

# How to predict conduction disturbances after transcatheter aortic valve replacement

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## ABSTRACT

Transcatheter aortic valve replacement (TAVI) has evolved into the gold standard management option for high-risk patients with severe aortic stenosis. Despite identifying procedural, electrocardiographic, and clinical predictors of important post-procedural conduction disturbances (left bundle branch block and high-degree atrioventricular block) and despite continuous technological refinement of transcatheter aortic valves, the rate of post-procedural conduction disturbance remains high and challenging to manage. New strategies are required to reduce the overall rate of post-procedural permanent pacemaker implantations. In this article, we will review the incidence, predictive factors, and clinical implications of conduction disturbances after TAVI.

**Key words:** conduction disturbances, left bundle branch block, permanent pacemaker implantation, right bundle branch block, transcatheter aortic valve implantation

## INTRODUCTION

Transcatheter aortic valve implantation (TAVI) has dramatically changed the treatment of patients with severe symptomatic aortic stenosis and is widely accepted as a valid alternative to cardiac surgery [1–8]. The number of TAVI procedures continue to grow worldwide, including in countries that have started their TAVI programs more recently. In Poland, for example, increasing numbers of patients are being treated with good results [9]. Due to technical refinements, the rate of most procedural complications has decreased over time, with subsequent better clinical outcomes [10, 11].

The incidence of conduction disturbances (high-degree atrioventricular block [HAVB] and new-onset left bundle-branch block [LBBB]) has, however, not decreased over time, and the adoption of newer-generation transcatheter heart valves (THV) is still limited by a clinically significant rate of permanent pacemaker implantation (PPI) [12–14]. Since chronic right ventricular pacing and intraventricular conduction disturbances have a well-known negative impact on left

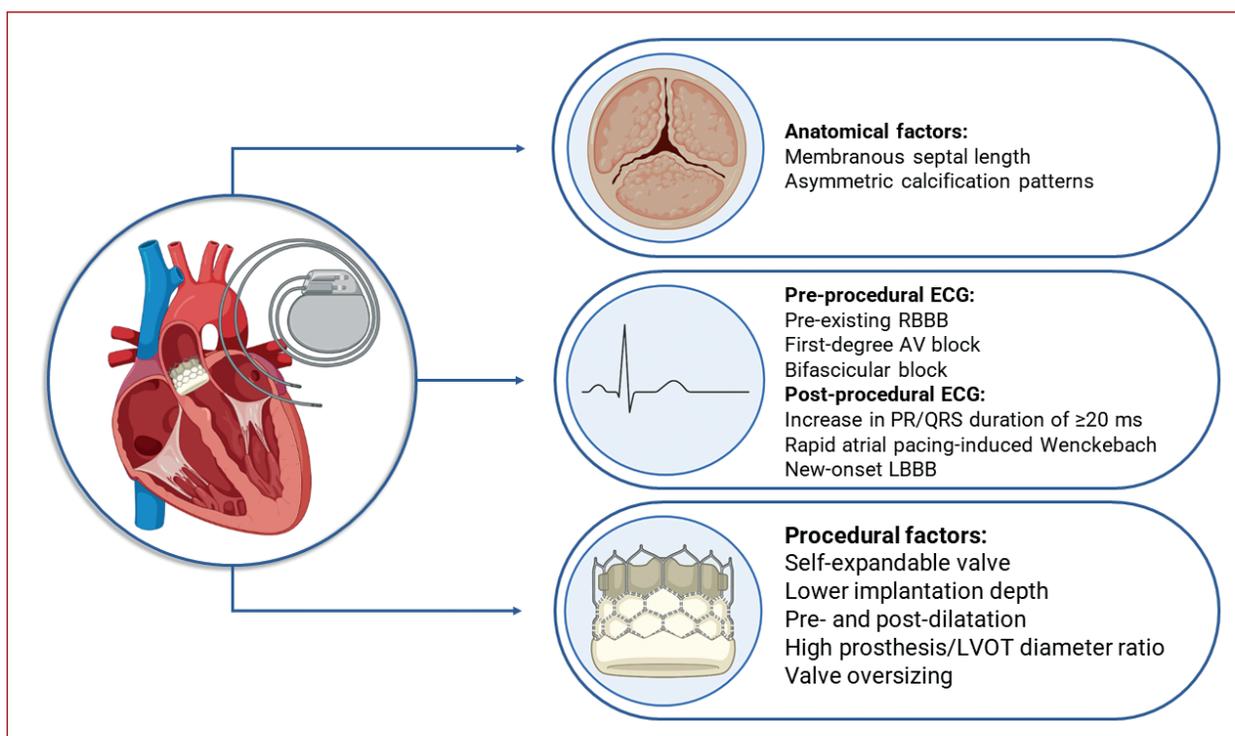
ventricular function [15, 16], the reduction of conduction disturbance after TAVI is a research priority.

