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Systematic Review/Meta-analysis

A Systematic Review of Delayed High-Grade Atrioventricular Block After Transcatheter Aortic Valve Implantation

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ABSTRACT

Background: High-grade atrioventricular block (HGAVB) is common after transcatheter aortic valve implantation (TAVI), often necessitating permanent pacemaker (PPM) implantation. Delayed HGAVB has varying definitions but typically refers to onset 48 hours after TAVI or following discharge and may cause syncope and sudden cardiac death. This review estimates the incidence of delayed HGAVB and identifies limitations of current literature.

Methods: A systematic review was performed of the following online databases: Medline, Cochrane, Web of Science, and Scopus. Studies that labelled the outcome of "delayed" or "late" atrioventricular block after TAVI were included; patients with previous PPM or aortic valve surgery were excluded. Initial search yielded 775 studies, which, after screening, was narrowed to 19 studies.

Results: Nineteen studies with 14,898 patients were included. Mean age was 81.7 years, and 46.3% were male. Mean Society of Thoracic

RÉSUMÉ

Contexte : L'apparition d'un bloc atrioventriculaire de haut degré (BAVHD) est fréquente après l'implantation valvulaire aortique par cathéter (IVAC), ce qui nécessite souvent l'implantation d'un stimulateur cardiaque permanent. Les définitions d'un BAVHD tardif varient, mais elles font habituellement référence à l'apparition du bloc 48 heures après l'IVAC ou après le congé de l'hôpital. Le bloc peut alors provoquer une syncope et une mort subite d'origine cardiaque. Cette analyse vise à estimer l'incidence de la formation d'un BAVHD tardif et à définir les lacunes dans les publications actuelles.

Méthodologie : Une analyse des études publiées dans les bases de données en ligne suivantes a été menée : Medline, Cochrane, Web of Science et Scopus. Les études dont le libellé comprenait l'issue du bloc atrioventriculaire tardif ou éloigné (« *delayed* » ou « *late* ») ont été retenues. Les patients qui avaient antérieurement reçu un stimulateur cardiaque permanent ou subi une intervention chirurgicale de la valve

High-grade atrioventricular block (HGAVB), which comprises third-degree or second-degree (Mobitz Type II) atrioventricular (AV) block, is not infrequent following transcatheter aortic valve implantation (TAVI), with a reported incidence between 9% and 26% and often necessitating permanent pacemaker (PPM) implantation.[1,2] The definition of delayed HGAVB varies in the literature but generally refers to the onset of HGAVB 48 hours after TAVI or following discharge, as per the most recent American College of Cardiology (ACC) consensus statement.[3] The current ACC and European Society of Cardiology (ESC) guidelines recommend (Class 1) permanent pacing in patients with persistent HGAVB at 24 to 48 hours post TAVI.[4]

The mechanism of HGAVB in TAVI is via mechanical compression of the bundle of His, left bundle branch, or—less commonly—the AV node. The bundle of His emerges and bifurcates at the base of the membranous ventricular septum, which explains why the membranous septal length and implantation depth are both powerful predictors of HGAVB post-TAVI.[5] Other predictors include pre-existing right bundle branch block (RBBB), self-expanding valves, significant oversizing, and a postprocedural increase in QRS or PR interval.[6-8] Electrophysiology study (EPS) including His-ventricular (HV) interval measurement and induction of AV Wenckebach through incremental atrial pacing have a strong negative but poor positive predictive value for PPM after TAVI.[9,10]

Despite multiple known predictors, there is currently no sensitive or specific method of identifying patients likely to develop HGAVB post-TAVI. Moreover, there is little understanding about the timing of delayed HGAVB; although predominantly occurring within the first week, HGAVB can also occur beyond 30 days.[11-13] When unrecognized,

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Surgeons (STS) score was 5.6%, and 31.3% of patients had known atrial fibrillation. The most common access site was transfemoral (84.8%), whereas balloon-expandable valves were used in 62.1%, self-expanding valves in 34.0%, and mechanically expanding valves in 3.9% of cases. The incidence of delayed HGAVB ranged from 1.7% to 14.6%, with significant methodologic heterogeneity noted among the included studies.

Conclusions: Delayed HGAVB is a common and potentially serious complication of TAVI, with similar risk factors to acute HGAVB. With a move toward an early discharge strategy post-TAVI, further prospective study of delayed HGAVB is warranted to improve understanding of predisposing factors, incidence, timing, and implications.

aortique ont été exclus. La recherche initiale a permis de recenser 775 études, nombre qui a été réduit à 19 après l'application des critères de sélection.

