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# Primary antiphospholipid syndrome in a male with myocardial infarction with non-obstructive coronary arteries and a history of stroke

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**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 procedural, electrocardiographic and clinical predictors of important post-procedural conduction disturbances (left bundle branch block [LBBB] and high-degree atrioventricular block [HAVB]) being identified, and 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 PPI. 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]. TAVI numbers continue to grow worldwide, including in nations that have started their TAVI programmes more recently. In Poland, for example, increasing numbers of patients are being treated and 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 newer-generation transcatheter heart valves (THV) are 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.

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 t 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 oedema, 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 need for PPI; this phenomenon is related to the regression of procedure related traumatic inflammation and oedema [18]. New-onset LBBB has been reported in a wildly variable percentage of TAVI performed with first-generation valves (4%–65%). The wide reported range is largely explained by the great variability in reporting, the types of valve and the different time-frames considered in the analysis [19]. Progressive refinements in valve design and standardization of the implantation technique has led to a reduction of acquired conduction disturbances since a higher implantation depth has been accepted as standard practice to minimize trauma to the conduction system [20]. The better device implantation technique has mitigated 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].

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, such 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 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 ≤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 for 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 for 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 for 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 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 consist predictors of new conduction abnormalities and PPI is the presence of baseline right bundle branch block (RBBB) (present in 10% to 14% of the patients), especially if associated with first-degree AV block [44–47]. RBBB and first degree AV block has been identified as a risk factor 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 a 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 nor pooled-analysis, 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 ≥140 ms (1 point), and valve oversizing ≥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 to 0.729). The risk for PPM requirement was stratified as follows: 7% risk of PPM with a score ≤ 3, 19% with a score 4 to 6, and 38% with a score ≥7.

**Modifiable factors**

During the procedural planning and procedural time, effort should be made to predict, avoid and manage any rhythm complication 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 disturbance 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 ventricle outflow tract, 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 higher rate of new PPI in comparison to BE valves even with latest generation of devices [56, 57], likely due to its stent design properties that influence the position of the valve frame within the left ventricular outflow tract (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 for 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].

Among the group of SE valves, the 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 and PPI [62, 63].

Finally, the choice of 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 demonstrated 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 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 improving procedural strategies. Valve implantation depth is a well-known procedural risk factor for new-onset of 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 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 RCC and LCC, that has the advantage of producing an elongation of the LVOT, making it possible to accurately position the prosthesis gaining a higher implantation depth (less than 3 mm). Data on cusp overlap technique

demonstrated excellent clinical and performance outcomes. A propensity score analysis comparing cusp overlap technique with a standard 3-cusp coplanar projection demonstrated that PPI rate was significantly reduced using 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 Optimize PRO study (171 patients) showed low PPI rates at 30-days (8.8%) achieved using 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 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. In details, a prospective study on 743 consecutive patients found that the rate of periprocedural bradyarrhythmic events (HAVB) was numerically lower among patients who continued BB 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 decrease over time. Most conduction disturbances, 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, and a PR interval <240 ms and QRS interval

<150 ms, or those in atrial fibrillation with QRS interval <140 ms, have a very low risk of new HAVB within 30 days [72]. In this low-risk category immediate removal of temporary pacemaker has been demonstrated to be a safe option [72] and telemetry monitoring after the procedure can be avoided [68].

In intermediate to high-risk categories (new LBBB or an increase in PR/QRS duration of ≥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 a. 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 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 hospital of up to 5 days should be considered [75].

**Late onset conduction disturbances**

Delayed conduction disturbances are classically 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 development of tissue oedema or inflammation, and in late stent expansion of SE valves that continue applying pressure on an already wounded area (also explaining the lower resolution rates of conduction abnormalities in these devices) [77].

Baseline RBBB (OR, 3.56; 95% CI, 1.07 to 11.77; $P = 0.03$) and change in PR interval (OR for each 10-ms increase 1.31; 95% CI, 1.18 to 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 bradyarrhythmic events after discharge. In the MARE Study [79, 80], 103 patients with new-onset LBBB after TAVI were followed up with 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 post-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 rhythm complications during all procedural steps and postprocedural monitoring.

- Selection of most appropriate device

- Optimization of valve delivery (minimize implantation depth, omit pre- and post-dilatation, avoid valve oversizing)
- 12-lead ECG immediately after the procedure could help to identify the risk of HAVB
- Longer period of continuous telemetry and the maintenance of transvenous temporary pacemaker if evidence of new-onset and advanced conduction abnormalities or significant baseline ECG changes
- Most conduction disturbances develop, and frequently regress, in the acute period (intra-procedurally or within 24 hours of the procedure). Therefore the optimal timing and indications of PPI is crucial
- After discharge, the risk of progression or new-onset of delayed conduction disturbances is low
- Follow-up visits and 12-lead ECG should be scheduled at 1-, 6- and 12-month.
- One year after the index procedure it is unlikely to have bradyarrhythmic events still related to TAVI.