In this review, we will analyze the incidence, predictors, and management strategies of conduction disturbances in patients undergoing TAVI.

## WHY IS THERE CONDUCTION DISTURBANCE AFTER TAVI? “KNOW YOUR ENEMY”: THE CONDUCTION SYSTEM

The anatomical relationship between the conduction system and the aortic valve complex explains the frequent association of the TAVI procedure and new-onset conduction disturbance. In the right atrium, the atrioventricular (AV) node is located within the apex of the triangle of Koch.

This is an important anatomical area demarcated by: the tendon of Todaro (continuation of the Eustachian valve of the inferior vena cava and the valve of the coronary sinus), the attachment of the septal leaflet of the tricuspid valve, and the orifice of the coronary sinus.



**Central illustration.** Summary of the predictors of permanent pacemaker implantation

Abbreviations: RBBB, right bundle branch block; LBBB, left bundle branch block; AV, atrioventricular; LVOT, left ventricular outflow tract

The apex of the triangle is formed by the convergence of the tendon of Todaro and the septal attachment of the tricuspid valve on the atrioventricular component of the membranous septum (MS). The atrioventricular node is located just inferior to the apex of the triangle, adjacent to the MS. The contiguity of these structures can explain the genesis and pathophysiology of periprocedural rhythm complications during TAVI.

The atrioventricular node continues as the bundle of His, piercing the MS and penetrating to the left through the central fibrous body.

On the left side, the conduction axis exits immediately beneath the MS and runs superficially along the crest of the ventricular septum, giving rise to the fascicles of the left bundle branch [17]. The upper segment of the bundle is closely related to the base of the interleaflet triangle separating the non-coronary and right coronary leaflets of the aortic valve; therefore, compression from the TAVI prosthesis threatens mechanical insult generating edema, as well as ischemia or hematoma of the surrounding tissues including the closely situated left bundle branch.

### INCIDENCE OF CONDUCTION DISTURBANCES AFTER TAVI

HAVB and new-onset LBBB are the most common conduction disturbances after TAVI. In almost half of cases, post-procedural conduction abnormalities regress or stabilize over time without the need for PPI; this phenomenon is related to the regression of procedure-related traumatic

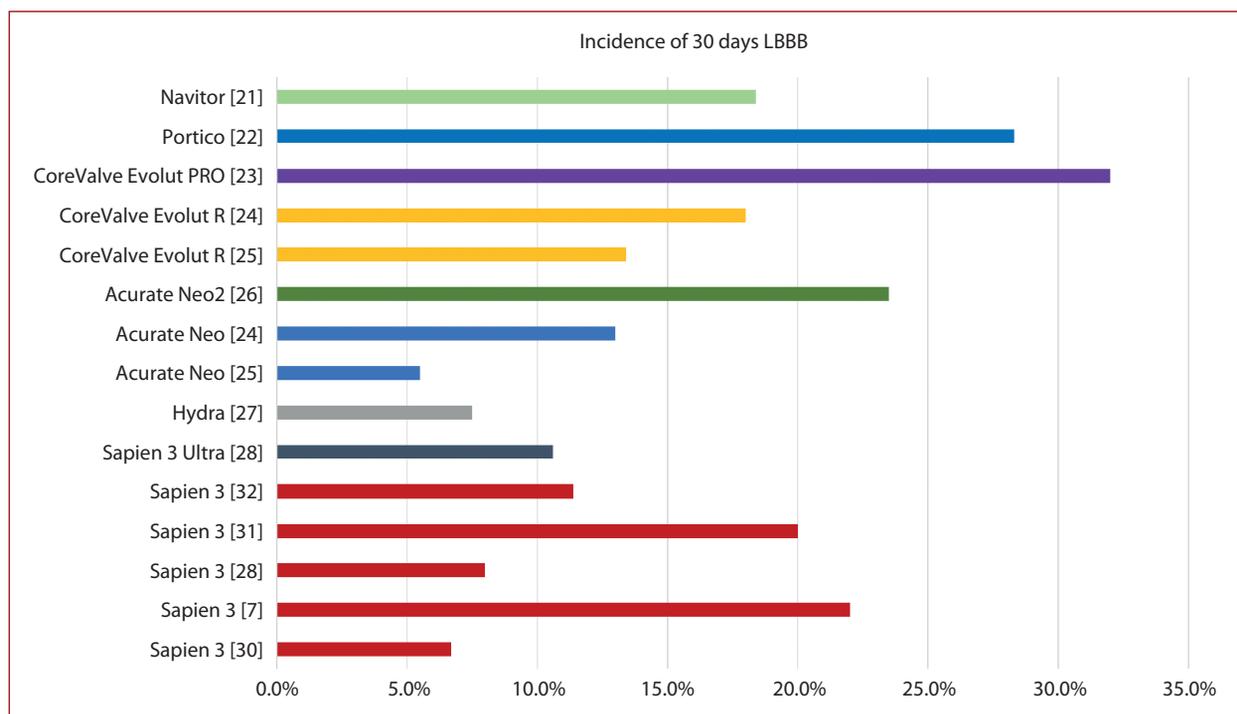
inflammation and edema [18]. New-onset LBBB has been reported in a variable percentage of TAVI performed with first-generation valves (4%–65%). The wide reported range is largely explained by the great variability in reporting, types of valves, and different time frames considered in the analysis [19]. Progressive refinements in valve design and standardization of the implantation technique have led to a reduction of acquired conduction disturbances since a greater implantation depth has been accepted as standard practice to minimize trauma to the conduction system [20]. The better device implantation technique has lowered the rate of LBBB with the latest generation THV (Figure 1) [7, 21–32].