Résultats : Dix-neuf études totalisant 14 898 patients ont été retenues. L'âge moyen était 81,7 ans, et 46,3 % des patients étaient des hommes. Le score STS (Society of Thoracic Surgeons) moyen était de 5,6 %, et 31,3 % des patients avaient une fibrillation auriculaire. Le point d'accès le plus fréquent était par l'artère fémorale (84,8 %). Des valves expansibles par ballonnet ont été utilisées dans 62,1 % des cas, des valves auto-expansibles dans 34,0 % des cas et des valves expansibles mécaniquement dans 3,9 % des cas. L'incidence du BAVHD tardif variait de 1,7 % à 14,6 %, mais la méthodologie était très hétérogène d'une étude à l'autre.

Conclusions : Le BAVHD tardif est une complication fréquente et potentiellement grave de l'IVAC, et ses facteurs de risque sont comparables à ceux du BAVHD aigu. Étant donné la volonté d'adopter une stratégie de congé précoce après une IVAC, une autre étude prospective sur le BAVHD tardif s'impose pour mieux comprendre les facteurs prédisposants, l'incidence, la chronologie et les implications.

HGAVB can lead to significant bradycardia, manifesting as presyncope, syncope, or sudden cardiac death. A substantial proportion of unexplained sudden cardiac deaths following TAVI may be secondary to unrecognized delayed HGAVB, given both adverse outcomes share similar predictors.[13,14]

As improved procedural technique and periprocedural care have reduced the length of post-TAVI hospital admissions, the incidence of delayed HGAVB necessitating PPM insertion following hospital discharge has increased.[15,16] This systematic review investigates the incidence of delayed HGAVB or new permanent pacemaker implantation in patients without a previous pacemakers or aortic valve surgeries and aims to identify the current limitations of the literature.

Methods

A systematic review searching the following electronic databases was performed: Medline, Scopus, Web of Science and Cochrane, from January 1, 2000, until May 15, 2022. Study screening was performed by 2 authors (K.R. and B.C.). Key words searched were "TAVI," "TAVR," "transcatheter aortic valve implantation," or "transcatheter aortic valve replacement" combined with "conduction disturbance," "bradycardia," "bradyarrhythmia," or "atrioventricular block." Free word and MeSH term searches were conducted on "TAVI," "TAVR," "transcatheter (aorta*)," and "block" or "pacemaker" or "bradycardia" or "conduction" or arrhythmia" combined with "delay" or "late." The review included all studies that measured the desired outcome of delayed HGAVB, had accessible results, and were published in English. Abstracts, case reports, conference presentations, editorials, and expert opinions were excluded. Review articles were omitted because of potential publication bias and result duplication.

Because of the varying definitions of delayed HGAVB, only studies that defined it as occurring at least 24 hours after the TAVI were included. There was no discrimination of total follow-up periods or valve design, and both prospective and retrospective studies were included.

Patients with previous permanent pacemaker implantation or aortic valve surgery were removed from the total population by the authors before calculating the incidence of delayed HGAVB.

A standardized data collection template was used for data extraction, including baseline demographics, study design, exclusion criteria, definition of delayed HGAVB and method of diagnosis, length of follow-up, valve types used, prevalence of pre-existing RBBB, prevalence of pre-existing atrial fibrillation, and incidence of delayed HGAVB.

Results

The initial search strategy yielded 775 results, and, after removal of duplicates, 370 studies were removed. Through title and abstract screening, a further 378 were removed, and 27 studies remained for full study review. After application of the selection criteria, 8 further studies were excluded. The remaining 19 studies were further screened, and a bias assessment was performed using the **R**isk **o**f **B**ias **i**n **N**on-randomised **S**tudies - of **I**nterventions (ROBINS-I)[17] (Fig. 1: **P**referred **R**eporting **I**tems for **S**ystemic Reviews and **M**eta-**A**nalyses [PRISMA] flow chart). Data extraction and critical appraisal were conducted by 2 reviewers (K.R. and B.C.), and results were reviewed by the senior investigators (P.H. and R.B.).

The 19 studies included in this review consisted of a total of 14,898 patients. Of the included studies, 11 (58%) were retrospectively performed, and 8 (42%) were prospectively performed. All studies were nonrandomized and observational. Delayed HGAVB was measured using a continuous monitoring method (either ambulatory event monitoring or an implantable loop recorder) in 7 (37%) of the studies, whereas the remainder used noncontinuous monitoring to measure the outcome, either through electrocardiography (ECG), clinical features, or clinician-initiated permanent pacemaker implantation.

