EDITORIAL

168  Pacemaker post transcatheter aortic valve replacement: A multifactorial risk?
    Noble S, Bendjelid K

173  Challenging situation of coronary artery anomaly associated with ischemia and/or risk of sudden death
    Ito S

177  Transcatheter aortic valve replacement in low-risk young population: A double edge sword?
    Bhogal S, Batta A

181  Hypoxia-inducible factor-1α in myocardial infarction
    Škrlec I, Kolomeichuk SN

186  Left bundle branch pacing set to outshine biventricular pacing for cardiac resynchronization therapy?
    Batta A, Hatwal J

MINIREVIEWS

191  Aspirin interruption before neurosurgical interventions: A controversial problem
    Kulikov A, Konovalov A, Pugnaloni PP, Bilotta F

SCIENTOMETRICS

199  The cardiovascular system at high altitude: A bibliometric and visualization analysis
    Zhao ML, Lu ZJ, Yang L, Ding S, Gao F, Liu YZ, Yang XL, Li X, He SY

CORRECTION

215  Correction: Establishment of a prediction model for prehospital return of spontaneous circulation in out-of-hospital patients with cardiac arrest
    Wang JJ, Zhou Q, Huang ZH, Han Y, Qin CZ, Chen ZQ, Xiao XY, Deng Z
## ABOUT COVER

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Pacemaker post transcatheter aortic valve replacement: A multifactorial risk?

Stephane Noble, Karim Bendjelid

Abstract

Pacemaker post-transcatheter aortic valve replacement is related to multifactorial risk. Nwaedozie et al brought to the body of evidence electrocardiogram and clinical findings. However, procedural characteristics have at least as much impact on the final need for a permanent pacemaker and potentially on the pacing rate. In this regard, long-term follow-up and understanding of the impact of long-term stimulation is of utmost importance.

Key Words: Transcatheter aortic valve replacement; Permanent pacemaker implantation; Conduction abnormalities; Right bundle branch block; Left bundle branch block

Core Tip: Since the first transcatheter aortic valve replacement (TAVR) in 2002, TAVR has become a recognized alternative therapy to symptomatic severe aortic stenosis independently of the surgical risk score. The multiple iterations of the delivery systems and transcatheter heart valves (THV) over time associated with better patient assessment and the growing experience and expertise of the operators improved the procedural and follow-up results. However, despite the possibility of repositioning and partially recapturing some of the self-expanding THV and generally higher implantation targets, the need for a permanent pacemaker remains the most frequent complication post-procedure.
INTRODUCTION

Since the first transcatheter aortic valve replacement (TAVR) in 2002, TAVR has become a recognized alternative therapy to symptomatic severe aortic stenosis independently of the surgical risk score. The multiple iterations of the delivery systems and transcatheter heart valves (THV) over time associated with better patient assessment and the growing experience and expertise of the operators improved the procedural and follow-up results[1-3]. However, despite the possibility of repositioning and partially recapturing some of the self-expanding THV and generally higher implantation targets, the need for a permanent pacemaker remains the most frequent complication post-procedure. Importantly, the left bundle branch travels commonly 2 to 3 mm below the base of the interleaflet triangle between the noncoronary and right coronary leaflets and is therefore at risk for interaction with the THV[4].

Conduction disturbances and the need for permanent pacemaker implantation post-TAVR are multifactorial and have an important clinical and economic impact (price of the pacemaker implantation, higher length of stay)[5]. In a multicenter European trial using balloon-expandable valves, conductance abnormalities were the second most common reason for prolonged hospitalization after logistic causes[6]. Delayed atrioventricular block can be seen up to 8 d post-TAVR in 7% of the cases, but patients without conduction abnormalities immediately post-TAVR did not present any delayed high-degree conduction disorder in a multicentric report including 1064 patients[7]. The European Society of Cardiology (ESC) guidelines on cardiac pacing gave a class I indication for permanent pacemaker implantation in the context of a complete atrioventricular block or new alternating bundle branch block and a class IIa for right bundle branch block and new conductance disturbance (PR prolongation or axis changes)[8]. Interestingly, a class IIa for ambulatory ECG monitoring or electrophysiology study was given in the setting of persistent new left bundle branch block > 150 ms or PR > 240 ms with no further prolongation during 48 h and a class IIb in the context of pre-existing conduction abnormalities with prolongation of > 20 ms of the QRS and PR interval.