### MODIFIABLE AND NON-MODIFIABLE RISK FACTORS INVOLVED IN CONDUCTION DISTURBANCES

#### Non-modifiable factors

##### Baseline anatomical factors

Men and women have distinct aortic root anatomy, independent of body surface area and height. Women have smaller annular dimensions, smaller sinuses, lower position of the left and right coronary artery ostia, and smaller ascending aortic diameters. These differences have implications on procedural planning and outcomes [33, 34], but they do not have any consistent impact on new-onset persistent LBBB or HAVB following TAVI [35–38].



**Figure 1.** Incidence of new-onset left bundle-branch block (LBBB) after transcatheter aortic valve replacement in the main registries and randomized clinical trials

Abbreviations: LBBB, left bundle branch block

The mechanism underlying the development of conduction disturbances after TAVR predominantly relates to the close anatomical proximity between the aortic annulus and the His bundle. The His bundle passes between the MS and the posterior crest of the muscular septum so that the inferior end of the MS can be considered an anatomic landmark for the left ventricular exit point of the conduction system. The distance between the aortic annulus and the membranous-muscular septal edge, measured by computed tomography (CT) represents a robust predictor of the development of new-onset conduction disturbance and PPI. This length appears to be inversely related to the risk of development of rhythm complications and an independent predictor of PPI [39, 40]. The INTERSECT registry highlighted that three risk groups could be identified based on MS length and its relationship with valve implantation depth: where an MS length  $\leq 3$  mm identifies a high-risk group for PPI ( $>20\%$ , Sapien 3 cohort odds ratio [OR], 6.96; 95% confidence interval [CI], 2.45–29.28; Evolut cohort OR, 3.14; 95% CI, 1.45–7.87), MS length 3–7 mm carries an intermediate risk of PPI (10%–20%, Sapien 3 cohort OR, 4.88; 95% CI, 1.75–20.37, Evolut cohort OR, 2.38; 95% CI, 1.21–5.87), and MS length  $> 7$  mm was deemed to be low risk of PPI ( $<10\%$ ) [41].

Another important anatomical factor for the prediction of PPI following TAVI is the presence of asymmetric calcification of the aortic valve. In a recent meta-analysis, the presence of elevated calcium load on the left coronary cusp (LCC) and on the non-coronary cusp (NCC) was a strong

predictor of PPI after TAVI [42]. This is probably due to an unequal distribution of radial forces on the aortic annulus and its surrounding structures, leading to a shift of the bioprosthesis away from calcification, towards the right coronary cusp (where the AV-bundle of His is located) [43]. The pattern of calcium distribution is, therefore, an important feature to take into account before TAVI.