Baseline characteristics

Overall, the mean age was 81.7 years; 46.3% of the patients were male, and the mean Society of Thoracic Surgeons (STS) score was 5.6% (Table 1). Almost one-third (31.5%) of

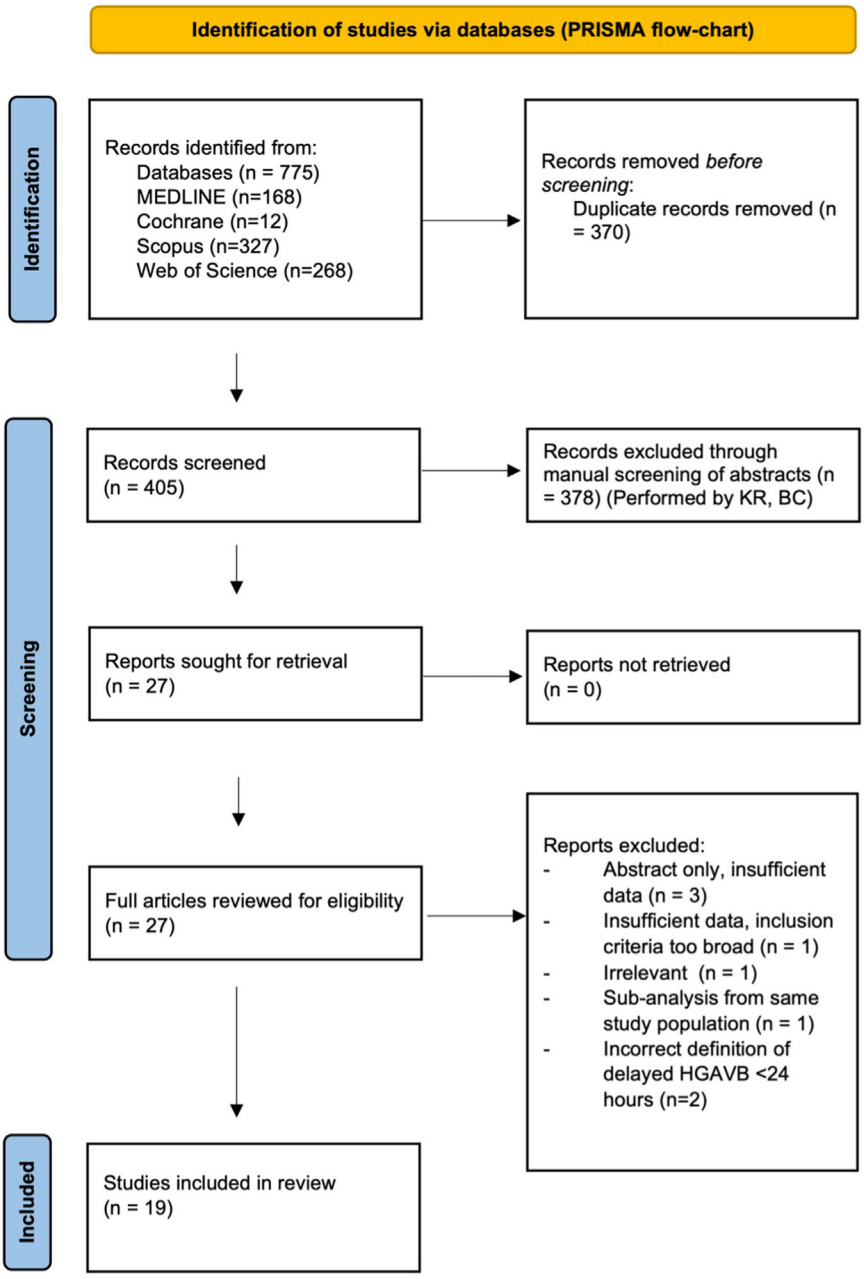

Figure 1. **P**referred **R**eporting **I**tems for **S**ystemic Reviews and **M**eta-**A**nalyses (PRISMA) Flowchart for identification, screening, and inclusion of studies.

patients were found to have pre-existing atrial fibrillation. The most commonly deployed valve type was balloon-expanding (62.1%), followed by self-expanding (34.0%), and then mechanically expanding valves (3.9%). The most common approach was transfemoral (84.8%).

Definition and incidence of delayed HGAVB

The definition of delayed HGAVB varied in the literature. Sixteen studies defined delayed HGAVB as either post-discharge, or between 24 and 72 hours following TAVI. The remainder defined delayed HGAVB as either after 7 days or after 30 days. Lengths of follow-up were also variable among the studies, ranging from 14 days to 5 years. Because of the variation in follow-up periods and influence on detection of the primary outcome, Tables 2 to 5 split the studies by total follow-up period.

