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EDITORIAL

# Pacemaker Implantation After Transcatheter Aortic Valve Replacement: A Necessary Evil Perhaps But Are We Making Progress?

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Percutaneous transcatheter aortic valve replacement (TAVR) has established itself as the preferred alternative to surgical valve replacement for inoperable high- and lower-surgical-risk patients with severe aortic stenosis, but is associated with significant risk of high-grade atrioventricular block and pacemaker implantation. A concerning trend is that the incidence of permanent pacemaker implantation (PPI) post-TAVR has actually increased significantly in recent trials that have tested latest-generation devices in intermediate- and low-risk patients.[1,2]

See Article by Bisson et al.

## MECHANISM OF INJURY TO THE CONDUCTION SYSTEM AFTER TAVR

Although some risk factors for PPI post-TAVR are operator dependent and may be potentially modifiable, such as depth of valve implantation, presence of baseline conduction system disease has remained one of the most reliable independent predictors for development of advanced atrioventricular block after TAVR, regardless of device used.[3] This was first demonstrated in an analysis of 1973 patients with severe aortic stenosis who underwent TAVR in the PARTNER (Placement of Aortic Transcatheter Valves) trial where pre-existing right bundle branch block and left anterior fascicular block at baseline ($P<0.001$) were shown to be electrocardiographic predictors for post-TAVR permanent pacemaker, and these findings have remained consistent in subsequent analyses.[4]

The extent of injury to the conduction system caused by mechanical trauma during TAVR is often capricious and not all cases of procedure-related atrioventricular block, even when initially severe, remain long-lasting. It is believed that anatomic variation in the length and location of the penetrating segment of the bundle of His and the depth of the proximal portion of the left bundle affect susceptibility to injury.[5] Given the dynamic nature of TAVR-related injury/inflammation, European Society of Cardiology guidelines for cardiac pacing suggest an observation period of at least 7 days to assess for potential return of functional atrioventricular conduction before deciding whether to move forward with implantation of a permanent pacemaker.[6] However, time for recovery from conduction disturbances is often unpredictable and may take longer than 1 week, contributing to wide variation in practice patterns for implantation.

Device selection has been demonstrated to be an important modifiable risk factor for post-TAVR PPI. Incidence of TAVR-related atrioventricular block requiring PPI was shown to be substantially higher with first-generation SE Corevalve than BE Sapien X3 devices. While improvements in design were incorporated into the latest BE technologies (Sapien 3, Sapien 3 Ultra), rates of PPI because of iatrogenic atrioventricular block have also increased considerably in comparison to the

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predecessor Sapien XT valve despite having tested newer BE valves in lower-risk populations.[7] Other device designs have aimed to lower risk of PPI after TAVR by mitigating trauma to the atrioventricular conduction system. In the SAVI TF (Symetis ACURATE neo Valve Implantation Using Transfemoral Access) registry, PPI was low using the ACURATE Neo valve despite its SE design, and in a prospective comparison the platform had lower incidence of post-TAVR PPI than other SE and BE valves ([Accurate Neo] 6% versus [Corevalve] 25% versus [Sapien XT] 11%; *P*=0.013) because of lower generation of radial forces and supra-annular position during deployment.[8,9] Unfortunately, in the SCOPE (Safety and Efficacy Comparison Of Two TAVI Systems in a Prospective Randomized Evaluation) I trial the ACURATE Neo valve did not meet noninferiority compared with the Sapien 3 valve for the primary efficacy end points of the study because of higher rates of a peri-vavular leak.[10]

## INSIGHTS FROM A 10-YEAR EXPERIENCE WITH PACEMAKER IMPLANTATION AFTER TAVR

In this issue of the *Journal of the American Heart Association* (*JAHA*), Fauchier et al[11] present the results of a systematic analysis of patient data from a national hospital administration database of 49 201 patients who had severe aortic stenosis and who underwent TAVI procedures using Edwards Sapien BE (Sapien XT and Sapien 3) or Medtronic SE (Corevalve and Evolut) bioprosthetic valves between 2010 and 2019. During study follow-up (mean 1.2 years; 59 041 patient-years), 27% of patients in the cohort underwent PPI post-TAVR with the majority performed within 30 days, which is a higher incidence than reported in most other large studies. As expected, the rate of PPI implantation was higher for SE than BE devices in the cohort, although the difference was only modestly higher than the Sapien XT group (Corevalve: hazard ratio [HR], 1.3 [95% CI, 1.21–1.4]; Evolut: HR, 1.25 [95% CI, 1.21–1.34]). A unique finding of the study was the lack of difference in the rate of PPI between patients who underwent TAVI with early and later generation BE technologies (Sapien 3: HR, 1.01 [95% CI 0.95–1.08] [reference Sapien XT]). However, PPI was lower in the Sapien 3 group during the first 30 days after TAVR, albeit with a small absolute difference (1.2%) between Sapien 3 and Sapien XT devices likely only reaching statistical significance because of the large number of patients in both groups. A curious finding of the study that merits further explanation was the higher incidence of late PPI performed in the Sapien 3 arm despite lower Charleston Comorbidity and Frailty Index scores than the Sapien XT arm. In the multivariate analysis, the usual suspects were confirmed as risk factors for PPI post-TAVI including age, right bundle branch block, hypertension, type 2 diabetes mellitus, history of myocardial infarction, and implantation of SE bioprosthetic valves. A novel finding of the study was that pre-existing left bundle branch block (LBBB) was identified as a predictor for PPI post-TAVR. Considering evidence that new-onset LBBB may be associated with adverse outcomes post-TAVR, higher presence of baseline LBBB in the Sapien 3 group than in the Sapien XT group (17.4% versus 12%) may have contributed to treatment bias, helping explain the higher incidence of PPI during later follow-up in the Sapien 3 group. However, it should be remembered that there is no conclusive evidence in the literature that pre-existing LBBB actually increases risk of trauma-related atrioventricular block after TAVR.