### Baseline ECG

Electrocardiography (ECG) is a simple and effective tool to evaluate and predict post-procedural new-onset conduction disturbance and the risk of PPI. One of the most powerful and consistent predictors of new conduction abnormalities and PPI is the presence of baseline right bundle branch block (RBBB) (present in 10% to 14% of patients), especially if associated with first-degree AV block [44–47]. RBBB and first-degree AV block have been identified as risk factors in over half of the studies evaluating predictors of conduction disturbance and PPI.

A large meta-analysis including 239 studies and a total of 981 168 patients confirmed that the most important predictors for PPI implant were pre-existing RBBB (RR, 3.12;  $P < 0.001$ ), bifascicular block (RR, 2.40;  $P = 0.002$ ), and isolated first-degree atrioventricular block (RR 1.44;  $P < 0.001$ ) [48].

The post-procedural outcomes of patients with pre-existing LBBB (about 10% of the population undergoing TAVI) are controversial. In a multicenter study, 3404 TAVI candidates were evaluated according to the presence or absence of LBBB on baseline ECG. Patients were treated

with both self-expandable (SE) and balloon-expandable (BE) valves. Pre-existing LBBB was present in 398 patients (11.7%) and was associated with significantly increased risk of early (but not late) PPI (AdjOR 1.51; 95% CI, 1.12–2.04), without any significant effect on overall mortality (AdjOR 0.94; 95% CI, 0.75–1.18) or cardiovascular mortality (AdjOR 0.90; 95% CI, 0.68–1.21) [49]. Nevertheless, these results are not uniformly confirmed by other studies or pooled analyses, hence the real impact of pre-existing LBBB in this subset is still not completely clear [50, 51].

Notably, post-procedural brady-arrhythmic events are not necessarily TAVI-related since 24-hour ECG monitoring the day before the procedure can identify new arrhythmias in 16.1% of patients and among patients who required post-procedural PPI, 31.4% had newly diagnosed HAVB or severe bradycardia before TAVI [52].

Different scores for the prediction of PPI after TAVI based on ECG criteria have been validated over the years. Kiani et al. [53] developed, in 2019, the Emory Risk Score for the prediction of PPI after TAVR. The variables included were: history of syncope (1 point), RBBB (2 points), QRS interval  $\geq 140$  ms (1 point), and valve oversizing  $\geq 16\%$  (1 point) with an area under the receiver operating characteristic (ROC) curve of 0.778 ( $P < 0.001$ ) and an OR of 2.2 per point increase ( $P < 0.001$ ). More recently, Shivamurthy et al. [54] introduced another scoring system in which the significant variables were: transfemoral approach (1 point), LBBB without bradycardia (2 points), sinus bradycardia without LBBB (3 points), RBBB (3 points), LBBB with sinus bradycardia (4 points), second-degree AVB (5 points) with a ROC curve of 0.6743 (95% CI, 0.618–0.729). The risk for PPM requirement was stratified as follows: 7% risk of PPM with a score  $\leq 3$ , 19% with a score of 4 to 6, and 38% with a score  $\geq 7$ .

### Modifiable factors

During the procedural planning and procedural time, effort should be made to predict, avoid, and manage any arrhythmia that potentially may arise.

### Transcatheter heart valve

Since the first transcatheter aortic valve implantation, with the Cribier-Edwards valve (Edwards Lifesciences, Irvine, CA, US) in 2002 [55], many THVs have been developed and approved for clinical use. Unfortunately, despite the advances in valvular design, rates of post-TAVI conduction disturbances have not significantly decreased over time: ranging from 4.0% to 24.0% with the Sapien 3; from 14.7% to 26.7% with the Evolut R; from 2.3% to 10.5% with the Acurate; and 15.2% with the Portico valve [22] (from 5.7% to 15% with the newer generation Navitor valve [21]).

Different valve design characteristics such as radial forces expressed by the scaffold, extension of the stent frame into the left ventricular outflow tract (LVOT), and the need for pre- and post-dilatation and implantation depth are implicated in the generation of rhythm complications.

Use of the Evolut family THV has been associated with a higher rate of new PPI in comparison to BE valves even with the latest generation of devices [56, 57], likely due to its stent design properties that influence the position of the valve frame within LVOT, and the high radial force exerted on the conduction system.