The incidence of delayed HGAVB or new delayed permanent pacemaker implantation, ranged from 1.7% to 14.6% across the included studies (Tables 2 to 5). Because of the high degree of heterogeneity, a pooled incidence was not calculated on all included studies. Instead, a subanalysis was performed on 5 prospective studies,[11,19,22,23,28] which used a

Table 1. Summary demographics (n = 19)

Summary baseline characteristics	Results
Total patients	14,898
Age, mean (SD)	81.7 (± 4.7)
Gender	
Male %	46.3
STS score, mean%	5.6
	*Total n = 11,498
Pre-existing atrial fibrillation, n (%)	4654 (31.3)
	*Total n = 14103
Pre-existing RBBB, n (%)	1144 (8.6)
	*Total n = 13,001
Valve type	
Balloon expandable, n (%)	9707 (62.1)
Self-expandable, n (%)	5305 (34.0)
Mechanically expandable, n (%)	608 (3.9)
Transfemoral access site, n (%)	10,395 (84.8)
	*Total n = 12,265

RBBB, right bundle branch block; SD, standard deviation; STS, Society of Thoracic Surgeons.

similar definition of delayed HGAVB (48 hours after TAVI or after discharge), had the lowest calculated risk of bias (low or low-moderate), and contained overall low heterogeneity (I^2 = 34%). The estimated overall incidence of these 5 studies was 5.17% (95% confidence interval [CI], 3.29-7.04) (Table 6).

Discussion

In this systematic review of 19 studies with 14,898 patients, the incidence of delayed HGAVB after TAVI ranged from 1.7% to 14.6%. There was significant variation among the study methodologies, which prohibited a meta-analysis and calculation of pooled incidence. However, a subanalysis of 5 select studies, with a similar definition of delayed HGAVB, yielded an estimated incidence of 5.17%. The major points of difference among the studies were their inclusion criteria, definitions of delayed HGAVB, follow-up periods, and methods of measuring HGAVB. Overall, more rigourously measured prospective data are required to better estimate the true incidence of this phenomenon.

A persistent confounder in all studies investigating AV block after TAVI is pre-existing subclinical conduction disease. Because of the proximity of the AV node to the aortic valve, calcium deposits often extend into the conduction system in patients with degenerative aortic stenosis, resulting in subclinical conduction disease even before their TAVI. It has been shown that by monitoring patients in the 24 hours before their TAVI, subclinical bradyarrhythmia was found in up to 6%.[33] Furthermore, the mean age of patients included in this review was 81.7 years, and advanced age—along with comorbidities such as diabetes, hypertension, and heart failure—are associated with left bundle branch block (LBBB) and bradyarrhythmia, irrespective of TAVI.[34–36]

The differing definitions of delayed HGAVB likely stem from the lack of consensus definition. Studies were included based on the self-labelled outcome of "delayed" or "late" HGAVB; however, the defined time period post-TAVI varied from as early as 2 hours postprocedure up to 30 days postprocedure. Studies that defined delayed HGAVB as temporally later than others, such as Biancari (2021), Fischer (2018), and Lee (2021), may have missed a significant proportion of patients. In the absence of a universally accepted definition of delayed HGAVB, it is important to consider what the correct or appropriate cut off may be.

From a patient-safety perspective, the highest risk of adverse outcomes from HGAVB is following hospital discharge, and thus this is perhaps the most practical definition of delayed HGAVB. Although this was incorporated as a definition in 5 studies, it is difficult to standardize time to discharge, as practices vary based on patients, operators, and institutions. Perhaps this is why 48 hours following TAVI was the most commonly used definition (n = 6). Considering that most TAVI patients are able to be discharged in the first 48 hours,[37] this may be the most appropriate definition. Creating a formalized definition can allow future studies—and larger national registries—to report this outcome homogeneously.

The method used to detect delayed HGAVB also varied among the literature, which also likely affected their results. The most accurate, or "gold-standard," measurement is via a continuous monitoring technique, such as an implantable loop recorder (ILR) or ambulatory electrocardiographic monitoring (AEM). However, this was only seen in 7 (33%) of the studies.

The remainder 14 studies used either periodic ECGs at designated time points, clinical symptoms, or treating physician-mandated pacemaker implantation based on these 2 previous features. These cross-sectional methods may miss HGAVB episodes that occurred transiently or remained subclinical, likely underestimating the true incidence. Similarly, post-TAVI pacemaker dependency has also been considered as a marker of persistent conduction disease; however, this measurement also appears flawed, as it fails to consider paroxysmal AV block.