With over 49 000 patients, the size of the study population is a major strength of the current analysis. Although incidence of PPI implantation was higher than findings reported in most other studies, the current analysis is insightful in view that it represents a real-world experience with a large number of operators minimizing the influence of individual practice variance. The investigators bring up a valid point that external pressure regarding length of stay in the hospital and hastening mobilization may have led to more "aggressive" decisions to proceed with PPI rather than fully wait out recovery of atrioventricular conduction or new-onset LBBB. Although follow-up data earlier than 30 days (ie, index hospitalization) were not made available in the current analysis, results from other studies have suggested that lack of clear guidance on appropriate timing for PPI and treatment bias have increased the proclivity for PPI in TAVR patients, as restoration of atrioventricular conduction after PPI has been reported in up to 50% of patients during follow-up. Another important limitation of the study was the decision to include patients with prior cardiovascular implantable devices in the analysis. As presence of existing cardiovascular implantable devices would have excluded patient eligibility for PPI post-TAVR, the higher proportion of existing cardiovascular implantable devices in patients who underwent SE valve implantation in the study may have led to underestimation of actual risk estimates for PPI, especially for the Corevalve SE arm (26.5% [Corevalve SE] versus 19.5% [reference Sapient XT]). Finally, many of the clinical variables identified in the multivariate analysis were only small to modest in size despite reaching statistical significance in the model. The predictors with largest effect size and therefore most clinically significant were presence of right bundle branch block and LBBB at baseline. For patients with existing right bundle branch block, incidence of PPI was higher in the first 30 days (odds ratio [OR], 2.21; [CI, 2.03–2.40]) than the rest of follow-up (OR, 1.34; [95% CI,

1.14–1.58]). Conversely, risk of PPI in patients with pre-existing LBBB was lower during the first 30 days (OR, 1.35; [95% CI, 1.27–1.42]) but increased on follow-up (OR, 1.75; [95% CI, 1.58–1.93]). From the results of the study it is unclear whether progression to complete heart block or other reasons led to PPI after 30 days in patients with existing LBBB at baseline.

## FUTURE OUTLOOK

The relevance of procedure-related conduction disturbance and subsequent permanent pacemaker placement is likely to increase as indications for TAVR expand further to younger and lower-risk patients. While mortality may not be higher in patients who undergo PPI after TAVR,[12] post-TAVR PPI is still a complication associated with increased length of stay, rehospitalizations, and other associated cost burdens. Furthermore, PPI is also associated with its own hazards such as risk of hematoma, vascular injury, serious infection, pneumothorax, lead dislodgement, and tricuspid regurgitation, potentially mitigating the advantages offered by TAVR. The future role of electrophysiology studies to stratify patients with equivocal findings on ECG post-TAVR needs to be studied further, but interpretation of electrophysiology study results are likely to be limited by the same constraints that challenge clinical assessment, given the dynamic nature of conduction system injury after TAVR and variable time length of recovery between patients. Because pacing and LBBB-induced cardiomyopathy remain a potential concern post-TAVR, cardiac resynchronization therapy may play an increased role in future management of TAVR patients. In a recently published study, De Pooter et al demonstrated feasibility of permanent His bundle pacing in a cohort (n=16) of patients with TAVR-induced LBBB. His bundle pacing with recruitment of the LBBB was obtained in 69% (11/16) of patients with significant narrowing of QRS duration. Although mean threshold for LBBB correction was somewhat high at 1.9 V±1.1 ms at 1.0 ms, threshold remained stable after 11 months of follow-up.[13]

## CONCLUSIONS

The current study by Fauchier and colleagues confirms that despite closing the gap with surgical valve replacement in terms of mortality and overall procedural safety, there has been minimal progress so far in reducing the incidence of procedure-related conduction abnormalities necessitating PPI despite technological advancements and increased operator experience. As the TAVR population continues to expand towards a younger and healthier population, traditional risk factors of value for older and high-risk patients will likely become less predictive for identifying patients at risk of requiring PPI before TAVR. Therefore, there is a pressing need to develop bioprosthetic devices and delivery systems that minimize trauma to the atrioventricular conduction system and establish clear clinical guidelines for indications for permanent pacemaker placement in patients after TAVR.

## ARTICLE INFORMATION

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