

Incidence of Conduction Disorders and Requirements for Permanent Pacemaker After Transcatheter Aortic Valve Implantation

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Abstract

Background: Transcatheter aortic valve implantation (TAVI) has become a therapeutic option for high-risk or non-operable patients with severe symptomatic aortic stenosis. Atrioventricular conduction disturbances requiring permanent pacemaker (PPM) are a common and clinically important complication.

Objectives: To evaluate the incidence of conduction disorders (CDs) after TAVI and the need for subsequent PPM implantation. To identify the predictors of postoperative PPM implantation.

Methods: Retrospective study. All patients who underwent TAVI in a public hospital from December/2011 to June/2016 were included. Multivariate analysis was conducted to establish the predictor of permanent pacemaker implantation. Survival curves were constructed by the Kaplan-Meier method. Statistically significant variables were those with p value < 0.05.

Results: 64 patients with AS underwent TAVI. Eleven patients were excluded. TAVI induced a new CD in 40 (77%) of the remaining 53 patients. The most common new CDs were 3rd degree AV block (32%) and left bundle branch block (30%). Sixteen patients (30,2%) underwent PPM implantation during the index hospitalization. On univariate analysis the risk factors for PPM implantation were CoreValve[®] use (OR: 1,76; P = 0,005), larger prosthesis implantation (P = 0,015), presence of a QRS \geq 120 ms (OR: 5,62; P = 0,012), and 1st degree AV block (OR: 13; P = 0.008). On multivariate analysis the presence of 1st degree AV block predicted the need for PPM.

Conclusion: TAVI induced CDs requiring PPM in 30% of the patients. The presence of 1st degree AV block predicted the need for PPM. (Int J Cardiovasc Sci. 2019;32(5):492-504)

Keywords: Atrioventricular Block; Bundle-Branch Block; Aortic Valve Stenosis/therapy; Transcatheter Aortic Valve Implantation/methods.

Introduction

Aortic stenosis (AoS) is the most common valve disease in developed countries, affecting approximately 3% of the population older than 75.¹ In Brazil, with an increase in life expectancy, a significant increase in cases of degenerative AoS is expected for the coming years.²

The mortality rate of patients with symptomatic AoS is approximately 50% in the first 2 years with no surgical treatment.^{3,4} Aortic valve replacement is associated with low mortality when performed in

patients without severe comorbidities.⁵ However, at least 30% of symptomatic patients with severe AoS are not operated because of the presence of comorbidities, ventricular dysfunction or old age.^{6,7} A less invasive form of treatment would be an attractive alternative for patients with high surgical risk.

Transcatheter aortic valve implantation (TAVI) is a recently developed technique for the treatment of symptomatic patients with severe AoS considered to be inoperable or at high surgical risk.⁸⁻¹³ The 2 types of aortic valve prosthesis most used for percutaneous

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implantation are: A CoreValve[®] (self-expanding) and Sapien[®] (balloon-expandable).^{11,12-16}

Percutaneous implantation has evolved a lot over the past years, but it presents some challenges. Conduction disorders requiring permanent pacemaker implantation are among the main complications of the procedure. TAVI is associated with a greater need for pacemakers compared to surgery, particularly when the CoreValve[®] prosthesis is used.¹⁷⁻²⁴

In addition to the greater need for permanent pacemaker implantation, a higher incidence of intraventricular conduction disorders has been demonstrated, notably left bundle branch block (LBBB) after TAVI. Several authors have shown that the development of LBBB after TAVI is associated with a greater need for pacemaker, ventricular dysfunction and increased long-term mortality.²⁵⁻²⁷

The objectives of this study are to determine the incidence of new conduction disorders and the need for a permanent pacemaker after TAVI, to identify predictors of the need for a permanent pacemaker, and to conduct an exploratory analysis to describe the long-term mortality of patients who developed conduction disorders.

Methodology

Retrospective study. The study included all patients undergoing TAVI in a major public cardiology hospital from December 2011 to June 2016. TAVI was recommended for patients with severe AoS considered to be inoperable or at high surgical risk by a Heart Team of clinical cardiologists, interventional surgeons and cardiac surgeons. The decision of surgical risk was obtained by calculating the EuroSCORE I.²⁸ The decision on the best form of treatment — clinical, surgical or TAVI — was taken by the Heart Team, considering the risk assessed by Euroscore and other variables not considered in the score but increased the surgical risk, such as the presence of porcelain aorta, fragility level, hostile chest and cirrhosis of the liver.

The feasibility of TAVI was determined after analysis of tomographic images from aortic measurements, aortic ring diameter, coronary artery height and femoral artery caliber. Some factors involved in planning the procedure, such as the best access route and the type and size of the prosthesis to be implanted, were defined by the surgical and interventional team after analysis of tomographic images. The prostheses used were CoreValve[®] from Medtronic, Sapien[®] from Edwards and Inovare[®] from

Braille. The access routes were transfemoral, transapical, transaortic and the subclavian artery. Transfemoral access was the preferred route in the absence of severe iliac or femoral artery disease. The transapical access route was recommended for patients with inadequate vascular access. The prostheses used for transapical access were Sapien[®] and Inovare[®]. All implants were performed under general anesthesia. Temporary transvenous pacemaker was implanted in all patients before the procedure and maintained for at least 48 hours.

The study was approved by the local research ethics committee and all patients undergoing TAVI signed an informed consent.

All data were collected by the first author of this manuscript by reviewing medical records. The electrocardiograms available in the medical records were ordered according to the dates they were taken. These electrocardiograms were divided into 4 groups: Pre-TAVI ECGs, ECGs taken after TAVI but still in the intensive care unit, ECGs after TAVI taken at the ward and ECGs taken at outpatient follow-up. The ECGs were analyzed independently by the author and a second cardiologist. The electrocardiographic reports followed the criteria defined by the Brazilian Guidelines on Electrocardiography.²⁹

The criterion used to recommend a permanent pacemaker still in the operating room after the TAVI was implanted was the presence of high-grade AVB or intrinsic rhythm of less than 40 beats per minute during inhibition of the temporary pacemaker. Recommendations of a permanent pacemaker while in hospital were determined by a team of clinical cardiologists, electrophysiologists and intensivists, considering the Brazilian and European guidelines for the implantation of artificial cardiac pacing devices.^{30,31}

Statistical analysis

Statistical analysis was performed using SPSS and Microsoft Excel.

The dichotomous variables possibly predicting the need for permanent pacemaker implantation during hospital stay were determined by preparing contingency tables and determining the odds ratio. The P value was calculated using Fisher's exact test. Every association with $P < 0.05$ was considered significant.

The continuous variables of normal distribution that were predictors of the need for permanent pacemaker

implantation during hospital stay were presented as mean \pm standard deviation, distribution variables other than normal were presented as median \pm interquartile range. Distribution of the continuous variables of patients who underwent permanent pacemaker implantation during hospital stay were compared using unpaired t test (used in normal distribution variables) or using the Mann-Whitney test (used in variables with distribution other than normal). Variables with p value $<$ 0.05 were considered statistically significant.