Limitations

In studies that used permanent pacemaker implantation as the defined time point for delayed HGAVB, it must be considered that the threshold often varies across centres, which is an important limitation of this study. For example, in centres in which permanent pacemakers may be implanted early because of high-risk features alone, there may be a potential underestimation of the incidence of delayed HGAVB.

Although the highest risk time period for HGAVB is immediately following TAVI, the risk appears to steadily reduce over time, persisting up to 12 to 24 months. Tables 2 to 5 divide the studies by grouping their follow-up periods. The 4 studies with "long" follow-up periods of greater than 1 year (Table 5), were all performed retrospectively with noncontinuous parameters to measure delayed HGAVB. Together, these studies made up 62% of the total participants included in the systematic review. By extending the follow-up period, there is an increased risk of capturing conduction disease unrelated to the initial TAVI.

The use of self-expanding valves is a well-documented risk factor for acute HGAVB. Historically, larger profile valves, such as the self-expanding Evolute (Medtronic, Dublin, Ireland) or Portico (Abbott, Chicago, Illinois, USA) platforms, as well as the now discontinued, mechanically-expanding Lotus valve (Boston Scientific, Marlborough, Massachusetts, USA) have resulted in higher rates of conduction abnormalities as they impart greater radial tension and require deeper implantation into the left ventricular outflow

Table 2. Studies with follow-up period up to 7 to 14 days

#	Author (year)	Country	Study type	Exclusion criteria	Special inclusion criteria	Delayed HGAVB definition	Measuring HGAVB	Maximum follow-up period	Total patients	Age (mean, year)	Male%	STS%	Pre-existing AF%	Pre-existing RBBB%	Valve used	% Trans femoral	% Incidence HGAVB	Bias (ROBINS-I tool)
1	De-Torres Alba (2018)[18]	Germany	Retro	Previous PPM, ViV	n/a	$\geq$ 48 hours	AEM	7 days	606	81.6	44.4	n/a	n/a	6.1	BE (100%)	94.4%	2.8%	Moderate
2	Muntane-Carol (2021)[19]	Canada, Spain	Pros-pective	Previous PPM, ViV	n/a	After discharge	AEM	14 days	459	79.0	54.7	3.6	27.5	9.4	BE (85.6%), SE (14.2%), ME (0.2%)	88.7%	4.6%	Low

AEM, ambulatory electrocardiographic monitoring; AF, atrial fibrillation; BE, balloon expandable; HGAVB, high-grade atrioventricular block; ME, mechanically expandable; PPM, permanent pacemaker; RBBB, right bundle branch block; ROBINS-I, **R**isk **o**f **B**ias **i**n **N**on-randomised **S**tudies - of **I**nterventions; SE, self-expandable; STS, Society of Thoracic Surgeons; ViV, valve-in-valve.

Table 3. Studies with follow-up period up to 30 to 90 days

#	Author (year)	Country	Study type	Exclusion criteria	Special inclusion criteria	Delayed HGAVB definition	Measuring HGAVB	Maximum follow-up period	Total patients	Age (mean, year)	Male%	STS%	Pre-existing AF%	Pre-existing RBBB%	Valve used	% Trans femoral	% Incidence HGAVB	Bias (ROBINS-I tool)
3	El-Sabawi (2021)[20]	USA	Retro	Previous PPM, ViV	n/a	$\geq$ 24 hours	Daily ECG until discharge, then periodic ECG guided by clinical features	30 days	953	81.1	56.1	7.1	37.5	12.5	BE (85.4%), SE (14.6%)	82.2%	3.5%	Moderate
4	Kagase (2021)[21]	Japan	Retro	Previous PPM, ViV	n/a	$\geq$ 24 hours and Complete (3rd degree) AV block only	Periodic ECG	30 days	696	85.4	33.5	7.9	19.7	12.7	BE (100%)	n/a	2.3%	Serious
5	Ream (2019)[11]	USA	Prosp	Previous PPM, ViV	n/a	$\geq$ 48 hours	AEM	30 days	148	78.0	54.1	n/a	29.7	17.3	BE (75.7%), SE (24.3%)	n/a	8.1%	Low-moderate
6	Tarakji (2022)[22]	USA	Prosp	Previous PPM, ViV	n/a	PPM insertion after discharge	AEM	90 days	96	80.3	71.9	n/a	17.7	17.9	BE (94.8%), SE (5.2%)	n/a	3.1%	Low-moderate
7	Tian (2019)[23]	USA	Prosp	Previous PPM, ViV	n/a	After discharge	AEM	30 days	197	81.0	61.9	6.4	37.6	17.3	BE (93.4%), SE (6.6%)	n/a	4.6%	Low-moderate
8	Toggweiler (2016)[24]	Switzerland	Prosp	Previous PPM, ViV	n/a	After first post procedure ECG	AEM 72 hours, periodic ECG thereafter	30 days	1064	82.0	47.7	6.2	22.0	5.0	BE (52.3%), SE (47.7%)	92.2%	6.7%	Moderate