## CONCLUSION

The high incidence of conduction disturbance 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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## REFERENCES

1. Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med. 2010; 363(17): 1597–1607, doi: 10.1056/NEJMoa1008232, indexed in Pubmed: 20961243.
2. Yakubov SJ, Adams DH, Watson DR, et al. Transcatheter aortic valve replacement using a self-expanding bioprosthesis in patients with severe aortic stenosis at extreme risk for surgery. J Am Coll Cardiol. 2014; 63(19): 1972–1981, doi: 10.1016/j.jacc.2014.02.556, indexed in Pubmed: 24657695.
3. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med. 2011; 364(23): 2187–2198, doi: 10.1056/NEJMoa1103510, indexed in Pubmed: 21639811.
4. Thourani VH, Kodali S, Makkar RR, et al. Transcatheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients: a propensity score analysis. Lancet. 2016; 387(10034): 2218–2225, doi: 10.1016/S0140-6736(16)30073-3, indexed in Pubmed: 27053442.
5. Leon MB, Smith CR, Mack MJ, et al. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. N Engl J Med. 2016; 374(17): 1609–1620, doi: 10.1056/NEJMoa1514616, indexed in Pubmed: 27040324.
6. Reardon MJ, Van Mieghem NM, Popma JJ, et al. Surgical or transcatheter aortic-valve replacement in intermediate-risk patients. N Engl J Med. 2017; 376(14): 1321–1331, doi: 10.1056/NEJMoa1700456, indexed in Pubmed: 28304219.
7. Pibarot P, Salaun E, Dahou A, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. N Engl J Med. 2019; 380(18): 1695–1705, doi: 10.1056/NEJMoa1814052, indexed in Pubmed: 30883058.
8. Popma JJ, Deeb GM, Yakubov SJ, et al. Transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. N Engl J Med. 2019; 380(18): 1706–1715, doi: 10.1056/NEJMoa1816885, indexed in Pubmed: 30883053.
9. Huczek Z, Rymuza B, Mazurek M, et al. Temporal trends of transcatheter aortic valve implantation in a high-volume academic center over 10 years. Kardiol Pol. 2021; 79(7-8): 820–826, doi: 10.33963/KP.a2021.0030, indexed in Pubmed: 34076883.
10. Carroll JD, Vemulapalli S, Dai D, et al. Procedural Experience for Transcatheter Aortic Valve Replacement and Relation to Outcomes: The STS/ACC TVT Registry. J Am Coll Cardiol. 2017; 70(1): 29–41, doi: 10.1016/j.jacc.2017.04.056, indexed in Pubmed: 28662805.

11. Vemulapalli S, Carroll JD, Mack MJ, et al. Procedural volume and outcomes for transcatheter aortic-valve replacement. N Engl J Med. 2019; 380(26): 2541–2550, doi: 10.1056/NEJMsa1901109, indexed in Pubmed: 30946551.
12. De Torres-Alba F, Kaleschke G, Diller GP, et al. Changes in the Pacemaker Rate After Transition From Edwards SAPIEN XT to SAPIEN 3 Transcatheter Aortic Valve Implantation: The Critical Role of Valve Implantation Height. JACC Cardiovasc Interv. 2016; 9(8): 805–813, doi: 10.1016/j.jcin.2015.12.023, indexed in Pubmed: 27017367.
13. Husser O, Pellegrini C, Kessler T, et al. Predictors of permanent pacemaker implantations and new-onset conduction abnormalities with the SAPIEN 3 balloon-expandable transcatheter heart valve. JACC Cardiovasc Interv. 2016; 9(3): 244–254, doi: 10.1016/j.jcin.2015.09.036, indexed in Pubmed: 26847116.
14. Meredith Am IT, Walters DL, Dumonteil N, et al. Transcatheter aortic valve replacement for severe symptomatic aortic stenosis using a repositionable valve system: 30-day primary endpoint results from the REPRISE II study. J Am Coll Cardiol. 2014; 64(13): 1339–1348, doi: 10.1016/j.jacc.2014.05.067, indexed in Pubmed: 25257635.
15. Khurshid S, Epstein AE, Verdino RJ, et al. Incidence and predictors of right ventricular pacing-induced cardiomyopathy. Heart Rhythm. 2014; 11(9): 1619–1625, doi: 10.1016/j.hrthm.2014.05.040, indexed in Pubmed: 24893122.
16. Zannad F, Huvelle E, Dickstein K, et al. Left bundle branch block as a risk factor for progression to heart failure. Eur J Heart Fail. 2007; 9(1): 7–14, doi: 10.1016/j.ejheart.2006.04.011, indexed in Pubmed: 16890486.
17. Piazza N, de Jaegere P, Schultz C, et al. Anatomy of the aortic valvar complex and its implications for transcatheter implantation of the aortic valve. Circ Cardiovasc Interv. 2008; 1(1): 74–81, doi: 10.1161/CIRCINTERVENTIONS.108.780858, indexed in Pubmed: 20031657.
18. Mangieri A, Montalto C, Pagnesi M, et al. TAVI and post procedural cardiac conduction abnormalities. Front Cardiovasc Med. 2018; 5: 85, doi: 10.3389/fcvm.2018.00085, indexed in Pubmed: 30018969.
19. Auffret V, Puri R, Urena M, et al. Conduction disturbances after transcatheter aortic valve replacement: current status and future perspectives. Circulation. 2017; 136(11): 1049–1069, doi: 10.1161/CIRCULATIONAHA.117.028352, indexed in Pubmed: 28893961.
20. Tang GHL, Zaid S, Michev I, et al. "Cusp-Overlap" View Simplifies Fluoroscopy-Guided Implantation of Self-Expanding Valve in Transcatheter Aortic Valve