For the multivariate analysis, logistic regression that included the variables with P value $<$ 0.25 in the univariate analysis was used. The selection of variables in the model was performed using the step-wise method.

Survival curves and pacemaker-free survival were constructed using the Kaplan-Meier method. Comparisons between the survival curves of patients undergoing implantation of different types of prostheses, and patients with conduction disorders or patients with no conduction disorders were compared using the Log-rank test. Again, results with P value $<$ 0.05 were considered statistically significant.

Results

Characteristics of the population and description of the procedure

From December 2011 to June 2016, 64 patients underwent TAVI at INC. Five patients with pacemakers and 6 patients with biological aortic prosthesis dysfunction were excluded before TAVI.

The mean age of the 53 patients included was 78.4 years and most of them were females (64.2%). The median of the EuroSCORE was 10.8% (Interquartile range: 7.95-16.8%). Mean ejection fraction was 58.8% with median of 62.4%. Table 1 shows the baseline characteristics of the 53 patients included in the study.

Table 2 describes the electrocardiographic findings of 52 of the 53 patients who underwent TAVI. The medical records of one of the 53 patients had no electrocardiogram available for analysis, but it was said that the patient was in sinus rhythm. Fourteen patients (26.4%) had atrial fibrillation and 39 were in sinus rhythm. The median PR interval of these patients was 160 ms (Interquartile range: 160-200 ms). The median duration of QRS complexes was 100 ms (Interquartile range: 80-140 ms) and LBBB was in 17% of the cases (9/52).

Table 1 - Characteristics of the 53 patients included in the study

	Number/total and (%)
Age (mean \pm SD)	78.4 \pm 18.11
Male sex	19/53 (35.8%)
Body mass index (mean \pm SD)	26.13 \pm 5.22
Cardiovascular risk factors:	
Hypertension	47/53 (88.7%)
Diabetes	14/53 (26.4%)
Dyslipidemia	48/53 (71.7%)
Smoking	11/53 (20.8%)
Coronary artery disease	28/53 (52.2%)
History of myocardial infarction	5/53 (9.41%)
History of PCI	10/53 (18.9%)
History of CABG surgery	6/53 (11.3%)
Others comorbidities:	
History of stroke or TIA	7/53 (13.2%)
Presence of porcelain aorta	12/53 (22.6%)
PASP $>$ 50 mmHg	13/53 (24.5%)
COPD	19/53 (17.0%)
Creatinine $>$ 2 mg/dl	4/53 (6.90%)
Pre-implantation symptoms:	
History of syncope	9/53 (17.0%)
NYHA II	10/53 (18.9%)
NYHA III or IV	43/53 (79.1%)
Use of negative chronotropic medication:	30/53 (56.6%)
Beta-blockers	25/53 (47.2%)
Calcium channel blocker	1/53 (1.90%)
Amiodarone	2/53 (3.80%)
Digoxin	5/53 (9.40%)
Etiology of valve disease:	
Degenerative AoS	50/53 (94.3%)
Bicuspid aortic valve	3/53 (5.70%)
EuroSCORE:	
EuroSCORE median [IQR]	10.8 [7.95 - 16.81]
EuroSCORE $>$ 15%	15/53 (28.3%)

Cont. Table 1 - Characteristics of the 53 patients included in the study

	Number/total and (%)
LV ejection fraction:	
LVEF (mean \pm SD)	58.83 \pm 16.67
LVEF < 40%	9/53 (17.0%)
LV/AO gradients in mmHg:	
Mean LV/AO grad (mean \pm SD)	53.4 \pm 18.7
Maximum LV/AO grad (mean \pm SD)	80.8 \pm 22.6
LV hypertrophy	44/53 (83.0%)
Mitral annulus calcification	28/53 (52.8%)

SD: standard deviation; IQR: interquartile range; PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting; TIA: transient ischemic attack; COPD: chronic obstructive pulmonary disease; LV: left ventricle; FE: ejection fraction; Grad: gradient; AO: aorta.

Table 2 - Echocardiographic characteristics of patients

	Number/total and (%)
Cardiac rhythm	
Sinus rhythm	39/53 (73.6%)
Atrial fibrillation or flutter	14/53 (26.4%)
HR (mean \pm SD)	
HR < 60 bpm	8/52 (15.1%)
First-degree AV block	7/41 (13.2%)
Median PR interval [IQR]	160 ms [160 – 200]
Median QRS duration [IQR]	100 ms [80 – 140]
LBBB	9/52 (17.0%)
RBBB	9/52 (17.0%)
LAHB	11/52 (20.8%)
LPHB	0/52 (0%)
LBBB or RBBB	18/52 (34.0%)
First-degree AVB or bundle branch block	20/52 (38.4%)

IQR: interquartile range; LBBB: left bundle branch block; RBBB: right bundle branch block; LAHB: left anterior hemiblock; LPHB: left posterior hemiblock; AVB: atrioventricular block.

Most patients (39 of 53 - 73.6%) had the CoreValve[®] prosthesis implanted. Eight received Sapien[®] (15.1%) and 6 received Inovare[®] (11.2%) (table 3). The sizes of the prostheses used were: number 20 (1 Inovare[®] prosthesis), number 23 (6 Sapien[®] prostheses), number 24 (1 Inovare[®] prosthesis), number 26 (1 Sapien[®] prosthesis, 2 Inovare[®] prostheses and 14 CoreValve[®] prostheses), number 28 (1 Inovare[®] prosthesis), number 29 (1 Sapien[®] prosthesis and 19 CoreValve[®] prostheses), number 30 (1 Inovare[®] prosthesis) and number 31 (6 CoreValve[®] prostheses). Balloon pre-dilation was performed in only 30% of the cases. In 7 patients, a second prosthesis was implanted (CoreValve[®] in CoreValve[®]). The femoral artery was the most used access route (81% of the cases) followed by the transapical route.

Incidence of new conduction disorders and need for pacemaker

Forty of the 52 patients (77%) developed new conduction disorders after TAVI, with 23 new atrioventricular conduction disorders, 13 new interventricular conduction disorders and 4 new mixed conduction disorders (first-degree AVB and concomitant LBBB). (Figure 1)

Twelve of the 52 (23%) ECG patients available for analysis did not develop new conduction disorders after TAVI. None of them died. Eight of these 12 patients had

Table 3 - Echocardiographic variables of the procedure

	Number/total
Type of prosthesis:	
CoreValve [®]	39/53 (73.6%)
Sapien [®]	8/53 (15.1%)
Inovare [®]	6/53 (11.2%)
Pre-dilatation with balloon	16/53 (30.2%)
Need for 2 nd valve (valve-in-valve)	7/53 (13.2%)
Prosthesis size in mm (mean \pm SD)	27 \pm 2.60
Access routes:	
Femoral artery	43/53 (81.1%)
Transapical	6/53 (11.3%)
Transaortic	3/53 (5.70%)
Subclavian artery	1/53 (1.90%)

normal AV and interventricular conduction before TAVI and remained without any conduction disorders after the procedure. Two patients had LBBB before TAVI and remained with LBBB after the procedure. One patient had an LAHB prior to TAVI and persisted with LAHB after the procedure and one patient who had first-degree AVB with RBBB maintained these electrocardiographic abnormalities after implantation.