In a meta-analysis conducted by Siontis et al. [58], patients receiving a CoreValve system had a 2.5-fold higher risk of PPI than those receiving a BE valve. The risk of PPI with the CoreValve family remained high even in the low-risk and intermediate-risk subgroups; the Evolut low-risk trial [8] demonstrated a 30-day need for PPI in 17.4% of patients, whereas in the SURTAVI study [6], the rate of PPI was 25.9% after TAVR with CoreValve or Evolut R devices. The recently published OPERA-TAVI registry confirmed these findings showing that Evolut PRO/PRO+ had a higher rate of PPI compared to Sapien 3 ULTRA (17.9% vs. 10.1%;  $P < 0.01$ ) [57].

In the group of SE valves, ACURATE neo and neo2 are associated with a lower rate of conduction disturbance and PPI compared with either Evolut platform (SCOPE II: 10.5% vs. 18.0%;  $P = 0.003$  [23]; Baggio et al. [59], 7.7% vs. 15.6%;  $P < 0.001$ ) or SAPIEN 3 valve (SCOPE I: 9.9% vs. 15.5%;  $P = 0.02$  [60]; MORENA registry 10.2% vs. 16.4%;  $P = 0.02$  [61]).

Pre- and post-dilatation have historically been considered mandatory steps during TAVI to facilitate device crossing and to ensure optimal valve expansion, especially in the case of THVs with low radial force. Pre-dilatation has been implicated in conduction disturbances during TAVI [62]; however, its role is still debatable, with growing evidence suggesting no significant impact on the development of periprocedural conduction disturbance or PPI [62, 63].

Finally, the choice of the right device size is of utmost importance. Valve oversizing, and a high prosthesis/LVOT diameter ratio leading to overstretching of the LVOT, is another well-known risk factor for PPI after TAVR [13, 38].

In valve-in-valve procedures, patients have been reported to have lower rates of PPI after transcatheter procedures. It has been hypothesized that the rigid structure of the pre-implanted stented valve allows less compression of the conduction system compared with native-valve TAVI recipients [64].

### Implant height

Since conduction disturbance and PPI have failed to decrease over time, despite optimization of valve technology, operators have tried to find new solutions to overcome the technological limits of devices and improve procedural strategies. Valve implantation depth is a well-known procedural risk factor for new-onset conduction disturbance due to the close anatomical relationship of the conduction system with the LVOT structures.

A first strategy to reduce rhythm complications during TAVI was identified by Jilaihawi et al. [65], who proposed an individualized, anatomically-guided tool for minimizing

implantation depth according to a CT-measured MS. They found that valve release at a depth lower than the MS significantly reduced the PPI rate (9.7% to 3%) and new-onset LBBB (25.8% to 9%).

Another technique to facilitate controlled implantation depth of SE valves is the use of the cusp-overlap projection; a coplanar projection made by overlapping the right coronary cusp (RCC) and LCC, which has the advantage of producing LVOT elongation, makes it possible to accurately position the prosthesis and gain a higher implantation depth (less than 3 mm). Data on the cusp overlap technique demonstrated excellent clinical and performance outcomes. A propensity score analysis comparing the cusp overlap technique with a standard 3-cusp coplanar projection demonstrated that the PPI rate was significantly reduced when using the cusp overlap technique (11.8% vs. 21.7%; RR, 0.54; 95% CI, 0.32–0.91;  $P = 0.03$ ). The results of the interim analysis of the Optimize PRO study (171 patients) showed low PPI rates at 30 days (8.8%) achieved using the cusp overlap technique with the Evolut PRO+ system and demonstrated that despite a higher implant, the technique was safe and no complications occurred [66].

Thanks to their short frame height, BE valves are commonly positioned and deployed perpendicular to the aortic valve annulus with minimal interaction with the conduction system using a standard 3-cusp coplanar projection. Nevertheless, deployment of BE valves using the cusp overlap technique has demonstrated a reduction of both new LBBB and PPI compared to standard 3 cusp projection (new-LBBB 5.3% vs. 12.2%;  $P < 0.001$ ; PPI 5.5% vs. 13.1%;  $P < 0.001$ ).

## DRUGS

To date, few data address the topic of beta-blocker discontinuation in patients undergoing TAVI. A prospective study on 743 consecutive patients found that the rate of periprocedural brady-arrhythmic events (HAVB) was numerically lower in patients who continued beta-blocker vs. those who did not (OR, 1.63; 95% CI, 0.95–2.8;  $P = 0.08$ ) with a significant reduction in PPI (20% vs. 13%;  $P = 0.02$ ) [67].