Replacement. JACC Cardiovasc Interv. 2018; 11(16): 1663–1665, doi: 10.1016/j.jcin.2018.03.018, indexed in Pubmed: 30139479.

21. Corcione N, Berni A, Ferraro P, et al. Transcatheter aortic valve implantation with the novel-generation Navitor device: Procedural and early outcomes. Catheter Cardiovasc Interv. 2022; 100(1): 114–119, doi: 10.1002/ccd.30179, indexed in Pubmed: 35557027.
22. Walther T, Manoharan G, Linke A, et al. Incidence of new-onset left bundle branch block and predictors of new permanent pacemaker following transcatheter aortic valve replacement with the Portico™ valve. Eur J Cardiothorac Surg. 2018; 54(3): 467–474, doi: 10.1093/ejcts/ezy078, indexed in Pubmed: 29534170.
23. Kroon HG, van Gils L, Ziviello F, et al. Impact of Baseline and Newly Acquired Conduction Disorders on Need for Permanent Pacemakers With 3 Consecutive Generations of Self-Expanding Transcatheter Aortic Heart Valves. Cardiovasc Revasc Med. 2022; 34: 40–45, doi: 10.1016/j.carrev.2021.01.025, indexed in Pubmed: 33547024.
24. Tamburino C, Bleiziffer S, Thiele H, et al. Comparison of Self-Expanding Bioprostheses for Transcatheter Aortic Valve Replacement in Patients With Symptomatic Severe Aortic Stenosis: SCOPE 2 Randomized Clinical Trial. Circulation. 2020; 142(25): 2431–2442, doi: 10.1161/CIRCULATIONAHA.120.051547, indexed in Pubmed: 33054367.
25. Pellegrini C, Garot P, Morice MC, et al. Permanent pacemaker implantation and left bundle branch block with self-expanding valves - a SCOPE 2 subanalysis. EuroIntervention. 2022 [Epub ahead of print], doi: 10.4244/EIJ-D-22-00558, indexed in Pubmed: 36128956.
26. Möllmann H, Holzhey DM, Hilker M, et al. The ACURATE neo2 valve system for transcatheter aortic valve implantation: 30-day and 1-year outcomes. Clin Res Cardiol. 2021; 110(12): 1912–1920, doi: 10.1007/s00392-021-01882-3, indexed in Pubmed: 34148125.
27. Chandra P, Jose J, Mattummal S, et al. Clinical evaluation of the Hydra self-expanding transcatheter aortic valve: 6 month results from the GENESIS trial. Catheter Cardiovasc Interv. 2021; 98(2): 371–379, doi: 10.1002/ccd.29733, indexed in Pubmed: 33876881.
28. Moriyama N, Lehtola H, Miyashita H, et al. Hemodynamic comparison of transcatheter aortic valve replacement with the SAPIEN 3 Ultra versus SAPIEN 3: The HomoSAPIEN registry. Catheter Cardiovasc Interv. 2021; 97(7): E982–E991, doi: 10.1002/ccd.29281, indexed in Pubmed: 32966682.
29. Mauri V, Reimann A, Stern D, et al. Predictors of Permanent Pacemaker Implantation After Transcatheter Aortic Valve Replacement With the SAPIEN 3. JACC Cardiovasc

Interv. 2016; 9(21): 2200–2209, doi: 10.1016/j.jcin.2016.08.034, indexed in Pubmed: 27832845.