Of the 53 patients included in the study, 16 (30.18%) had a permanent pacemaker implanted before discharge. The pacemaker was implanted in the operating room after TAVI in 11 of the 16 patients (68.7%). These 11 patients maintained complete atrioventricular block and escape rhythm with enlarged QRS complexes during pacemaker inhibition at the end of the procedure. In 5 patients, the pacemaker recommendation occurred between the 3rd and the 8th day after the procedure. CAVB was the recommendation of pacemaker implant in 5 of the 6 patients. In 1 patient, the pacemaker was recommended by second-degree AVB.

Four of the 53 patients (7.5%) died before discharge. All deaths occurred in female patients. Three died of

complications related to the procedure in the first 24 hours of implantation and one death occurred 48 days after TAVI due to cardiogenic shock. All patients who died had developed new conduction disorders (Figure 1).

Predictors of the need for pacemaker

Forty-nine patients were discharged. Table 4 compares the characteristics of the 16 patients who underwent pacemaker implantation with the characteristics of the 33 who were discharged without the need for pacemaker implantation. In the univariate analysis, the percentage of patients with QRS complexes ≥ 120 ms and first-degree AVB was higher in the group that was discharged with permanent pacemaker than in those who did not need this device. QRS ≥ 120 ms was present in 68.8% of the patients who had pacemakers implanted and in 28.1% of those who did not have pacemakers implanted (odds ratio: 5.62; 95% CI 1.52 to 20.80; $p = 0.012$). First-degree AVB was found in 50% of the patients who had pacemakers implanted and in 7.1% of those who did not have it implanted. (Table 4)

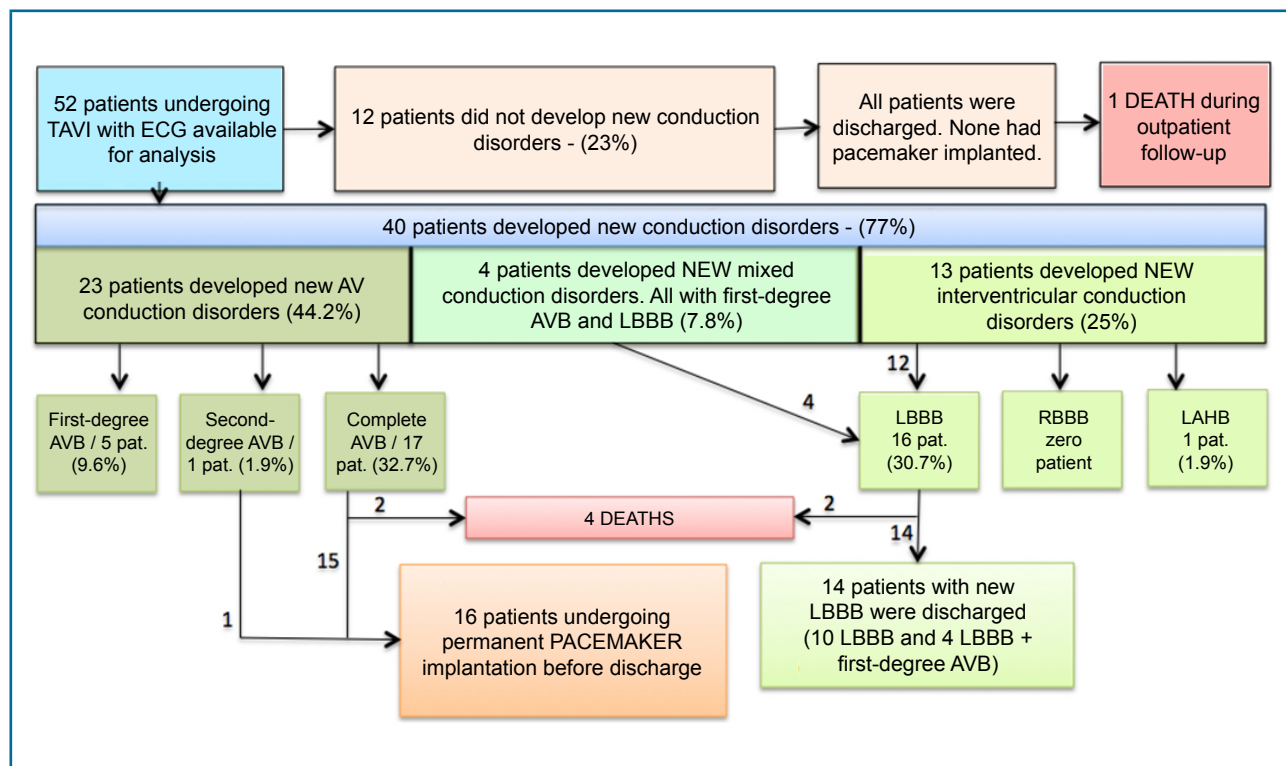


Figure 1 - New conduction disorders after transcatheter aortic valve implantation.

TAVI: transcatheter aortic valve implantation; dis.: disorder; LBBB: left bundle branch block; RBBB: right bundle branch block; LAHB: left anterior hemiblock; IV: intraventricular; AV: atrioventricular; AVB: atrioventricular block; pat.: patients.

Table 4 - Comparison of characteristics of patients who were discharged with and without permanent pacemaker

	33 patients were discharged without permanent pacemaker	16 patients had permanent pacemaker implanted while in hospital	Odds ratio (95% CI), p value
Clinical variables:			
Age (mean ± SD)	79.09 ± 8.46	78.63 ± 8.4	0.857
Male sex	12/33 (36.4%)	7/16 (43.8%)	0.756
Hypertension	29/33 (87.9%)	14/16 (87.5%)	1.00
Diabetes	10/33 (30.3%)	3/16 (18.8%)	0.501
Dyslipidemia	22/33 (66.7%)	12/16 (75%)	0.743
Smoking	8/33 (24.2%)	2/16 (12.5%)	0.463
Coronary artery d.	17/33 (51.5%)	9/16 (53.3%)	0.771
History of myocardial infarction	5/33 (15.2%)	0/16 (0.0%)	0.158
History of PCI	6/33 (18.2%)	4/16 (25%)	0.708
History of CABG surgery	6/33 (19%)	0/16 (0.0%)	0.158
History of syncope	7/33 (21.2%)	1/16 (6.3%)	0.245
Neg. chron. medication	19/33 (57.6%)	9/16 (56.3%)	1.00
Median Euroscore [IQR]	10.9 [8.57 - 17.65]	10.25 [6.92 - 14.20]	0.675
Echocardiographic variables:			
HR (mean ± SD)	72.78 ± 11.29	73.43 ± 16.8	0.870
HR < 60 bpm	4/32 (12.5%)	4/16 (25%)	0.413
QRS duration in ms Median [IQR]	100 [80 - 120]	140 [100 to 160]	0.013
QRS ≥ 120 ms	9/32 (28.1%)	11/16 (68.8%)	5.62 [1.52 - 20.80] p = 0.012
Median PR interval [IQR]	160 [160 - 200]	190 [160 to 250]	0.984
Atrial fibrillation or flutter	7/33 (21.2%)	6/16 (37.5%)	0.304
First-degree AV block	2/28 (7.1%)	5/10 (50.0%)	13.00 [1.95 - 86.80] p = 0.008
LBBS	4/32 (12.5%)	5/16 (31.3%)	0.137
RBSB	3/32 (9.4%)	5/16 (30.0%)	0.096
LAHB	5/32 (15.6%)	5/16 (31.3%)	0.266
Echocardiographic variables:			
LVEF (mean ± SD)	58.78 ± 17.82	55.65 ± 14.88	0.540
Max AO LV grad (mean ± SD)	80.0 ± 23.1	80.0 ± 20.4	0.989
HVE on Echo	26/33 (78.8%)	15/16 (93.8%)	0.245
Mitral annulus calcification	15/33 (45.5%)	10/16 (62.5%)	0.363

