Cardiac conduction disturbances after transcatheter aortic valve replacement: much remains to be learned

Tamim Nazif, MD; Susheel K. Kodali*, MD

Columbia University Medical Center and New York Presbyterian Hospital, New York, NY, USA

Over the past decade, transcatheter aortic valve replacement (TAVR) has emerged as a less invasive alternative to surgical aortic valve replacement (SAVR) for high-risk surgical candidates and the treatment of choice for inoperable patients with symptomatic, severe aortic stenosis (AS). Recently, there has been explosive growth in the clinical adoption of TAVR worldwide. With this increasing role, intense research efforts have focused on understanding and reducing procedural complications of TAVR, the most common of which are cardiac conduction disturbances.

Two reports in the current issue of EuroIntervention, by Houthuizen et al and Lange et al, focus on cardiac conduction disturbances after TAVR. The study by Houthuizen et al elaborates on the incidence, fate, and clinical impact of left bundle branch block (LBBB), the most frequent conduction disturbance after TAVR1. The report of Lange et al, on the other hand, explores the impact of balloon aortic valvuloplasty (BAV) balloon sizing on the occurrence of the most threatening conduction disturbance after TAVR, complete atrioventricular block requiring permanent pacemaker implantation (PPI)2. These complications occur with varying frequency after TAVR, and it is of critical importance to understand their aetiologies, clinical implications, and possible means of prevention.

New-onset LBBB is the most frequent conduction disturbance to complicate both SAVR and TAVR. The incidence of new LBBB after SAVR has been reported to range from 6 to 20%3-5. Following TAVR, the exact frequency varies with the transcatheter heart valve (THV) system used and the elapsed time from the procedure. The rate of new LBBB with the Edwards SAPIEN valve (ESV; Edwards Lifesciences, Irvine, CA, USA) is similar to SAVR, with recent large series reporting rates ranging from 10 to 30%6-7. The incidence of new LBBB with the Medtronic CoreValve (MCV; Medtronic, Minneapolis, MN, USA) is substantially higher, ranging from approximately 40 to 55% in large series8,9. While the wide range of rates across studies may reflect differences in populations, it may also be due to differences in definition, intensity of surveillance, and time of assessment of LBBB after TAVR.

In the current study, Houthuizen et al analysed the occurrence of LBBB after TAVR in 476 patients (223 MCV, 253 ESV) without pre-existing LBBB or pacemaker. The overall rate of new LBBB was similar to previously published reports: approximately 37% overall, 54% after MCV, and 22% after ESV. However, this study makes an important contribution in its close examination of the time course of development and resolution of new LBBB. It is notable that the vast majority of new LBBB developed within 24 hours of the procedure (86%) or during the index hospitalisation (98%). In agreement with prior studies, the authors also found that a significant proportion of new LBBB after TAVR resolve over time6-8. Importantly, the degree of resolution of new LBBB was significantly less with MCV than ESV (28% vs. 56%). The fact that new LBBB is both substantially more frequent and also less likely to resolve with MCV may have important implications for the choice of THV in certain patients, such as those with reduced left ventricular function in whom dyssynchrony may lead to worsening cardiac function and clinical heart failure.

Importantly, the authors also propose a new classification scheme for the time course of new LBBB after TAVR, in which LBBB is defined as acute, subacute, or chronic based on occurrence within 24 hours, from 24 hours to discharge, and after discharge, respectively. LBBB is further classified as transient or persistent based on whether or not it remains at one year. Of note, this definition of “persistent” differs from prior studies, which have used the term to refer to LBBB persisting at hospital discharge6-7. Furthermore, in our recent analysis from the PARTNER trial, we demonstrated that the vast majority of LBBB resolution occurred by 30 days, which may also be a candidate time point for defining “persistent”. The Valve Academic Research Consortium (VARC), which standardised definitions for many TAVR endpoints, has recommended systematic reporting of data on conduction disturbances, but has stopped short of proposing specific definitions9. It may, therefore, be hoped that the new classification scheme proposed by Houthuizen et al will be a first step in clarifying the vague, often confusing terminology that currently exists in the literature regarding LBBB after TAVR.