## POSTPROCEDURAL FACTORS: RECOGNIZE THE RED FLAGS

### Early phase, in-hospital monitoring

After TAVI, most conduction disturbances develop in the acute period (intra-procedurally or within 24 hours of the procedure) [19]. TAVI-induced HAVB (60% to 98%) [68, 69] and LBBB (85% to 94%) [70] mainly occur during the most traumatic stages of the procedure such as balloon pre-dilatation and valve expansion. Some cases of bundle branch block have also been associated with guidewire insertion and manipulation across the aortic valve. After this timeframe, only a small proportion of patients develop subacute conduction abnormalities, and the incidence rate of these events decreases over time. Most conduction dis-

turbances, such as LBBB or even HAVB, tend to be transient with complete recovery of normal conductive function [71].

The first ECG performed immediately post-procedure has been proposed as a key tool to screen patients at increased risk of HAVB.

Patients with normal sinus rhythm with no RBBB, a PR interval  $< 240$  ms and QRS interval  $< 150$  ms, or those in atrial fibrillation with a QRS interval  $< 140$  ms, have a very low risk of new HAVB within 30 days [72]. In this low-risk category, immediate removal of a temporary pacemaker has been demonstrated to be a safe option [72], and telemetry monitoring after the procedure can be avoided [68].

In the intermediate to high-risk categories (new LBBB or an increase in PR/QRS duration of  $\geq 20$  ms with or without pre-existing RBBB, HAVB), expert consensus recommends maintaining transvenous pacing ability for at least 24 hours because of the increased risk of early progression to HAVB [73].

Krishnaswamy et al. [74] tested the use of rapid atrial pacing up to 120 bpm, with the temporary pacing wire, to uncover latent conduction disturbance and predict the need for PPI. The authors found that patients who did not develop pacing-induced Wenckebach AV block had a very low need for permanent pacing within 30 days, with a negative predictive value for PPI in the group without Wenckebach AV block of 98.7%.

The 2021 European Society of Cardiology (ESC) guidelines on cardiac pacing suggest that in patients with dynamic progression of post-procedural conduction abnormalities (new BBB with dynamic prolongation of QRS and/or PR), an extended monitoring period in the hospital of up to 5 days should be considered [75].

### Late-onset conduction disturbances

Delayed conduction disturbances are conventionally defined as those occurring  $> 48$  hours after TAVI or hospital discharge. The incidence of this disturbance is reported to be around 10% [76].

The pathophysiological mechanisms of delayed conduction system injury can be identified in the development of tissue edema or inflammation and in late stent expansion of SE valves that continue applying pressure on an already wounded area (which also explains the lower resolution rates of conduction abnormalities in these devices) [77].

Baseline RBBB (OR, 3.56; 95% CI, 1.07–11.77;  $P = 0.03$ ) and change in PR interval (OR for each 10-ms increase 1.31; 95% CI, 1.18–1.45;  $P \leq 0.001$ ) were found to be independently associated with advanced delayed conduction abnormalities [78]. Less is known regarding the incidence of brady-arrhythmic events after discharge. In the MARE study [79, 80], 103 patients with new-onset LBBB after TAVI were followed up with an implantable cardiac monitor. Data showed that up to 16% of patients had HAVB episodes at 2-year follow-up (leading to PPI in 66% of them) and that most events occurred in the early phase after TAVI (50%

and 80% within the first and fourth months, respectively, with only 1 event after 12 months).

In summary, TAVI operators should aim to prevent and identify arrhythmia during all procedural steps and post-procedural monitoring through:

- Selection of the most appropriate device
- Optimization of valve delivery (minimize implantation depth, omit pre- and post-dilatation, avoid valve over-sizing)
- Performing 12-lead ECG immediately after the procedure, which could help to identify the risk of HAVB
- Longer period of continuous telemetry and maintenance of transvenous temporary pacemaker if there is evidence of new-onset and advanced conduction abnormalities or significant baseline ECG changes
- Observing patients in the acute period (intra-procedurally or within 24 hours of the procedure) as most conduction disturbances develop and frequently regress in that period. Therefore, the optimal timing and indications of PPI are crucial.

After discharge, the risk of progression or new-onset delayed conduction disturbances is low. Follow-up visits and 12-lead ECG should be scheduled at 1, 6, and 12 months. One year after the index procedure, it is unlikely for patients to have brady-arrhythmic events still related to TAVI.

## CONCLUSION

The high incidence of conduction disturbances after valve implantation still represents a major challenge in the management of patients after TAVI. Despite the significant body of knowledge on this complication, certain challenges need to be addressed to optimize the TAVR procedure in daily practice.

## Article information

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