Cont. Table 4 - Comparison of characteristics of patients who were discharged with and without permanent pacemaker

	33 patients were discharged without permanent pacemaker	16 patients had permanent pacemaker implanted while in hospital	Odds ratio (95% CI), p value
Variables related to the implant:			
CoreValve® implant	21/33 (63.6%)	16/16 (100%)	1.76 [1.33 - 2.33] p = 0.005
2 nd valve required	3/33 (9.1%)	4/16 (25%)	0.195
Femoral access	27/33 (81.8%)	15/16 (93.8%)	0.401
Prosthesis size in mm	26.87 ± 2.50	28.56 ± 1.96	

IQR: interquartile range; LBBB: left bundle branch block; RBBB: right bundle branch block; LAHB: left anterior hemiblock; LPHB: left posterior hemiblock; AVB: atrioventricular block.

The CoreValve® implant was associated with the pacemaker implant in a statistically significant way in the univariate analysis (odds ratio: 1.76; (95% CI: 1.33 to 2.33; p = 0.005). All patients undergoing permanent pacemaker implantation were CoreValve® patients. Larger prostheses were also associated with a greater need for permanent pacemaker implantation (Table 4).

In the multivariate analysis, the only variable considered to be an independent predictor of the need for pacemaker implantation after TAVI was the presence of first-degree AVB before implantation of the prosthesis. (Odds ratio: 13.00; 95% CI 1.95 to 86.80; p = 0.008).

Survival of patients undergoing TAVI: Median follow-up of the 53 patients undergoing TAVI was 363 days with an interquartile range of 86.5 to 755.5 days. During this follow-up, 13 (24.5%) died (4 during index admission and 9 at outpatient follow-up). Eight of the 9 patients who died during follow-up had either LBBB or permanent pacemaker. The survival of patients who did not develop new conduction disorders was higher than those with new conduction disorders, but this result was not statistically significant (p = 0.26). (Figure 2)

Nineteen (35.8%) of the 53 patients had pacemakers implanted throughout the study (16 during index admission and 3 at outpatient follow-up). Pacemaker-free survival was significantly lower in the group of patients who had CoreValve® implanted, in patients who had first-degree AVB before TAVI and in those with QRS complex greater than 120 ms before TAVI. Pacemaker-free survival was also lower in patients who had RBBB prior to TAVI. This result was not statistically significant (p = 0.08) (Figures 3 and 4).

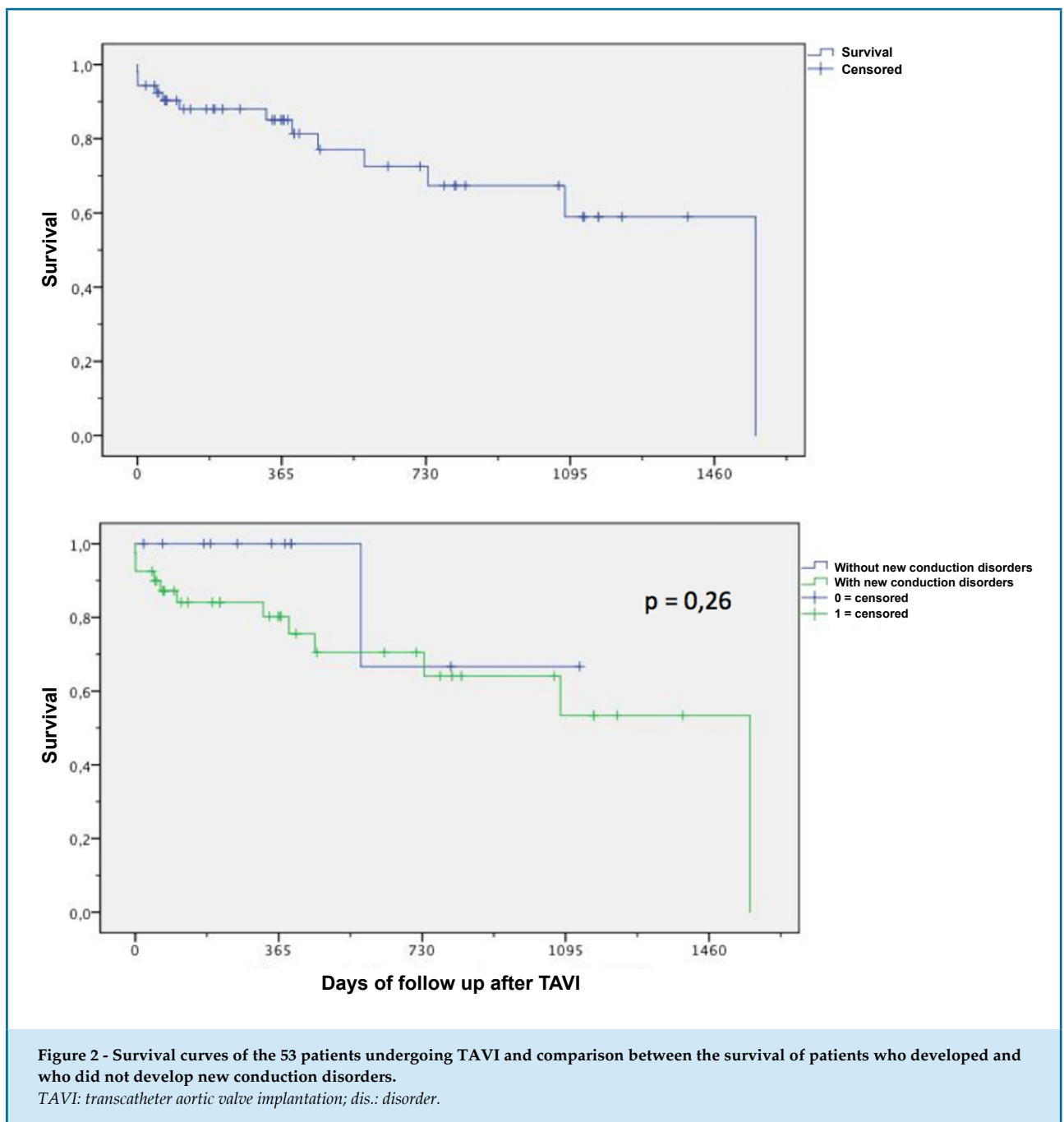
Discussion

The benefits of TAVI include: improved functional class and quality of life, increased ejection fraction and increased short- and long-term survival.⁹⁻¹² Despite some favorable clinical outcomes, complications such as the development of LBBB and AVB requiring pacemakers are a source of concern.