30. Sammour Y, Banerjee K, Kumar A, et al. Systematic Approach to High Implantation of SAPIEN-3 Valve Achieves a Lower Rate of Conduction Abnormalities Including Pacemaker Implantation. Circ Cardiovasc Interv. 2021; 14(1): e009407, doi: 10.1161/CIRCINTERVENTIONS.120.009407, indexed in Pubmed: 33430603.
31. Unzué L, García E, Díaz-Antón B, et al. Left Bundle Branch Block after Transcatheter Aortic Valve Implantation with Edwards Sapien 3 Valve: Influence of the Valve Depth Implantation. Cardiovasc Revasc Med. 2019; 20(11): 949–955, doi: 10.1016/j.carrev.2019.01.006, indexed in Pubmed: 30745060.
32. Sammour YM, Lak H, Chahine J, et al. Clinical and echocardiographic outcomes with new-onset left bundle branch block after SAPIEN-3 transcatheter aortic valve replacement. Catheter Cardiovasc Interv. 2023; 101(1): 187–196, doi: 10.1002/ccd.30488, indexed in Pubmed: 36378620.
33. Aggarwal SR, Clavel MA, Messika-Zeitoun D, et al. Sex differences in aortic valve calcification measured by multidetector computed tomography in aortic stenosis. Circ Cardiovasc Imaging. 2013; 6(1): 40–47, doi: 10.1161/CIRCIMAGING.112.980052, indexed in Pubmed: 23233744.
34. Hamdan A, Barbash I, Schwammenthal E, et al. Sex differences in aortic root and vascular anatomy in patients undergoing transcatheter aortic valve implantation: A computed-tomographic study. J Cardiovasc Comput Tomogr. 2017; 11(2): 87–96, doi: 10.1016/j.jcct.2017.01.006, indexed in Pubmed: 28139364.
35. Bleiziffer S, Ruge H, Hörer J, et al. Predictors for new-onset complete heart block after transcatheter aortic valve implantation. JACC Cardiovasc Interv. 2010; 3(5): 524–530, doi: 10.1016/j.jcin.2010.01.017, indexed in Pubmed: 20488409.
36. Regazzoli D, Chiarito M, Cannata F, et al. Transcatheter Self-Expandable Valve Implantation for Aortic Stenosis in Small Aortic Annuli: The TAVI-SMALL Registry. JACC Cardiovasc Interv. 2020; 13(2): 196–206, doi: 10.1016/j.jcin.2019.08.041, indexed in Pubmed: 31883714.
37. Schymik G, Tzamalis P, Bramlage P, et al. Clinical impact of a new left bundle branch block following TAVI implantation: 1-year results of the TAVIK cohort. Clin Res Cardiol. 2015; 104(4): 351–362, doi: 10.1007/s00392-014-0791-2, indexed in Pubmed: 25388650.
38. Giustino G, Van der Boon RMA, Molina-Martin de Nicolas J, et al. Impact of permanent pacemaker on mortality after transcatheter aortic valve implantation: the PRAGMATIC

(Pooled Rotterdam-Milan-Toulouse in Collaboration) Pacemaker substudy. EuroIntervention. 2016; 12(9): 1185–1193, doi: 10.4244/EIJV12I9A192, indexed in Pubmed: 27753605.

39. Aslan S, Demir AR, Çelik Ö, et al. Usefulness of membranous septum length in the prediction of major conduction disturbances in patients undergoing transcatheter aortic valve replacement with different devices. Kardiol Pol. 2020; 78(10): 1020–1028, doi: 10.33963/KP.15538, indexed in Pubmed: 32735407.
40. Hamdan A, Guetta V, Klempfner R, et al. Inverse Relationship Between Membranous Septal Length and the Risk of Atrioventricular Block in Patients Undergoing Transcatheter Aortic Valve Implantation. JACC Cardiovasc Interv. 2015; 8(9): 1218–1228, doi: 10.1016/j.jcin.2015.05.010, indexed in Pubmed: 26292585.
41. Hokken TW, Muhemin M, Okuno T, et al. Impact of membranous septum length on pacemaker need with different transcatheter aortic valve replacement systems: The INTERSECT registry. J Cardiovasc Comput Tomogr. 2022; 16(6): 524–530, doi: 10.1016/j.jcct.2022.07.003, indexed in Pubmed: 35872136.
42. Maier O, Piayda K, Afzal S, et al. Computed tomography derived predictors of permanent pacemaker implantation after transcatheter aortic valve replacement: A meta-analysis. Catheter Cardiovasc Interv. 2021; 98(6): E897–E907, doi: 10.1002/ccd.29805, indexed in Pubmed: 34076343.
43. Fujita B, Kütting M, Seiffert M, et al. Calcium distribution patterns of the aortic valve as a risk factor for the need of permanent pacemaker implantation after transcatheter aortic valve implantation. Eur Heart J Cardiovasc Imaging. 2016; 17(12): 1385–1393, doi: 10.1093/ehjci/jev343, indexed in Pubmed: 26758411.
44. Watanabe Y, Kozuma K, Hioki H, et al. Pre-Existing Right Bundle Branch Block Increases Risk for Death After Transcatheter Aortic Valve Replacement With a Balloon-Expandable Valve. JACC Cardiovasc Interv. 2016; 9(21): 2210–2216, doi: 10.1016/j.jcin.2016.08.035, indexed in Pubmed: 27832846.
45. Auffret V, Webb JG, Eltchaninoff H, et al. Clinical Impact of Baseline Right Bundle Branch Block in Patients Undergoing Transcatheter Aortic Valve Replacement. JACC Cardiovasc Interv. 2017; 10(15): 1564–1574, doi: 10.1016/j.jcin.2017.05.030, indexed in Pubmed: 28734885.
46. Egger F, Nürnberg M, Rohla M, et al. High-degree atrioventricular block in patients with preexisting bundle branch block or bundle branch block occurring during transcatheter aortic valve implantation. Heart Rhythm. 2014; 11(12): 2176–2182, doi: 10.1016/j.hrthm.2014.07.014, indexed in Pubmed: 25034184.

