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Original article

Anemia as a Predictor of Transient Pacemaker Dependency After TAVI

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Abstract

Background: Transcatheter aortic valve implantation (TAVI) has emerged as an effective and safe treatment for severe aortic stenosis in the last decades compared for surgical aortic valve replacement. However, it stills associated with high risk of conduction abnormalities requiring pacemaker implantation. Our study aimed to examine factors associated with transient conduction abnormities that don't require pacemaker on long term. ***Methods:*** Retrospective analysis of all consecutive patients who underwent TAVI between 2010 and 2019 in Kaplan Medical Center, Rehovot, Israel. ***Results:*** Pre-TAVI haemoglobin levels were significantly lower in patients who developed transient CA compared to patients who develop persistent conduction abnormalities and were pacemaker dependent on follow up. Similarly, urea levels were higher in in patients with transient conduction abnormalities. ***Conclusion:*** Transient conduction abnormalities following TAVI are not uncommon. Correction of anaemia and volume depletion prior to TAVI may decrease the incidence of these transient conduction abnormalities and hence, decrease the fraction of unnecessary permanent pacemaker implantations in the long term. Watchful waiting may be wise in anaemic patients who develop CA after TAVI. The cut-off for haemoglobin levels prior to TAVI is yet to be determined.

Keywords: ***anemia, aortic stenosis, TAVI, pacemaker, conduction abnormalities.***

Introduction

Transcatheter aortic valve implantation (TAVI) is considered the procedure of choice for managing severe aortic stenosis in patients with intermediate to high surgical risk for aortic valve replacement (AVR) [1,2]. Even in patients with low surgical risk, TAVI is considered noninferior, if not superior, to AVR [3,4]. Even though TAVI is associated with a lower morbidity and mortality than AVR, the development of conduction abnormalities (CA) requiring permanent pacemaker (PPM) implantation is considered one of the most common complications of TAVI [5-8]. The incidence of post-TAVI PPM implantation ranges between 5% for the balloon expandable Core Valve prosthesis and up to 25% for the self-expanding Edawards SAPIEN prosthesis [9]. In comparison, PPM implantation post-AVR occurs in about 7% of the cases [10].

The development of CA post-TAVI is believed to occur due to mechanical stress of the prosthesis on the heart's conduction system owing to its proximity to the aortic valve apparatus [11-12]. Former studies identified multiple independent predictors for developing CA requiring PPM implantation, such as preexisting RBBB and the use of self-expanding prostheses (SEV) compared to balloon expanding valves (BEV) [13-15]. In addition, studies also found that these CA are transient in an about 50% of the cases [16,17], with some CA occurring 48 hours or more post-TAVI and even after five days [18].

Transient and late appearing CA and their impact on PPM dependency are of important significance for the management of patient undergoing TAVI, both pre- and post-procedure.

The aim of our study is to examine post-TAVI PPM dependency at implantation and at one-year follow-up (F/U) to assess laboratory predictors that are associated with an immediate transient PPM dependency. The results would provide guidance to pre-TAVI patient management thereby minimizing the incidence of transient CA requiring PPM implantation.

Methods

Population

Analysis of all consecutive patients who underwent TAVI between 2010 and 2019 in Kaplan Medical Center, Rehovot, Israel. Patient data were retrospectively collected and were entered into a dedicated database. A total of 370 patients underwent TAVI, all via transfemoral access. Twenty patients with preexisting PPM were excluded. Out of 350 patients, 82 patients (23.4%) underwent PPM implantation post-TAVI. Sixty-four patients (78%) received a BEV while 18 patients (22%) receive a SEV. All patients underwent coronary evaluation prior to TAVI and all patients signed an informed consent for the procedure and the data collection, allowing intra-institutional data analysis.

TAVI

The decisions for TAVI vs. AVR, valve type, valve size, and access were made by a multidisciplinary team consisting of a cardiac surgeon, an interventional cardiologist, an echocardiographic specialist and a radiologist. The decision for a pre-TAVI balloon aortic valvuloplasty was made by the interventional cardiologist at the time of the procedure. The procedures were performed in a hybrid room with a cardiac surgeon available if needed.

Electrocardiograph (ECG) and PPM implantation

Full 12-lead ECG records were obtained for pre-TAVI, and post-TAVI (immediate, 24 hours, 48-72 hours and at discharge). After TAVI, all patients were monitored by continuous one lead telemetry. The decision for PPM implantation and the mode of pacing was made after consulting with an electrophysiologist according to the accepted guidelines for PPM implantation.