The high incidence of conduction disorders after TAVI can be explained by the anatomical proximity of the conduction system to the aortic valve.³² TAVI involves the exclusion of valve tissue by the prosthesis and compression of the annulus and adjacent structures, including the fibrous skeleton of the heart and the conduction system. A necropsy study of a patient who had CAVB after TAVI demonstrated the presence of a hematoma in the interventricular septum that compressed the bundle of His.³³

In this study, 77% of the patients developed new conduction disorders during index admission. These findings are identical to those described by Fraccaro et al. in 64 patients undergoing TAVI,²⁴ and very similar to those described in the studies by Calvi et al., who found new conduction disorders in 68% of the 30 patients who underwent the procedure.²³

In this study, it was found that 30.7% of the patients developed LBBB. This finding is similar to that described by Houthuizen et al., who found a new LBBB in 34% of the 679 patients who underwent TAVI.²⁵ The incidence of LBBB after TAVI can range from 4 to 65% depending on the prosthesis used. According to Martinez et al., the frequency of a new LBBB after the



implantation of a self-expanding prosthesis ranges from 22 to 65%, while with the use of a balloon-expandable prosthesis, it ranges from 4 to 30.2%.³⁴ In the study by Testa et al., the onset of LBBB after TAVI was observed in 43% of the 1,060 patients treated with the CoreValve® prosthesis. According to this author, the presence of LBBB is associated with a higher rate of pacemaker implantation up to 30 days after TAVI.²⁶

Sixteen of the 53 patients (30.2%) included in this study had a permanent pacemaker implanted

during index admission. In a review of 42 studies, the recommendation for pacemaker implantation after TAVI ranged from 4 to 51%.¹⁹ The highest incidence was described by Akin et al.¹⁷ and the lowest one was found in the study by Eltchaninoff et al.¹⁶

The risk factors for the need for a permanent pacemaker after TAVI found in this study in the univariate analysis were: use of CoreValve® prosthesis, implantation of larger prostheses, QRS complex \geq 120 ms and first-degree AVB. In this study, all of the 16

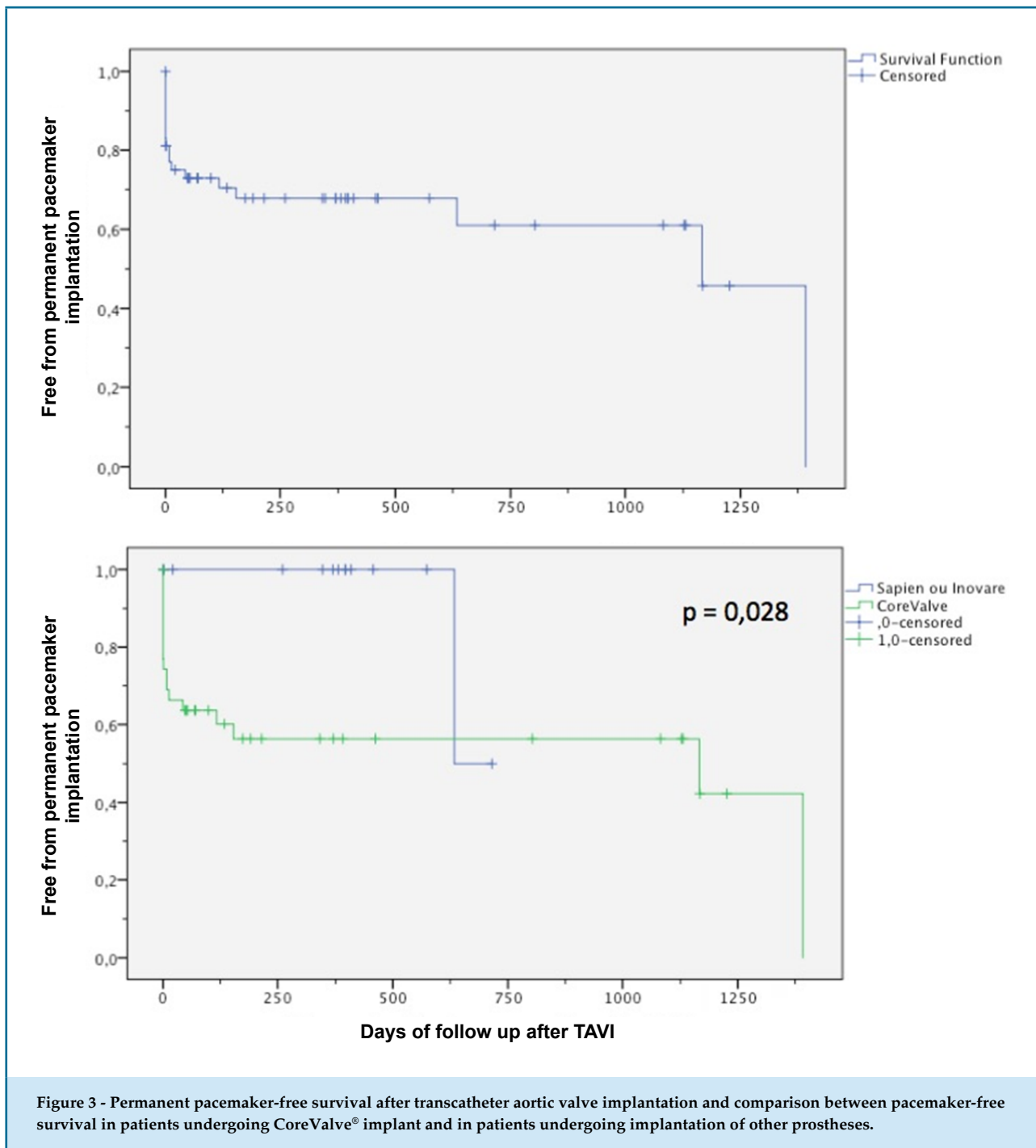


Figure 3 - Permanent pacemaker-free survival after transcatheter aortic valve implantation and comparison between pacemaker-free survival in patients undergoing CoreValve® implant and in patients undergoing implantation of other prostheses.

patients who needed a pacemaker had the CoreValve® prosthesis implanted. Other authors also demonstrated that the need for a permanent pacemaker with the CoreValve® prosthesis is significantly higher compared to the Sapien® prosthesis.^{16-19,21-24} In the study by Piazza et al., who used the CoreValve® prosthesis, the pacemaker implant rate was 19% in 91 patients evaluated.²² In the PARTNER study, which used Sapien® prostheses, this

rate was 3.8% in 699 patients evaluated up to 30 days after the procedure.¹⁰ In the study by Aktug et al., 20 of the 72 patients (28%) who had the CoreValve® prosthesis implanted required a permanent pacemaker, whereas only 4 of the 82 patients (5%) who had Sapien® implanted required the device.³⁵