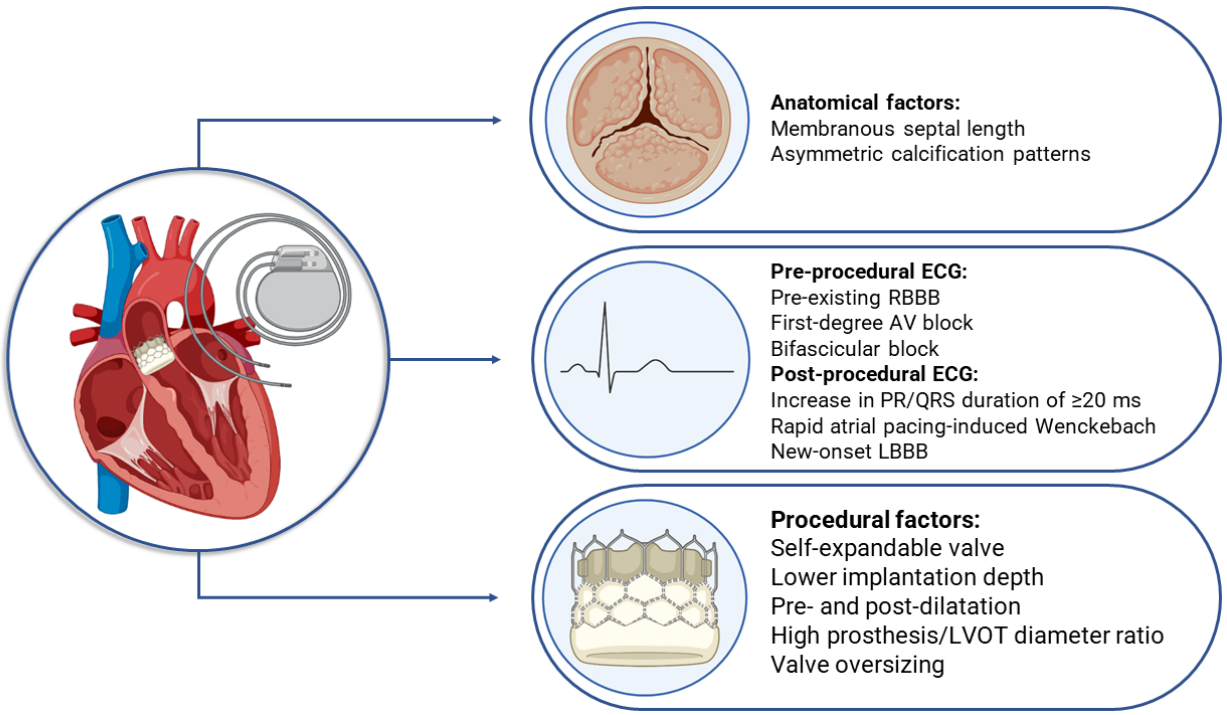
47. Chorianopoulos E, Krumsdorf U, Pleger ST, et al. Incidence of late occurring bradyarrhythmias after TAVI with the self-expanding CoreValve(®) aortic bioprosthesis. Clin Res Cardiol. 2012; 101(5): 349–355, doi: 10.1007/s00392-011-0398-9, indexed in Pubmed: 22179559.
48. Abu Rmilah AA, Al-Zu'bi H, Haq IU, et al. Predicting permanent pacemaker implantation following transcatheter aortic valve replacement: A contemporary meta-analysis of 981,168 patients. Heart Rhythm O2. 2022; 3(4): 385–392, doi: 10.1016/j.hroo.2022.05.001, indexed in Pubmed: 36097458.
49. Fischer Q, Himbert D, Webb JG, et al. Impact of Preexisting Left Bundle Branch Block in Transcatheter Aortic Valve Replacement Recipients. Circ Cardiovasc Interv. 2018; 11(11): e006927, doi: 10.1161/CIRCINTERVENTIONS.118.006927, indexed in Pubmed: 30571207.
50. Sammour Y, Sato K, Kumar A, et al. Impact of baseline conduction abnormalities on outcomes after transcatheter aortic valve replacement with SAPIEN-3. Catheter Cardiovasc Interv. 2021; 98(1): E127–E138, doi: 10.1002/ccd.29309, indexed in Pubmed: 33010100.
51. Shoar S, Batra S, Gulraiz A, et al. Effect of pre-existing left bundle branch block on post-procedural outcomes of transcatheter aortic valve replacement: a meta-analysis of comparative studies. Am J Cardiovasc Dis. 2020; 10(4): 294–300, indexed in Pubmed: 33224576.
52. Urena M, Hayek S, Cheema AN, et al. Arrhythmia burden in elderly patients with severe aortic stenosis as determined by continuous electrocardiographic recording: toward a better understanding of arrhythmic events after transcatheter aortic valve replacement. Circulation. 2015; 131(5): 469–477, doi: 10.1161/CIRCULATIONAHA.114.011929, indexed in Pubmed: 25466975.
53. Kiani S, Kamioka N, Black GB, et al. Development of a Risk Score to Predict New Pacemaker Implantation After Transcatheter Aortic Valve Replacement. JACC Cardiovasc Interv. 2019; 12(21): 2133–2142, doi: 10.1016/j.jcin.2019.07.015, indexed in Pubmed: 31699374.
54. Shivamurthy P, Vejpongsa P, Gurung S, et al. Validation of scoring system predicting permanent pacemaker implantation after transcatheter aortic valve replacement. Pacing Clin Electrophysiol. 2020; 43(5): 479–485, doi: 10.1111/pace.13910, indexed in Pubmed: 32270881.
55. Cribier A, Eltchaninoff H, Bash A, et al. Percutaneous transcatheter implantation of an aortic valve prosthesis for calcific aortic stenosis: first human case description.