Follow up (F/U) after PPM implantation

Standard electrocardiography was assessed in the VVI mode with a backup frequency of 30 beats/minute. PPM dependency was defined as intrinsic ventricular rhythm of less than 30 beats/minute over 30 seconds, consistent with previous studies [19].

Statistical analysis

All data for continuous variables are expressed as mean ± standard deviation or median and interquartile range (IQR) as appropriate. Categorical variables are reported as numbers and percentages. Continuous variables between the various study groups were tested for normality using the Shapiro-Wilk test and when an abnormal distribution was found, non-parametric tests were performed. The Mann-Whitney test was performed to compare two groups, and the Kruskal-Wallis test was conducted to compare three or more groups. When the distribution was normal, a t-test was used. Chi-square tests were used for the relationship between two categorical variables. A P value < 0.05 was considered statistically significant. Data were analyzed using SPSS 25.

Results

Out of the 82 patients, 19 patients (23%) were lost to follow-up and only 63 (77%) patients were evaluated at the one-year F/U at our unit. One patient was excluded since he was PPM dependent at implantation and at the one-year F/U. Out of the 62 patients (age 82.4, 30 males), 49 patients (79%) were not PPM dependent at implantation and at the one-year F/U (group 1), five patients (8%) were dependent at one year but not at implantation (group 2), eight patients (13%) were transiently dependent at implantation but not at one year (group 3). (Figure 1). The patients' baseline characteristics did not differ significantly between the three groups except for BSA which was lower in group 3 (median 1.71, IQR: 1.56-1.76) compared to group 1 (median 1.83, IQR: 1.71-1.92, P=0.034) and group 2 (median 1.95, IQR: 1.86-1.96, P= 0.013) as shown in **Table 1**.

Pre-TAVI laboratory tests were compared between the three groups (**Table 2**). Pre-TAVI white blood cells (WBC) and their differential, platelets, creatinine, albumin and protein levels did not differ significantly between the three groups. Pre-TAVI haemoglobin levels were significantly lower in group 3 (median 10.65, IQR: 10.35-11.10 vs median 11.60, IQR: 11.00-12.60, P = 0.039 with group 1 and median 12.20, IQR:11.80-13.20, P = 0.019 with group 2). Urea levels pre-TAVI were significantly higher in group 3 compared to group 2 (median 73.5, IQR: 58-103 vs median 39, IQR: 39-47, P =0.027). There was no significant difference between group 3 and 1 regarding urea levels (median 73.5, IQR: 58-103 vs median 53.00, IQR: 39.50-66.00, P= 0.062).