Due to its longer length (53 to 55 mm), the CoreValve® prosthesis extends from the ascending aorta to the LV

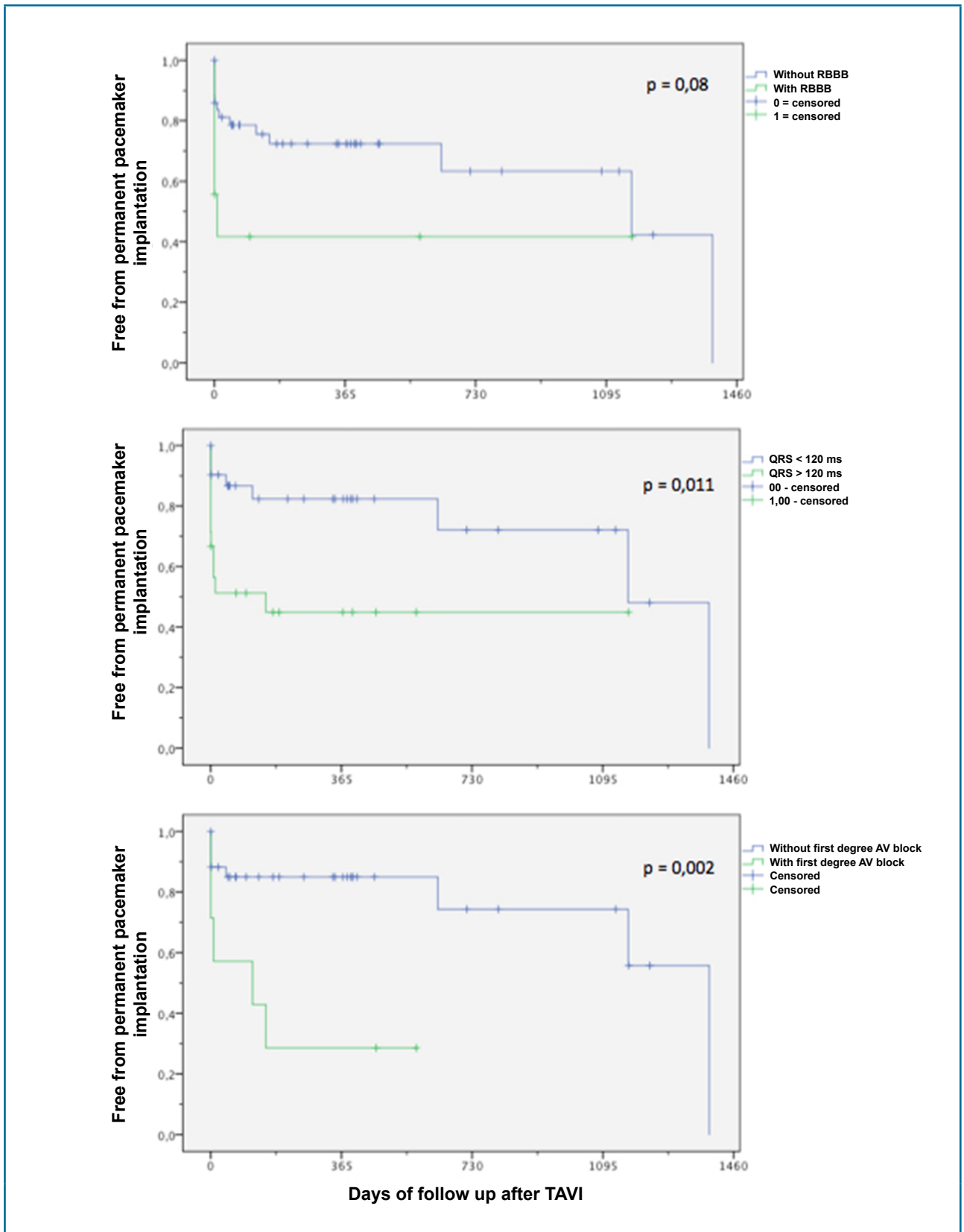


Figure 4 - Comparison between pacemaker-free survival in RBBB and non-RBBB patients, in patients with QRS > 120 ms and in those with QRS < 120 ms and in patients with first-degree AVB and in those without first-degree AVB. RBBB: right bundle branch block; AVB: atrioventricular block; TAVI: transcatheter aortic valve implantation.

outflow tract. During implantation, the lower third of the prosthesis may compress the interventricular septum and the conduction system.^{19,22,24,36} The Sapien[®] prosthesis extends a few millimeters below the annular plane. The lower incidence of conduction disorders with the Sapien[®] prosthesis is due to a higher implant and less extension of the prosthesis in the LV outflow tract.^{19,22,24}

The implantation of larger prostheses was associated with a greater need for pacemakers in this study. The mean prosthesis size of patients who had pacemaker implanted was significantly higher than that of those who did not have any pacemaker implanted. The implantation of larger prostheses was also a predictor of the need for pacemakers after TAVI in a multicenter study that evaluated 243 patients in the UK.³⁶

The presence of previous conduction disorders is a risk factor for the development of AVB in both conventional surgery and TAVI.^{19,20} In this study, patients with history of first-degree AVB had a 13-fold higher risk of pacemaker implantation compared to those without first-degree AVB. The presence of first-degree AVB before TAVI was also a predictor of the need for pacemakers in the FRANCE-TAVI Registry¹⁶ and in the studies by De Carlo et al. and Bleiziffer et al.^{37,38}

In this study, patients with QRS complex duration ≥ 120 ms had a 5-fold increased risk of pacemaker implantation compared to those who did not have the same ECG finding before TAVI. The presence of previous conduction disorders was an independent predictor of the need for pacemakers in a meta-analysis published by Siontis et al.¹⁹

In the multivariate analysis, the only variable considered to be an independent predictor of the need for pacemaker implantation after TAVI was the presence of first-degree AVB before implantation of the prosthesis. It should be noted that this is a retrospective design study that reports the initial experience of a single center with a small sample size. Thus, the multivariate analysis presented has low statistical power, which means that there is a considerable chance of type II error. Despite these limitations, the results found were similar to those described in the literature.