Circulation. 2002; 106(24): 3006–3008, doi: 10.1161/01.cir.0000047200.36165.b8, indexed in Pubmed: 12473543.

56. Erkapic D, De Rosa S, Kelava A, et al. Risk for permanent pacemaker after transcatheter aortic valve implantation: a comprehensive analysis of the literature. J Cardiovasc Electrophysiol. 2012; 23(4): 391–397, doi: 10.1111/j.1540-8167.2011.02211.x, indexed in Pubmed: 22050112.
57. Costa G, Saia F, Pilgrim T, et al. Transcatheter Aortic Valve Replacement With the Latest-Iteration Self-Expanding or Balloon-Expandable Valves: The Multicenter OPERA-TAVI Registry. JACC Cardiovasc Interv. 2022; 15(23): 2398–2407, doi: 10.1016/j.jcin.2022.08.057, indexed in Pubmed: 36121242.
58. Siontis GCM, Jüni P, Pilgrim T, et al. Predictors of permanent pacemaker implantation in patients with severe aortic stenosis undergoing TAVR: a meta-analysis. J Am Coll Cardiol. 2014; 64(2): 129–140, doi: 10.1016/j.jacc.2014.04.033, indexed in Pubmed: 25011716.
59. Baggio S, Pagnesi M, Kim WK, et al. Comparison of transcatheter aortic valve replacement with the ACURATE neo2 versus Evolut PRO/PRO+ devices. EuroIntervention. 2023; 18(12): 977–986, doi: 10.4244/EIJ-D-22-00498, indexed in Pubmed: 36093795.
60. Lanz J, Kim WK, Walther T, et al. Safety and efficacy of a self-expanding versus a balloon-expandable bioprosthesis for transcatheter aortic valve replacement in patients with symptomatic severe aortic stenosis: a randomised non-inferiority trial. Lancet. 2019; 394(10209): 1619–1628, doi: 10.1016/S0140-6736(19)32220-2, indexed in Pubmed: 31570258.
61. Husser O, Kim WK, Pellegrini C, et al. Multicenter Comparison of Novel Self-Expanding Versus Balloon-Expandable Transcatheter Heart Valves. JACC Cardiovasc Interv. 2017; 10(20): 2078–2087, doi: 10.1016/j.jcin.2017.06.026, indexed in Pubmed: 29050625.
62. Lange P, Greif M, Vogel A, et al. Reduction of pacemaker implantation rates after CoreValve® implantation by moderate predilatation. EuroIntervention. 2014; 9(10): 1151–1157, doi: 10.4244/EIJV9I10A195, indexed in Pubmed: 24561731.
63. Auffret V, Regueiro A, Campelo-Parada F, et al. Feasibility, safety, and efficacy of transcatheter aortic valve replacement without balloon predilation: A systematic review and meta-analysis. Catheter Cardiovasc Interv. 2017; 90(5): 839–850, doi: 10.1002/ccd.27040, indexed in Pubmed: 28403562.