AEM, ambulatory electrocardiographic monitoring; AV, atrioventricular; BE, balloon-expandable; ECG, electrocardiogram; HGAVB, high-grade AV block; PPM, permanent pacemaker; RBBB, right bundle branch block; ROBINS-I, **R**isk **o**f **B**ias **i**n **N**on-randomised **S**tudies - of **I**nterventions; SE, self-expandable; STS, Society of Thoracic Surgeons; ViV, valve-in-valve.

Table 4. Studies with follow-up period of 1 year

#	Author (year)	Country	Study type	Exclusion criteria	Special inclusion criteria	Delayed HGAVB definition	Measuring HGAVB	Maximum follow-up period	Total patients	Age (mean, year)	Male%	STS%	Pre-existing AF%	Pre-existing RBBB%	Valve used	% Trans femoral	% Incidence HGAVB	Bias (ROBINS-I tool)
9	Chorianopoulos (2012)[25]	Germany	Retro	Previous PPM, ViV	n/a	≥ 48 hours	Periodic ECG, clinical decision for PPM	1 year	130	81.3	41.5	n/a	n/a	13.8	SE (100%)	100.0%	7.7%	Moderate
10	Khan (2022)[26]	USA	Retro	Previous PPM, ViV	n/a	≥ 7 days	Clinical decision for PPM	1 year	285	83.9	47.4	n/a	23.5	7.5	BE (79.6%), SE (20.4%)	89.5%	7.4%	Moderate
11	Lee (2021)[27]	Japan	Retro	Previous PPM, ViV	n/a	≥ 1 month	AEM until discharge, periodic ECG thereafter	1 year	246	85.0	34.6	6.4	22.0	14.0	BE (23.2%), SE (70.3%)	n/a	4.1%	Moderate
12	Mangieri (2018)[13]	Italy	Retro	Previous PPM, ViV, acute HGAVB < 48 hours	n/a	≥ 48 hours	Periodic ECG and clinical decision for PPM	1 year	611	84.4	43.7	6.9	31.6	6.1	BE (51.7%), SE (42.1%), ME (4.6%)	100.0%	8.8%	Moderate
13	Reiter (2021)[28]	Austria	Pros-pective	Previous PPM, ViV, permanent AF, acute HGAVB < 48 hours	n/a	≥ 48 hours and complete (third degree) AV block only	ILR	1 year	59	80.3	39.0	n/a	n/a	6.8	SE (100%)	100.0%	11.9%	Low to Moderate
14	Rodes-Cabau (2018)[29]	Spain	Pros-pective	Previou PPM, ViV	Persistent LBBB post TAVI day 3	≥ 72 hrs	ILR	1 year	103	80.0	42.7	5.0	26.2	0	BE (48.5%), SE (51.5%)	86.4%	14.6%	Serious
15	Tovia-Brodie (2017)[20]	Israel	Pros-pective	Previous PPM, ViV	Persistent LBBB post TAVI day 2	PPM insertion after discharge	Clinical decision for PPM	1 year	81	82.0	42.0	3.3	11.1	0	BE (32.1%), SE (67.9%)	n/a	3.7%	Serious

AEM, ambulatory electrocardiographic monitoring; AF, atrial fibrillation; AV, atrioventricular; BE, balloon-expandable; ECG, electrocardiogram; HGAVB, high-grade AV block; ILR, implantable loop recorder; LBBB, left bundle branch block; ME, mechanically expandable; PPM, permanent pacemaker; RBBB, right bundle branch block; ROBINS-I, **R**isk **o**f **B**ias **i**n **N**on-randomised **S**tudies - of **I**nterventions; SE, self-expandable; STS, Society of Thoracic Surgeons; TAVI, transcatheter aortic valve implantation; ViV, valve-in-valve.

tract.[38,39] A possible exception is the AcurateNeo (Boston Scientific) self-expanding valve, is engineered to impart more balanced symmetrical radial force, which may explain the comparatively lower pacemaker rates.[40]

Different inclusion criteria among the studies are also an influential determinant of delayed HGAVB. Four of the studies selectively included patients with pre-existing bundle branch block, a well-documented risk factor for post-TAVI acute pacemaker implantation. Rodes-Cabau (2018), Tovie-Brodie (2017), and Fischer (2018) only included patients with pre-existing or new-persistent LBBB post-TAVI. LBBB is common post-TAVI, occurring in up to 40% of patients[41] and independently results in a 3-fold increased risk of PPM post-TAVI.[42]

Similarly, RBBB has a prevalence of 10% to 14%[14,43,44] in patients before TAVI and correlates with up to a 5-fold greater risk of pacemaker implantation.[14,44] Among the included studies, the prevalence of pre-existing RBBB ranged from 5.0% to 17.9%, and thus this variability may also account for differing outcomes.