Other factors associated with the development of conduction disorders after TAVI, such as depth of self-expanding prostheses and calcification in the outflow tract were not evaluated in this study. The excessively low valve implantation was associated with the development of conduction disorders after TAVI in some

series published in the literature.^{19,22,24} Piazza described a significant correlation between the depth of the implant in the LVOT and the onset of LBBB after implantation of self-expanding prosthesis.²²

History of conduction disorders after TAVI is not well understood yet, because it is a relatively new technology and further studies are required to say the best course of action to be taken in the development of conduction disorders. Implantation of permanent pacemaker after TAVI is justified among seniors with cardiac structural disease. Potential problems related to the use of provisional transvenous pacemaker, such as ventricular perforation, infection, prolonged immobilization and longer hospital stay, contribute to reduced threshold of indication of permanent artificial cardiac pacing. It is known that displacement of the electrode of the provisional pacemaker can cause catastrophic failures with potentially serious consequences, exposing the patient to the risk of asystole and death. These facts justify the decision of implanting permanent pacemaker earlier, a conduct supported by experts, but not based on the results of randomized studies, as these are not available in this particular situation.³⁹

On the other hand, implantation of permanent pacemaker is also not risk-free. Elderly patients with multiple comorbidities have an increased risk of hematoma, pocket infection and endocarditis. Besides, cardiac pacing may lead to interventricular dyssynchrony and worsening of long-term ventricular function.⁴⁰ In a sub-analysis of the PARTNER study, the presence of pacemaker was an independent predictor of mortality in one year.²¹

In this study, 8 of the 9 patients who died during follow-up had either LBBB or permanent pacemaker. Houthuizen et al. demonstrated an association between new LBBB after TAVI and increased mortality.²⁵ The 60% increase in 1-year mortality in patients who developed new LBBB after TAVI in the study by Houthuizen et al. suggests that the onset of LBBB after TAVI is a serious complication, which attenuates the benefit achieved by the procedure.

It should be noted that in this study the prostheses used were first-generation prostheses. Despite the technological development of the new prostheses and the experience gained with the procedure, the incidence of conduction disorders after TAVI is still a source of concern and has inconsistent results depending on the prosthesis used. The need for a permanent pacemaker

is at least 2-fold higher after Sapien3® implantation compared to the first generation Sapien® prosthesis.³⁹ The need for a permanent pacemaker using the Medtronic Evolut® prosthesis is lower (11.7 - 25%) compared to the CoreValve® prosthesis (9 - 38%), although with a relatively high incidence.³⁹

Conduction disorders requiring permanent pacemaker implantation remain a common complication after TAVI and may have a negative impact on the patients' prognosis.^{21,25,26,27,39} Strategies to reduce these complications are of great importance before extending TAVI to low-risk patients in whom these complications may have an even greater impact on prognosis.

Conclusions

TAVI caused the development of conduction disorders in the vast majority of patients. Seventy-seven percent of the patients developed new conduction disorders, the most frequent of which is complete AV block (32%) and left bundle branch block (30%).

Approximately 30% of the patients required a permanent pacemaker implanted during hospitalization.

A QRS complex with duration ≥ 120 ms, the presence of first-degree AVB, implantation of larger prostheses and the use of CoreValve were associated with the need for a permanent pacemaker in the univariate analysis.

In the multivariate analysis, the only variable considered to be an independent predictor of the need for pacemaker implantation after TAVI was the presence of first-degree AVB.

The survival of patients who developed new conduction disorders after TAVI was numerically worse than the survival of the rest of the population. This result was not statistically significant. The lack of statistical

significance can be attributed to the relatively short analysis time and small sample size.

Author contributions

Conception and design of the research: Santos MC, Azevedo FS, Rodrigues LCD, Weksler C, Colafranceschi AS, Lacerda GC. Acquisition of data: Santos MC, Azevedo FS, Rodrigues LCD, Colafranceschi AS, Lacerda GC. Analysis and interpretation of the data: Santos MC, Lamas CC, Lacerda GC. Statistical analysis: Santos MC, Lacerda GC. Writing of the manuscript: Santos MC, Lacerda GC. Critical revision of the manuscript for intellectual content: Santos MC, Lamas CC, Weksler C, Colafranceschi AS, Lacerda GC.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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Ethics approval and consent to participate

This study was approved by the Ethics Committee of the *Instituto Nacional de Cardiologia* under the protocol number 1.334.739. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

References

- Lindroos M, Kupari M, Heikkilä J, Tilvis R. Prevalence of aortic valve abnormalities in the elderly: An echocardiographic study of a random population sample. *J Am Coll Cardiol*. 1993;21(5):1220-5.
- Grinberg M, Accorsi TA. Aortic stenosis in the elderly: a Brazilian perspective. *Arq Bras Cardiol*. 2009;2(2):e9-12, e36-9.
- Ross J, Braunwald E. Aortic stenosis. *Circulation*. 1968;38(1 Suppl):61-7.
- Turina J, Hess O, Sepulcri F, Kraysenbuehl HP. Spontaneous course of aortic valve disease. *Eur Heart J*. 1987;8(5):471-83.
- Shahian DM, O'Brien SM, Filardo G, Ferraris VA, Haan CK, Rich JB, et al; Society of Thoracic Surgeons Quality Measurement Task Force. The society of Thoracic Surgeons 2008 cardiac surgery risk models: parte 3- valve plus coronary artery bypass grafting surgery. *Ann Thorac Surg*. 2009;88(1 Suppl):S43-62.
- Bouma BJ, Van den Brink RBA, Van der Meulen JHP, Verheul HA, Cheriex EC, Hamer HP, et al. To operate or not on elderly patients with aortic stenosis: the decision and its consequences. *Heart*. 1999;82(2):143-8.
- Iung B, Cachier A, Baron G, Messika-Zeitoun D, Delahaye F, Tornos P, et al. Decision-making in elderly patients with severe aortic stenosis: why are so many denied surgery?. *Eur Heart J*. 2005;26(24):2714-20.
- Cribier A, Eltchaninoff H, Tron C, Bauer F, Agatiello C, Nercolini D, et al. Treatment of calcific aortic stenosis with the percutaneous heart