64. Reul RM, Ramchandani MK, Reardon MJ. Transcatheter aortic valve-in-valve procedure in patients with bioprosthetic structural valve deterioration. Methodist Debakey Cardiovasc J. 2017; 13(3): 132–141, doi: 10.14797/mdcj-13-3-132, indexed in Pubmed: 29743998.
65. Jilaihawi H, Zhao Z, Du R, et al. Minimizing permanent pacemaker following repositionable self-expanding transcatheter aortic valve replacement. JACC Cardiovasc Interv. 2019; 12(18): 1796–1807, doi: 10.1016/j.jcin.2019.05.056, indexed in Pubmed: 31473236.
66. Jilaihawi H, Zhao Z, Du R, et al. Minimizing permanent pacemaker following repositionable self-expanding transcatheter aortic valve replacement. JACC Cardiovasc Interv. 2019; 12(18): 1796–1807, doi: 10.1016/j.jcin.2019.05.056, indexed in Pubmed: 31473236.
67. Younis A, Orvin K, Nof E, et al. The effect of periprocedural beta blocker withdrawal on arrhythmic risk following transcatheter aortic valve replacement. Catheter Cardiovasc Interv. 2019; 93(7): 1361–1366, doi: 10.1002/ccd.28017, indexed in Pubmed: 30489692.
68. Toggweiler S, Stortecky S, Holy E, et al. The electrocardiogram after transcatheter aortic valve replacement determines the risk for post-procedural high-degree AV block and the need for telemetry monitoring. JACC Cardiovasc Interv. 2016; 9(12): 1269–1276, doi: 10.1016/j.jcin.2016.03.024, indexed in Pubmed: 27339844.
69. Guetta V, Goldenberg G, Segev A, et al. Predictors and course of high-degree atrioventricular block after transcatheter aortic valve implantation using the CoreValve Revalving System. Am J Cardiol. 2011; 108(11): 1600–1605, doi: 10.1016/j.amjcard.2011.07.020, indexed in Pubmed: 21880290.
70. Massoullié G, Bordachar P, Ellenbogen KA, et al. New-Onset left bundle branch block induced by transcutaneous aortic valve implantation. Am J Cardiol. 2016; 117(5): 867–873, doi: 10.1016/j.amjcard.2015.12.009, indexed in Pubmed: 26742470.
71. Nazif TM, Chen S, Kodali SK. Disarming the ticking time bomb: post-procedure electrocardiography predictors of high-degree conduction disturbances after transcatheter aortic valve replacement. JACC Cardiovasc Interv. 2018; 11(15): 1527–1530, doi: 10.1016/j.jcin.2018.07.003, indexed in Pubmed: 30093057.
72. Jørgensen TH, De Backer O, Gerds TA, et al. Immediate post-procedural 12-lead electrocardiography as predictor of late conduction defects after transcatheter aortic valve replacement. JACC Cardiovasc Interv. 2018; 11(15): 1509–1518, doi: 10.1016/j.jcin.2018.04.011, indexed in Pubmed: 30093055.

73. Rodés-Cabau J, Ellenbogen KA, Krahn AD, et al. Management of conduction disturbances associated with transcatheter aortic valve replacement: JACC Scientific Expert Panel. J Am Coll Cardiol. 2019; 74(8): 1086–1106, doi: 10.1016/j.jacc.2019.07.014, indexed in Pubmed: 31439219.
74. Krishnaswamy A, Sammour Y, Mangieri A, et al. The utility of rapid atrial pacing immediately post-tavr to predict the need for pacemaker implantation. JACC Cardiovasc Interv. 2020; 13(9): 1046–1054, doi: 10.1016/j.jcin.2020.01.215, indexed in Pubmed: 32305392.
75. Glikson M, Nielsen JC, Kronborg MB, et al. 2021 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy. Eur Heart J. 2021; 42(35): 3427–3520, doi: 10.1093/eurheartj/ehab364, indexed in Pubmed: 34455430.
76. Ream K, Sandhu A, Valle J, et al. Ambulatory rhythm monitoring to Detect Late high-grade atrioventricular block following transcatheter aortic valve replacement. J Am Coll Cardiol. 2019; 73(20): 2538–2547, doi: 10.1016/j.jacc.2019.02.068, indexed in Pubmed: 31118148.
77. Houthuizen P, van der Boon RMA, Urena M, et al. Occurrence, fate and consequences of ventricular conduction abnormalities after transcatheter aortic valve implantation. EuroIntervention. 2014; 9(10): 1142–1150, doi: 10.4244/EIJV9I10A194, indexed in Pubmed: 24273252.
78. Mangieri A, Lanzillo G, Bertoldi L, et al. Predictors of advanced conduction disturbances requiring a late (≥48 h) permanent pacemaker following transcatheter aortic valve replacement. JACC Cardiovasc Interv. 2018; 11(15): 1519–1526, doi: 10.1016/j.jcin.2018.06.014, indexed in Pubmed: 30093056.
79. Rodés-Cabau J, Urena M, Nombela-Franco L, et al. Arrhythmic burden as determined by ambulatory continuous cardiac monitoring in patients with new-onset persistent left bundle branch block following transcatheter aortic valve replacement: the MARE study. JACC Cardiovasc Interv. 2018; 11(15): 1495–1505, doi: 10.1016/j.jcin.2018.04.016, indexed in Pubmed: 30031719.
80. Muntané-Carol G, Urena M, Nombela-Franco L, et al. Arrhythmic burden in patients with new-onset persistent left bundle branch block after transcatheter aortic valve replacement: 2-year results of the MARE study. Europace. 2021; 23(2): 254–263, doi: 10.1093/europace/euaa213, indexed in Pubmed: 33083813.