In the present issue of the Journal, Nwaedozie et al[9] assessed the effects of baseline nonspecific interventricular conduction delay and supraventricular arrhythmia on post-TAVR permanent pacemaker need and also reported the impact of permanent pacemaker implantation on clinical outcomes at one year. In this regard, they retrospectively analyzed the single-center cohort of a tertiary hospital in central Wisconsin, United States involving 357 patients who underwent a TAVR (95.2% of transfemoral approach) between January 2012 and December 2019 using balloon-expandable and self-expanding THV in 53.8% and 46.2%, respectively.

One of the strengths of the study is that they analyzed the rate of pacemaker dependency at follow-up, which was as high as 78.9% one month post-pacemaker implantation. In addition, board-certified cardiologists reviewed the ECG. They found a permanent pacemaker rate of 16% at one year with no significant differences between self-expanding (17.6%) and balloon-expandable (14.6%) THV. Their pacemaker rates are similar to the Medtronic self-expanding THV in the Evolut Low-Risk trial (17.4% at 30 d and 19.4% at one year) and slightly above what we could expect with the Edwards SAPIEN 3 balloon-expandable valve (PARTNER 3 trial: 6.6% at 30 d and 7.5% at one year)[10,11]. The median time of implantation in the study by Nwaedozie et al[9] was 2 d, and half of the patients underwent pacemaker implantation within 48 h post-TAVR. Complete atrioventricular block was the predominant indication (66.7%) and the other indications were as follows: left ventricle dysfunction (10.5%), symptomatic bradycardia (8.8%), and symptomatic second atrioventricular block (1.8%).

The main findings of this trial are that pre-TAVR type II Diabetes Mellitus and QRS duration > 120 ms, regardless of the presence of bundle branch block were predictors of permanent pacemaker need post-TAVR. They also demonstrated a linear association between post-TAVR permanent pacemaker rate for every 20 ms prolongation of the QRS duration above 100 ms. Finally, at one year, there were more heart failure hospitalizations (28% vs 14%, P = 0.022) and myocardial infarction (9% vs 2%, P = 0.031) in the group requiring a permanent pacemaker.

The limitations of this report are related to the design of the study which is a retrospective analysis of a single center experience with a relatively small number of patients (n = 357) treated over 8 years. During this long period, there were multiple THV iterations, implantation technique refinements, and a regular expansion of the indication creating a heterogenous population. The results have to be brought into perspective. Indeed, not only does the baseline ECG influence the post-procedural risk of permanent pacemaker need (particularly the presence of a right bundle branch block[5]), but also the left ventricular outflow tract (LVOT) anatomy and the calcium burden and repartition as well as the valve type used (i.e., balloon-expandable vs self-expanding THV), and finally patient and procedural characteristics (i.e., the height of implantation, percentage of oversizing, the technique of implantation, pre- and post-dilatation, resheathing and recapture).

Recently, the best clinical practices concerning the view of valve deployment have progressively switched from a three-cusp view to a combination of cusp overlap and three-cusp views, particularly for the self-expanding valves[12]. When using the cusp-overlap view, we focus on the non-coronary cusp which is on the left side of the screen, whereas the right and left cusps are superimposed on the right side of the screen. This view allows the elongation of the LVOT and subsequently a more precise height of implantation. It also contributes to eliminating the parallax of the delivery catheter, deploying the valve in a true coplanar view, and better aligning the THV commissures[12]. The cusp overlap technique
has been associated with a lower pacemaker implantation rate at 30 d than the conventional technique in a meta-analysis including 1227 Medtronic Evolut valves (cusp overlap technique: 641 vs co-planar view: 586).