- valve: mid-term follow-up from the initial feasibility studies: the French experience. *J Am Coll Cardiol.* 2006;47(6):1214-23.
9. Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, et al; PARTNER Trial Investigators. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med.* 2010;363(17):1597-607.
 10. Smith CR, Leon MB, Mack MJ, Miller DC, Moses JW, Svensson LG, et al; PARTNER Trial Investigators. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med.* 2011;364(23):2187-98.
 11. Makkar RR, Fontana GP, Jilalawi H, Kapadia S, Pichard AD, Douglas PS, et al; PARTNER Trial Investigators. Transcatheter aortic-valve replacement for inoperable severe aortic stenosis. *N Engl J Med.* 2012;366(18):1696-704.
 12. Adams DH, Popma JJ, Reardon MJ, Yakubov SJ, Coselli JS, Deeb GM, et al; U.S. CoreValve Clinical Investigators. Transcatheter aortic-valve replacement with a self-expanding prosthesis. *N Engl J Med.* 2014;370(19):1790-8.
 13. Holmes DR Jr, Mack MJ, Kaul S, Agnihotri A, Alexander KP, Bailey SR, et al. 2012 ACCF/AATS/SCAI/STS expert consensus document on transcatheter aortic valve replacement. *J Am Coll Cardiol.* 2012;59(13):1200-54.
 14. Grube E, Schuler G, Buellesfeld L, Gerckens U, Linke A, Wenaweser P, et al. Percutaneous aortic valve replacement for severe aortic stenosis in high-risk patients using the second- and current third-generation self-expanding CoreValve prosthesis: device success and 30-day clinical outcome. *J Am Coll Cardiol.* 2007;50(1):69-76.
 15. Bosmans JM, Kefer J, De Bruyne B, Herijgers P, Dubois C, Legrand V, et al. 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(5):762-7.
 16. Eltchaninoff H, Prat A, Gilard M, Leguerrier A, Blanchard D, Fournial G, et al. Transcatheter aortic valve implantation: early results of the France (French Aortic National CoreValve and Edwards) registry. *Eur Heart J.* 2011;32(2):191-7.
 17. Akin I, Kische S, Parankaya L, Schneider H, Rehders TC, Trautwein U, et al. Predictive factors for pacemaker requirement after transcatheter aortic valve implantation. *BMC Cardiovasc Disord.* 2012 Oct;12:87.
 18. Jilalawi H, Chakravarty T, Weiss RE, Fontana GP, Forrester J, Makkar RR. Meta-analysis of complications in aortic valve replacement: comparison of Medtronic-Corevalve, Edwards-Sapien and surgical aortic valve replacement in 8536 patients. *Catheter Cardiovasc Interv.* 2012; 80(1):128-38.
 19. Siontis GC, Juni P, Pilgrim T, Stortecky S, Büllsfeld L, Meier B. Predictors of permanent pacemaker implantation in patients with severe aortic stenosis undergoing TAVR: a meta-analysis. *J Am Coll Cardiol.* 2014;64(2):129-40.
 20. Hasan Basri E, Nihan K, Hasan A, Omeroglu SN, Kirali K, Guler M, et al. Risk factors for requirement of permanent pacemaker implantation after aortic valve replacement. *J Cardiac Surg.* 2006;21(3):211-5.
 21. Dizon JM, Nazif TM, Hess PL, Biviano A, Garan H, Douglas PS, et al. Chronic pacing and adverse outcomes after transcatheter aortic valve implantation. *Heart.* 2015;101(20):1655-71.
 22. Piazza N, Onuma Y, Jesserun E, Kint PP, Maugenes AM, Anderson RH, et al. Early and persistent intraventricular conduction abnormalities and requirements for pacemaking after percutaneous replacement of the aortic valve. *JACC Cardiovasc Interv.* 2008;1(3):310-6.
 23. Calvi V, Puzangara E, Pruiti GP, Conti S, Di Grazia A, Ussia GP, et al. Early conduction disorders following percutaneous aortic valve replacement. *Pacing Clin Electrophysiol.* 2009;32(Suppl 1):S126-30.
 24. Fraccaro C, Buja G, Tarantini G, Gasparetto V, Leoni L, Razzolini R, et al. Incidence, predictors, and outcomes of conduction disorders after transcatheter self-expandable aortic valve implantation. *Am J Cardiol.* 2011;107(5):747-54.
 25. Houthuizen P, Van Garsse LA, Poels TT, de Jaegere P, van der Boon RM, Swinkels BM, et al. Left bundle-branch block induced by transcatheter aortic valve implantation increases risk of death. *Circulation.* 2012;126(6):720-8.
 26. Testa L, Latib A, De Marco F, De Carlo M, Agnifili M, Latini RA, et al. Clinical impact of persistent left bundle-branch block after transcatheter aortic valve implantation with CoreValve Revalving System. *Circulation.* 2013;127(12):1300-7.
 27. Urena M, Mok M, Serra V, Dumont E, Nombela-Franco L, DeLarochellière R, et al. Predictive factors and long-term clinical consequences of persistent left bundle branch block following transcatheter aortic valve implantation with a balloon-expandable valve. *J Am Coll Cardiol.* 2012;60(18):1743-52.
 28. Nashef SA, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R. European system for cardiac operative risk evaluation (EuroSCORE). *Eur J Cardiothorac Surg.* 1999;16(1):9-13.
 29. Guimaraes JJ, Nicolau JC, Polanczyk CA, et al. Diretrizes de interpretação de eletrocardiograma de repouso. *Arq Bras Cardiol.* 2003;80(Suppl 2):1-63.
 30. European Society of Cardiology (ESC); European Heart Rhythm Association (EHRA), Brignole M, Auricchio A, Baron-Esquivias G, Bordachar P, Boriani G, Breithardt OA, et al. 2013 ESC guidelines on cardiac pacing and cardiac resynchronization therapy. *Europace.* 2013;15(8):1070-118.
 31. Martinelli Filho M, Zimmerman LI, Lorga AM, Vasconcelos JTM, Rassi A Jr. Guidelines for Implantable Electronic Cardiac Devices of the Brazilian Society of Cardiology. *Arq Bras Cardiol.* 2007;89(6):e210-e238.
 32. Piazza N, de Jaegere P, Schultz C, Becker AE, Serruys PW, Anderson RH. Anatomy of the aortic valvar complex and its implications for transcatheter implantation of the aortic valve. *Circ Cardiovasc Interv.* 2008;1(1):78-81.
 33. Moreno R, Dobarro D, Lopéz de Sá E, Prieto M, Morales C, Calvo Orbe L, et al. Cause of complete atrioventricular block after percutaneous aortic valve implantation. Insights from a necropsy study. *Circulation.* 2009;120(5):e29-30.
 34. Martinez-Selles M, Bramlage P, Thoenes M, Schymik G. Clinical significance of conduction disturbances after aortic valve intervention: current evidence. *Clin Res Cardiol.* 2015;104(1):1-12.
 35. Aktug O, Dohmen G, Brehmer K, Koos R, Altiok E, Deserno V, et al. Incidence and predictors of left bundle branch block after transcatheter aortic valve implantation. *Int J Cardiol.* 2012;160(1):26-30.
 36. Khawaja MZ, Rajani R, Cook A, Khavandi A, Moynagh A, Chowdhary S, et al. Permanent pacemaker insertion after Corevalve Transcatheter aortic valve implantation. *Circulation.* 2011;123(9):951-96.
 37. De Carlo M, Giannini C, Bedogni F, Klugmann S, Brambilla N, De Marco F, et al. Safety of a conservative strategy of permanent pacemaker implantation after transcatheter aortic CoreValve implantation. *Am Heart J.* 2012;163(3):492-9.
 38. Bleiziffer S, Ruge H, Horer J, Klugmann S, Brambilla N, De Marco F, et al. Predictors for new-onset complete heart block after transcatheter aortic valve implantation. *JACC Cardiovasc Interv.* 2010;3(5):524-30.
 39. Auffret V, Puri R, Urena M, Chamandi C, Rodriguez-Gabella T, Philippon F, et al. Conduction disturbances after transcatheter aortic valve replacement. *Circulation.* 2017;136(11):1049-69.
 40. Wilkoff BL, Cook JR, Epstein AE, Greene HL, Hallstrom AP, Hsia H, et al. Dual chamber and VVI implantable defibrillator trial investigators. Dual-chamber pacing or ventricular backup pacing in patients with an implantable defibrillator: The DAVID trial. *JAMA.* 2002;288(24):3115-23.