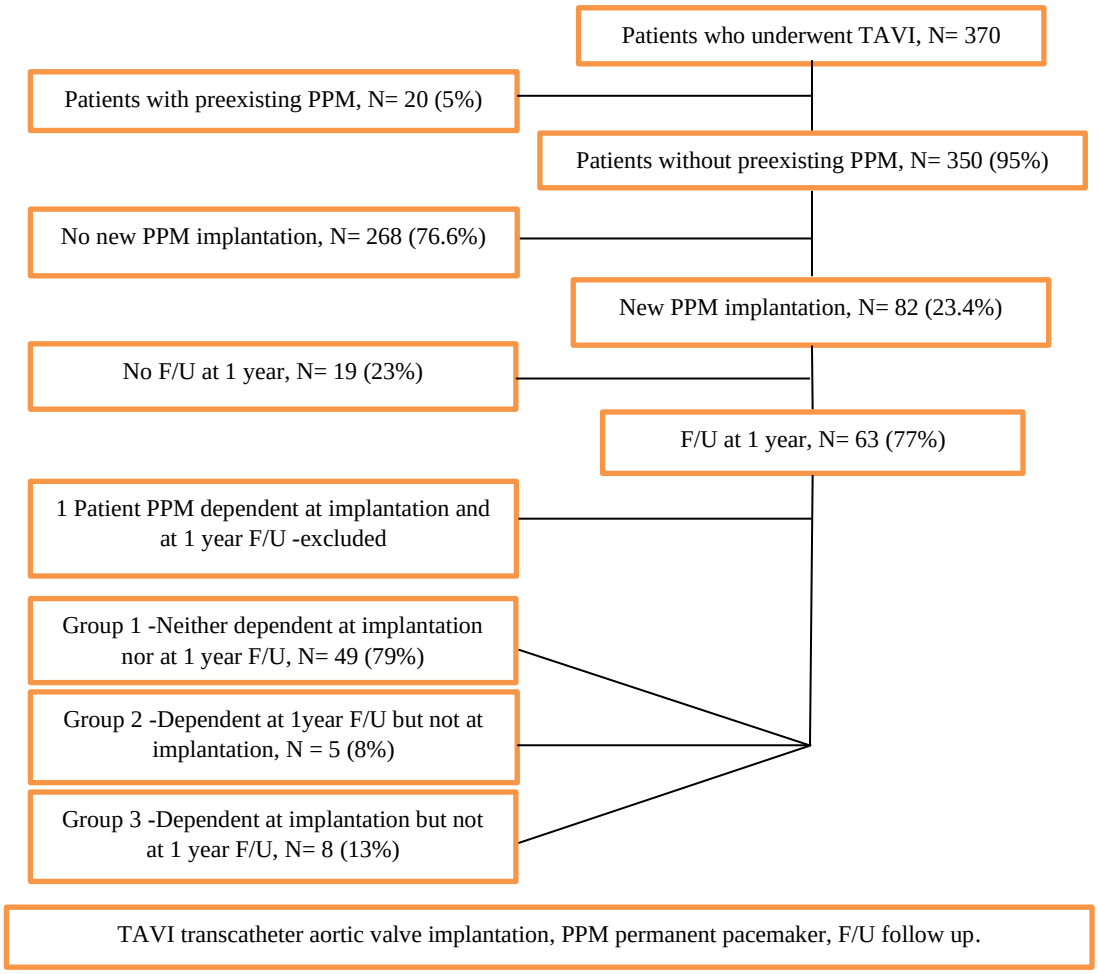

Figure 1: flowchart of the entire study population

Table 1: Baseline characteristics of the study population

	Group 1*	Group 2º	Group 3#	p-value
N (%)	49 (79%)	5 (8%)	8 (13%)	
Age (median [IQR])	82.00 [77.00-87.00]	82.00 [81.00-85.00]	85.50 [82.75-89.00]	0.297
Gender, male (%)	25 (51.0)	3 (60.0)	2 (25.0)	0.34
Weight (median [IQR])	75.00 [69.00-84.00]	80.00 [79.00-85.00]	67.50 [57.25-73.75]	0.053
Height (median [IQR])	165.00 [158.00-170.00]	170.00 [160.00-175.00]	156.00 [153.75-165.00]	0.092
BMI (median [IQR])	28.12 [25.21-30.91]	28.12 [26.12-33.91]	24.73 [23.63-29.38]	0.341
BSA (median [IQR])	1.83 [1.72-1.92]	1.95 [1.86-1.96]	1.71 [1.56-1.76]	0.022
Hypertension (%)	45 (91.8)	5 (100.0)	6 (75.0)	0.245
Diabetes mellitus (%)	25 (51.0)	2 (40.0)	2 (25.0)	0.373
Dyslipidaemia (%)	36 (73.5)	5 (100.0)	5 (62.5)	0.313
Smoker (%)	4 (8.3)	1 (20.0)	1 (12.5)	0.681
AF/AFL (%)	10 (20.8)	1 (20.0)	1 (12.5)	0.86
CAD (%)	23 (46.9)	3 (60.0)	2 (25.0)	0.403
PVD (%)	7 (14.3)	2 (40.0)	0 (0.0)	0.137
CVA (%)	2 (4.1)	1 (20.0)	0 (0.0)	0.227
CABG (%)	5 (14.3)	0 (0.0)	0 (0.0)	0.614

* Pacemaker independent at implantation and at one year follow-up
º Pacemaker dependent at one year follow-up but not at implantation
Transient pacemaker dependent at implantation but not at one year follow-up

BMI body mass index, BSA body surface area, AF/AFL atrial fibrillation/flutter, CAD coronary artery disease, PVD peripheral vascular disease, CVA cerebrovascular accident, CABG coronary artery bypass graft