In the cusp overlap technique, the implantation height was 1.03 mm higher and the incidence of pacemaker rate was 9.8% compared to 20.6% in the conventional technique[13]. However, the incidence of a left bundle branch block did not differ. In a propensity-matched analysis on a small Spanish cohort (92 patients in each group with no baseline characteristic differences), there was a significant reduction of new onset of left bundle branch block and reduced P wave and QRS widening at one year in the cusp overlap technique group compared to the conventional technique group[14]. There was also a significant reduction in a combined primary endpoint including pacemaker implantation, hospitalization and cardiovascular death at one year[14]. Recently, the interim analysis of the Optimize PRO TAVR study showed again the benefit of the cusp overlap technique in 400 patients[15]. This study reports the absence of moderate or severe paravalvular leak and the lowest pacemaker rate (9.8% at 30 d) in a multicenter prospective study with the Evolut platform using the cusp overlap technique and an "optimized TAVR care pathway". The pacemaker rate was as low as 5.7% when the 4-step cusp overlap technique was precisely followed.

Importantly, Nwaedozie et al[9] did not report data on the procedural depth of THV implantation which is a major predictor of the need for a permanent pacemaker post-TAVR. To emphasize the role of the implantation technique and volume-outcome relationship, in a sub-analysis of the Evolut low-risk trial, there was a substantial variation in the rate of permanent pacemaker implantation from site to site in this study including 699 patients from 84 centers, with a lower rate of pacemaker need in high volume centers[3,16]. The sites with a low pacemaker rate had higher implantation at the non-coronary and left coronary sinus levels and fewer patients with an implantation depth of more than 5 mm[16].

Finally, the long-term pacemaker implantation after TAVR are conflicting. Right ventricular pacing is associated with electromechanical dyssynchrony, left ventricular remodeling, increased risk of atrial fibrillation, and tricuspid regurgitation. In a series of 377 post-TAVR patients at one year, a stimulation rate > 40% of the time was associated in a propensity-matched analysis with a higher risk of cardiovascular mortality and hospitalization for heart failure[17]. More physiological pacing such as cardiac resynchronization in cases of reduced left ventricular ejection fraction is recommended to decrease the adverse outcome. His bundle or conduction system stimulation is also a more physiological pacing, which should be promoted. Of note, in the later series, 6 patients had His stimulation with no event or hospitalization during follow-up. In 2020, a meta-analysis including 30 studies showed a higher risk at one year of all-cause death and heart failure hospitalization after new onset of left bundle branch block or peri-procedural pacemaker implantation[18]. In addition, post TAVR new onset of left bundle branch block was associated with an increased risk of cardiac death and need for pacemaker implantation at one year[18]. In a recent meta-analysis of 31 studies with a mean follow-up of 22 months, new permanent pacemaker implantation after TAVR was associated with a higher risk of all-cause death and heart failure hospitalization[19]. Conversely, data from the nationwide, population cohort study with 3420 TAVR performed between 2008 and 2018 in Sweden, 481 (14.1%) required permanent pacemaker implantation within 30 d post procedure[20]. With a median follow-up of 2.7 years, there was no difference in long-term survival between patients who were not or were implanted with a permanent pacemaker (survival at 5 and 10 years: 52.7% and 10.9% in the pacemaker group and 53.8% and 15.3% in the group without a pacemaker, respectively).

**CONCLUSION**

In conclusion, pacemaker post-TAVR is related to multifactorial risk. Nwaedozie et al[9] brought to the body of evidence ECG and clinical findings, but procedural characteristics have at least as much impact on the final need for a permanent pacemaker and potentially on the pacing rate. Long-term follow-up and understanding of the impact of long-term stimulation is of utmost importance.

**FOOTNOTES**

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