Clinical implications of delayed HGAVB

Approximately 9% of all cardiac death up to 2 years post-TAVI is from unexplained sudden cardiac death, which has retrospectively been attributed to bradycardiac arrest secondary to delayed HGAVB in the absence of other obvious causes.[45] Although delayed HGAVB can be prevented and treated with timely pacemaker implantation, the threshold varies across centres, and although not in the scope of this review, remains a key decision after TAVI.

Although pacemaker implantation remains common after TAVI, it may cause cardiac dyssynchrony and progression of tricuspid regurgitation. There are conflicting results in 2 major studies evaluating the long-term outcomes of patients requiring new pacemakers after TAVI[46,47]; however, a recent meta-analysis suggested higher all-cause mortality and heart failure-related rehospitalization.[47] Regardless, with a paradigm shift toward TAVI in younger patients and those at low surgical risk, methods to prevent conduction disease are paramount. In addition, conduction-system pacing may result in shorter QRS, better ventricular synchrony, and improved hemodynamic results compared with right ventricular pacing, and may help to improve the prognosis of post-TAVI conduction disease.[48]

Therefore, the absence of conduction abnormalities have been a key criteria in classifying patients as "low discharge risk" in 2 large North American studies,[16,49] which validated early discharge following TAVI. The presence of pre-existing RBBB, persistent new LBBB, along with the use of self-expanding valves have generally been viewed as much higher risk for early discharge because of the risk of impending HGAVB. For this reason, perhaps such high-risk patients should be monitored in hospital for at least 48 hours post-TAVI, and clinicians may even consider longer-term postdischarge ambulatory rhythm monitoring and earlier follow-up. The current European Society of Cardiology (ESC) pacing guidelines recommend (Class IIA) permanent pacing in patients with pre-existing RBBB with any new conduction disease noted post TAVI. Similarly, it is recommended that in patients with new LBBB above 150 ms, or PR intervals above 240 ms, the use of continuous rhythm monitoring, or the

Table 5. Studies with variable and longer follow-up periods of over 1 year

#	Author (year)	Country	Study type	Exclusion criteria	Special inclusion criteria	Delayed HGAVB definition	Measuring HGAVB	Maximum follow-up period	Total patients	Age (mean, year)	Male%	STS%	Pre-existing AF%	Pre-existing RBBB%	Valve used	% Transfemoral	% Incidence HGAVB	Bias (ROBINS-I tool)
16	Biancari (2021)[12]	Finland	Retro	Previous PPM, ViV	n/a	PPM insertion ≥ 30 days	Clinical decision for PPM	5 years	1897	81.2	44.2	4.5	40.9	n/a	BE (68.5%), SE (20.7%), ME (10.8%)	n/a	6.2%	Moderate
17	Elchinova (2021)[30]	Switzerland	Retro	Previous PPM, ViV, all patients with acute HGAVB	n/a	PPM insertion after discharge	Periodic ECG and clinical decision for PPM	Variable, median 1095 days	1059	81.7	47.2	5.4	33.9	6.3	BE (52.3%), SE (40.8%), ME (6.7%)	89.1%	4.3%	Moderate
18	Fischer (2018)[31]	Canada	Retro	Previous PPM, ViV	LBBB on baseline ECG	PPM insertion ≥ 30 days	Periodic ECG and clinical decision for PPM	Variable, median 22 months	3404	81.0	47.3	5.5	27.8	0	BE (53.9%), SE (45.8%)	81.2%	1.7%	Serious
19	Kooistra (2020)[32]	The Netherlands	Retro	Previous PPM, ViV	n/a	PPM insertion ≥ 48 hours	Telemetry (48 hours), periodic ECG guided by clinical decision to implant PPM	5 years	2804	82.0	44.5	n/a	34.6	11.0	BE (55.8%), SE (36.7%), ME (7.2%)	75.7%	2.2%	Moderate

AF, atrial fibrillation; BE, balloon-expandable; ECG, electrocardiogram; HGAVB, high-grade atrioventricular block; LBBB, left bundle branch block; ME, mechanically expandable; PPM, permanent pacemaker; RBBB, right bundle branch block; ROBINS-I, **R**isk **o**f **B**ias **i**n **N**on-randomised **S**tudies - of **I**nterventions; SE, self-expandable; STS, Society of Thoracic Surgeons; ViV, valve-in-valve.