Table 2: Pre-TAVI laboratory tests

	Group 1*	Group 2º	Group 3#	p-value
N (%)	49 (79%)	5 (8%)	8 (13%)	
HG (median [IQR])	11.60 [11.00-12.60]	12.20 [11.80-13.20]	10.65 [10.35-11.10]	0.035
WBC (median [IQR])	6.85 [5.96-8.20]	6.80 [6.70-9.10]	6.35 [5.68-8.33]	0.771
NEUT% (median [IQR])	66.00 [58.90-70.10]	64.50 [60.60-72.10]	64.15 [62.00-75.40]	0.719
LYM% (median [IQR])	22.60 [18.50-27.20]	24.50 [17.70-27.00]	21.25 [15.90-27.92]	0.922
MONO% (median [IQR])	7.50 [6.10-9.20]	8.10 [7.80-9.00]	7.75 [5.45-10.28]	0.669
EOS% (median [IQR])	2.60 [1.90-4.00]	2.10 [1.50-4.60]	2.20 [1.30-2.92]	0.588
BASO% (median [IQR])	0.40 [0.40-0.60]	0.60 [0.30-0.80]	0.30 [0.27- 0.40]	0.071
PLT (median [IQR])	197.50 [167.00-237.50]	240.00 [195.00-255.00]	227.00 [197.25-262.75]	0.290
Albumin (median [IQR])	3.90 [3.77-4.10]	3.90 [3.70-4.00]	3.75 [3.60-4.03]	0.387
Protein (median [IQR])	6.85 [6.57-7.30]	6.90 [6.70-7.33]	7.05 [6.60-7.40]	0.862
CREA (median [IQR])	1.06 [0.87-1.38]	0.95 [0.90-1.10]	1.16 [1.02-1.52]	0.429
Urea (median [IQR])	53.00 [39.50-66.00]	39.00 [39.00-47.00]	73.50 [58.00-103.25]	0.047

* Pacemaker independent at implantation and at one year follow-up
º Pacemaker dependent at one year follow-up but not at implantation
Transient pacemaker dependent at implantation but not at one year follow-up

HG hemoglobin, WBC white blood cells, NEUT neutrophils, LYM lymphocytes, MONO monocytes, EOS eosinophils, BASO basophils, PLT platelets, CREA creatinine

Discussion

PPM implantation is a common and significant complication following TAVI, occurring in 23.4% of patients in our cohort, which is comparable to previously published data [9]. Conduction abnormalities necessitating PPM implantation may be transient in an appreciated fraction of patients. In the study of Van der Boon et al., partial or even complete resolution of AVB occurred in 20 out of the 30 patients who receive PPM after BEV. This may suggest impaired conduction due to edema and inflammation as seen in postmortem examinations. Other factors, such as hypotension, may occur during rapid right ventricular pacing for aortic balloon valvuloplasty and/or valve deployment. This may induce myocardial ischemia affecting the conduction system in the heart [16]. Elderly patients with diffuse atherosclerotic disease and impaired homeostasis may be at higher risk of ischemia and hence the development of CA [20]. In our trial, pre-TAVI hemoglobin levels were significantly lower in patients who developed transient CA. Similarly, urea levels were higher in this group of patients. Previous data show a clear association between pre-TAVI anemia and a worse outcome including a higher one-year mortality [21]. Pre-TAVI low hemoglobin levels may be associated with a type of ischemia relative to the normal conduction system in the heart leading to the appearance of transient CA that requires PPM implantation in the immediate period after TAVI. Similarly, higher urea levels with normal creatinine levels may reflect more depleted intravascular blood volume (dehydration) and a relative ischemia to the heart's conduction system. The mean age of patients in group 3 was 85.5 vs 82 years in group 1 and 2. Although not statistically significant, due to the small sample size, it may reflect an increase in the risk of ischemia during TAVI (more advanced atherosclerosis and/or impaired homeostasis). Correction of the anemia and a cautious volume expansion pre-TAVI, especially in older patients, may decrease the rate of transient CA following TAVI and hence, the rate of PPM implantation and length of hospital stay.

Limitations of our study

This is a retrospective study with a small number of patients in the three groups, which influences the statistical power of this study. Although pacemaker dependence was defined as intrinsic ventricular rhythm lower than 30 bpm consistent with prior published articles, this does not mean that patients with intrinsic rhythms higher than 30 bpm should not have undergone PPM implantation. Some patients develop transient complete AVB without an escape rhythm or develop CA causing significant symptoms and hence, they should undergo PPM implantation.

A prospective trial with a higher number of patients is needed. Identifying intrinsic rhythm and ventricular pacing percentages is mandatory even if the patient is not PPM dependent.

Conclusion

Transient conduction abnormalities following TAVI are not uncommon. Correction of anemia and volume depletion prior to TAVI may decrease the incidence of these transient conduction abnormalities and hence, decrease the fraction of unnecessary permanent pacemaker implantations in the long term. Watchful waiting may be wise in anemic patients who develop CA after TAVI. The cutoff for hemoglobin levels prior to TAVI is yet to be determined.

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