The clinical impact of new-onset LBBB after TAVR received substantial attention after a study in 2012 by Houthuizen et al reported higher one-year mortality in patients with new LBBB after TAVR with either ESV or MCV5. However, multiple subsequent publications, including large cohorts of patients treated with both ESV and MCV, have failed to substantiate this finding6-8. In contrast to these

*Corresponding author: Columbia University Medical Center and New York Presbyterian Hospital, 722 W 168th St, New York, NY, 10032, USA. E-mail: sk2427@columbia.edu

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studies, Houthuizen et al once again report an association of new-onset LBBB with mortality, this time with a median follow-up of 915 days. However, this finding must be interpreted with caution given the likely overlap of the current patient population with the previously published cohort and the failure of other groups to replicate the findings in independent populations. Although there may be differences in definitions and patient characteristics that explain the discrepancy with other studies, it is also possible that the association of new LBBB with mortality is due to unidentified confounders. Furthermore, given the known incomplete pacemaker dependency of patients who undergo PPI after TAVR, it is not clear that PPI within 30 days should be an exclusion criterion when analysing the clinical impact of new LBBB. The ongoing debate regarding the impact of new LBBB on mortality does not, however, imply that it is benign, given its association with PPI and impaired recovery of left ventricular function\textsuperscript{4-6}. Unfortunately, analyses of these additional endpoints was not possible in the current study.

The other important conduction disturbance after TAVR is complete atrioventricular block and related conduction abnormalities requiring PPI. Contemporary studies have reported PPI rates ranging from 3% to 7% after isolated SAVR for AS. Recent, large-scale meta-analyses have shown similar average PPI rates after TAVR with ESV (5.9 to 6.5%)\textsuperscript{9-15}. However, PPI rates with MCV are reported to be significantly higher (24.5-25.8%)\textsuperscript{13-15}. Multiple studies have examined predictors of PPI after TAVR and have clearly established the use of MCV and pre-existing RBBB as the most reliable and potent predictors of PPI\textsuperscript{13,16}. More limited studies have identified an array of other electrocardiographic, anatomic, and procedural risk factors for PPI. Important among these are modifiable, procedural risk factors, such as depth of THV implantation\textsuperscript{9,17}.

More recently, BAV has been identified as another potentially modifiable, procedural risk factor for conduction disturbances after TAVR\textsuperscript{18,19}. While the incidence of PPI after isolated BAV is less than 1.5%, studies have shown that up to half of all conduction disturbances during TAVR occur prior to valve deployment, most often during BAV\textsuperscript{20,22}. As postulated by Lange et al, this suggests a “two-hit model”, in which an initial conduction system injury during BAV is exacerbated and becomes permanent due to a second injury from THV deployment. It is therefore rational that avoidance of BAV during TAVR may minimise conduction disturbances, including PPI. Several small pilot studies have now shown that TAVR with both MCV and ESV may be feasible without BAV and that this strategy may minimise conduction disturbances\textsuperscript{18,23}.

A prior, small study of patients treated with MCV showed that the ratio of the BAV balloon diameter, but not the THV prosthesis, to the aortic valve annulus was associated with conduction disturbances\textsuperscript{22}. The current study by Lange et al extends this work by analysing the impact of BAV balloon size on PPI in a larger cohort of 237 patients without prior pacemaker who underwent TAVR with MCV. In this analysis, the overall incidence of PPI was 21.1%, but was significantly higher when a 25 mm balloon was used (27.1%) than when a 23 mm or smaller balloon was used (15.4%) for the BAV. Furthermore, when stratified by THV size (26 or 29 mm), there was a step-wise increase in PPI rate with each increase in balloon size. The association of balloon size with PPI remained significant after multivariable adjustment for differences in baseline patient characteristics. Overall, these results suggest that pacemaker rates after TAVR may be safely decreased by using the smallest possible BAV balloon.

There are several limitations of this analysis that should be considered. First, the rationale for choosing different balloon sizes in individual cases was not discussed. It remains possible that smaller balloons were utilised in patients in whom conduction disturbances or other complications were feared and that unidentified confounders, such as the burden of calcification, affected the result. The indications for PPI were also not provided, although the authors state that pacemakers were only placed at their institution for complete atrioventricular block or symptomatic bradycardia. Finally, the potential impact of BAV size on THV valve areas and rates of paravalvular regurgitation were not investigated. Additional, prospective studies are necessary to understand better the impact on clinical outcomes of minimising the balloon size or deferring BAV altogether.

Cardiac conduction disturbances, including LBBB and complete atrioventricular block or other abnormalities requiring PPI, are the most frequent complication of TAVR. The studies in this issue of EuroIntervention contribute to our understanding of the aetiology, time course, and clinical impact of conduction disturbances. Future studies should aim to further this understanding with a particular focus on clinical implications and modifiable risk factors.

**Conflict of interest statement**

T. Nazif has served as a consultant for Edwards Lifesciences. S. Kodali serves on the steering committee and is a consultant for Edwards Lifesciences and Claret Medical, and is a member of the scientific advisory board of Thubrikar Aortic Valve Inc.

**References**