Table 6. Subanalysis of selected prospective studies with continuous monitoring methods and lowest assessment of bias

Author (year)	Study type	Delayed HGAVB definition	Method of measuring HGAVB	Follow-up	Patients	Valve type	Total delayed HGAVB events	% incidence of delayed HGAVB	Bias (ROBINS-I tool)
Muntane-Carol (2021)[19]	Prospective	After discharge	AEM	14 days	459	BE (85.6%), SE (14.2%), ME (0.2%)	21	4.6%	Low
Ream (2019)[11]	Prospective	≥ 48 hours	AEM	30 days	148	BE (75.7%), SE (24.3%)	12	8.1%	Low to moderate
Reiter (2021)[28]	Prospective	≥ 48 hours and complete (third degree) AV block only	ILR	1 year	59	SE (100%)	7	11.9%	Low to moderate
Tarakji (2022)[22]	Prospective	PPM insertion after discharge	AEM	3 months	96	BE (94.8%), SE (5.2%)	3	3.1%	Low to moderate
Tian (2019)[23]	Prospective	After discharge	AEM	30 days	197	BE (93.4%), SE (6.6%)	9	4.6%	Low to moderate

n = 959; incidence (%) of delayed HGAVB (IV, random, 95% confidence interval) = 5.17 (3.29-7.04); Heterogeneity: I^2 = 34%.

AEM, ambulatory electrocardiographic monitoring; AV, atrioventricular; BE, balloon expandable; HGAVB, high-grade AV block; ILR, implantable loop recorder; IV, instrumental variable; ME, mechanically expandable; PPM, permanent pacemaker; ROBINS-I, **R**isk **o**f **B**ias **i**n **N**on-randomised **S**tudies - of **I**nterventions; SE, self-expandable.

measurement of a HV interval over 70 ms, can aid in decision making.[4]

Because of the difficulty in predicting delayed HGAVB, various studies have evaluated the use of EPS to risk stratify patients further. It may serve a role in intermediate-risk patients, such as those with a new persistent LBBB or RBBB or PR prolongation over 40 ms after TAVI. One group demonstrated that an absolute increase in HV interval pre- and post-TAVI, or an absolute HV interval > 65 ms post-TAVI may predict subsequent AV block.[10] The use of the HV interval post-TAVI to predict delayed HGAVB has been subsequently validated by future studies that have used cutoffs between 55 ms and 70 ms.[50,51] Rapid atrial pacing provoked second-degree AV block (AV Wenkebach cycle length) may also have utility, with Krishnaswamy et al.[9] demonstrating that patients who did not develop pacing-induced AV Wenkebach up to 120 beats per minute had extremely low likelihood of requiring permanent pacemaker implantation. Other risk factors for acute high-grade AV block include the use of deeply implanted valves, along with patient factors such as aortic valve calcification and short membranous septum length.[20]

A current actively recruiting Australian study, Prospective Observational Study on the Accuracy of Predictors of High-Grade Atrioventricular **Conduct**ion Block After **T**rans-catheter **A**ortic **V**alve **I**mplantation (CONDUCT-TAVI [ACTRN12621001700820]), is aiming to provide further clarity on clinical predictors of delayed HGAVB by studying conduction disturbances in transfemoral TAVI patients with implantable loop recorders for 2 years. This study will prospectively analyze the frequency and timing of delayed HGAVB post-TAVI as well as evaluate 12-lead ECG, computed tomography, and EPS-based risk factors.

Conclusions

Despite the heterogeneity within currently published literature, it is evident that delayed HGAVB is not infrequent after TAVI, with important clinical ramifications. With newer-generation valves, greater experience, and higher implant depths, pacemaker rates are steadily reducing.

Predicting delayed HGAVB remains difficult, and further study into novel methods, such as using targeted pre- and post-TAVI EPS measuring the membranous septum length and quantifying cusp calcification, may assist us moving forward. In the future, a consensus definition of delayed HGAVB, along with well-powered prospective studies that incorporate continuous rhythm monitoring for extended periods are most likely to advance our understanding.

Ethics Statement

The research reported has adhered to relevant ethical guidelines.

Patient Consent

The authors confirm that patient consent is not applicable to this article, as it is a systematic review of published literature.

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Disclosures

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