**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

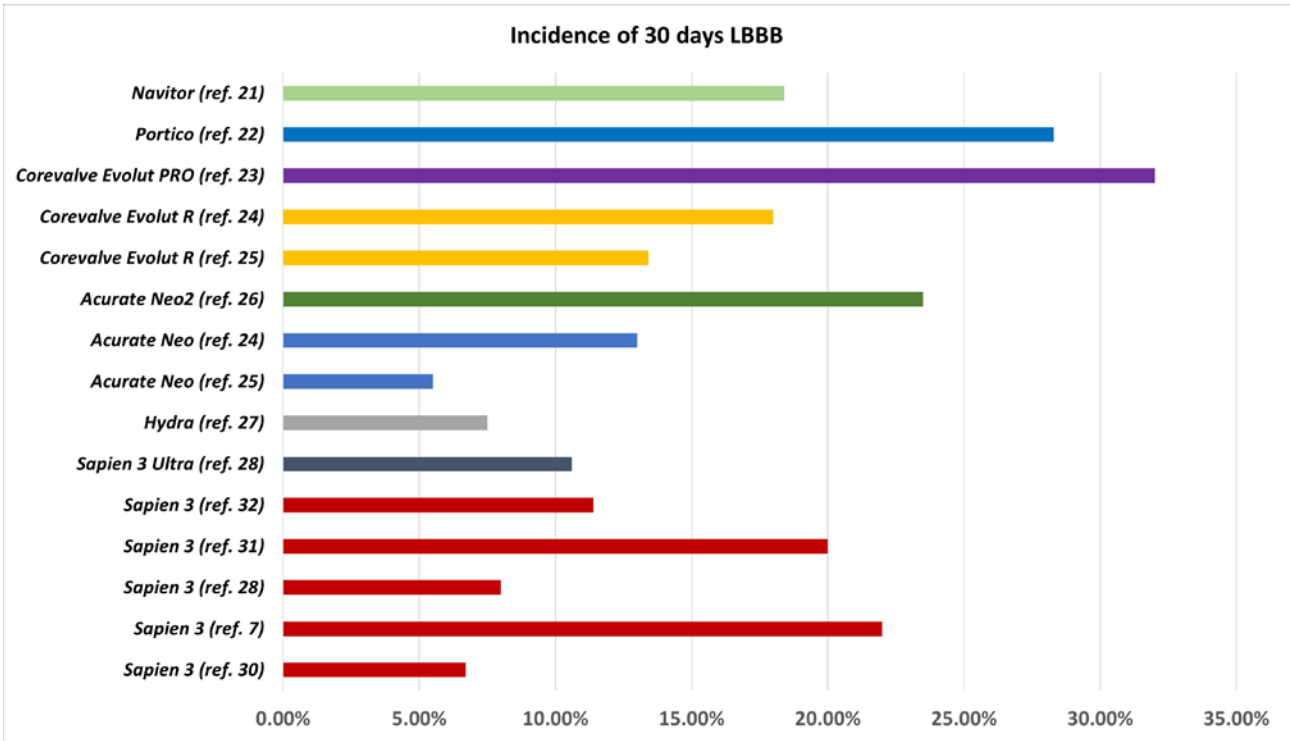



**Figure 1.** Incidence of new-onset left bundle-branch block (LBBB) after transcatheter aortic valve replacement in the main registries and randomized clinical trials

Abbreviations: LBBB, left bundle branch block

emic (yellow arrows) (**C**)