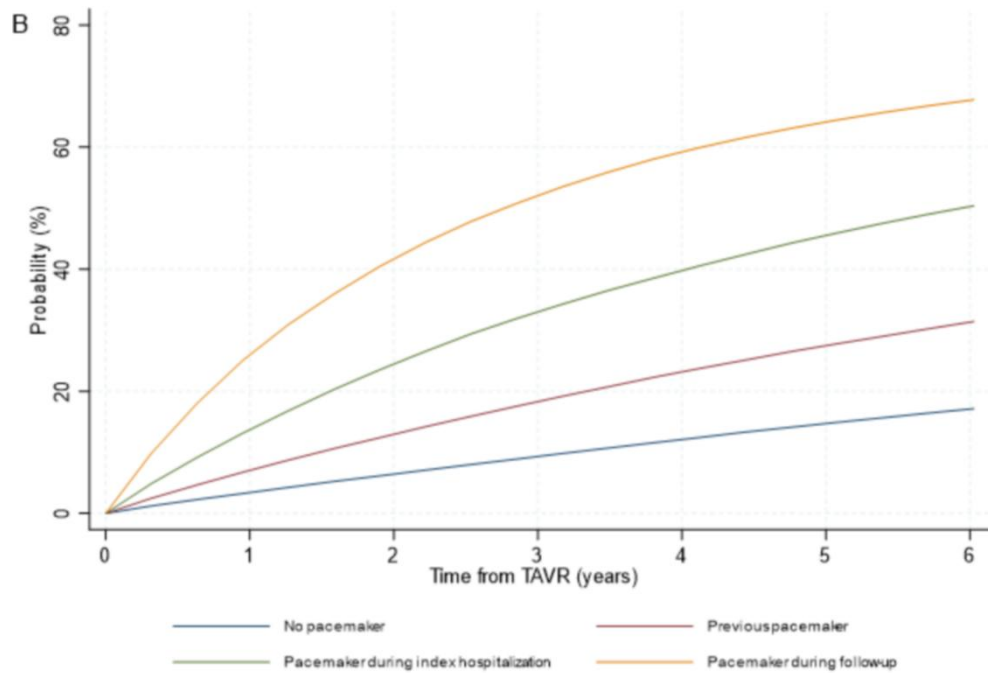
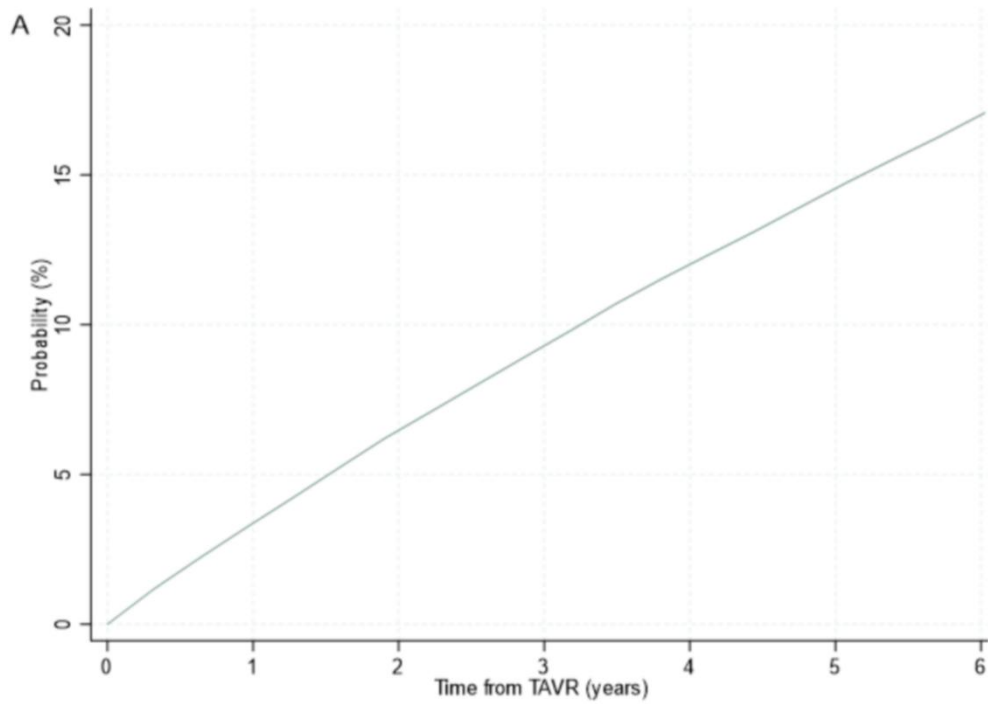


PPI: Permanent pacemaker implantation

X) Supplementary Figure 3 – Adjusted probabilities of transitioning from post-TAVR status to all-cause mortality heart failure hospitalization

Panel A: Probability over time in the overall population

Panel B: Probability over time according to PPI status



PPI: Permanent pacemaker implantation

