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Review

Current Opinions on New-Onset Left Bundle Branch Block after Transcatheter Aortic Valve Replacement and the Search for Physiological Pacing

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Abstract

Transcatheter aortic valve replacement possesses a high validity for patients with aortic stenosis who are considered high risk for aortic valve replacement surgery, nowadays it is also considered for patients with intermediate risk or even lower risk in certain situations. The incidence of new conduction abnormalities remains to be a tough problem, in particular, left bundle branch block. New-onset left bundle branch block is a major concern despite improvements in valve technology, and it may affect postoperative prognosis. Understanding the anatomical relationship between the conduction system and the aortic root, clarify factors related to the procedure, devices, and patients, might help to reduce the conduction abnormalities. Physiological pacing has emerged as a reasonable pacing strategy for patients with cardiac insufficiency post-valve replacement, especially combined with left bundle branch block. The purpose of this review is to summarize the current opinion on the incidence of new-onset left bundle branch block associated with transcatheter aortic valve replacement, to offer insights into its anatomical and procedural causes, clinical consequences, and more importantly, the prospect of applying physiological pacing as a therapeutic method for these patients.

Keywords: transcatheter aortic valve replacement; His-purkinje conduction system pacing; left bundle branch block; desynchrony

1. Introduction

Transcatheter aortic valve replacement (TAVR) has been proved effective and has been becoming a solid therapeutic alternative for high-risk patients with severe aortic stenosis (AS). Nowadays, it is also considered for patients with intermediate risk even lower risk patients in certain situations [1,2]. However, conduction abnormalities remain the major complications of this procedure. Conduction disturbances in this setting mainly include complete atrioventricular block (AVB) and new onset left bundle branch block (LBBB), which partly offset the benefit of this remarkable technology. The mechanism of conduction abnormalities following TAVR may be explained by the close anatomical relationship between the implantation site of the aortic artificial valve and the conduction system, with the incidence varying among different implantation techniques and the morphology of the artificial valve used [3,4]. These complications limit the application of TAVR in patients who are younger or at low-risk for surgical operations [1,5]. The incidence of complete AVB following TAVR is well described and permanent pacemaker implantation (PPI) is recommended as a remedy. However, the reported incidence of new onset LBBB following TAVR has a substantial variation. For new onset LBBB, controversy remains regarding the definition, cause, incidence, and its effect on cardiac function. The optimal strategy for new onset LBBB in this population has not been clearly established yet. Cardiac resynchronization therapy (CRT) has been proven to improve clinical outcomes in patients with left ventricular dyssynchrony. Recently, His bundle pacing (HBP) and left bundle branch pacing (LBBP), also known as His-purkinje conduction system pacing (HPCSP), have been introduced as an alternative modality of physiological pacing to achieve electrical synchrony of the left ventricle [6]. HPCSP can capture His bundle region or left bundle branch directly and make the excitation pass down along the physiological pathway, which is a more physiological pacing mode. Researchers have reported the feasibility and safety of HPCSP. Increasingly more research is focusing on HPCSP in post-TAVR patients, including its effect on cardiac function and mortality of TAVR related new onset LBBB. For the special population of postoperative LBBB in TAVR, further studies are needed to illustrate the pathophysiological basis of postprocedural conduction block, factors influencing its outcome, the optimal timing of pacing therapy, and the impact of physiological pacing techniques on the prognosis of these patients.

2. Pathogenesis, Predictive Factors of New Onset LBBB

The anatomical relationship between the aortic artificial valve and the cardiac conduction system is the basis of

postoperative conduction abnormalities in TAVR. His bundle is close to the aortic valve when it crosses the central fibrous body and reaches the interventricular septal membrane, and the left bundle branch is close to the bottom of the fibrous triangle between the non-coronary sinus valve and the right coronary valve. Direct mechanic injury, including edema, inflammation, and ischemia, may occur during the insertion of the guide wire, balloon dilation, and valve implantation [7–10]. In addition, the following factors may affect the occurrence of LBBB: (a) Baseline features of the patients: such as preexisted conduction abnormalities and aortic valve calcification increase the incidence of conduction block after TAVR [11,12]; (b) Procedural factors, the membranous interventricular septum length and the implantation depth considering the membranous septum length is an important factor regarding the development of LBBB or AVB. The risk of LBBB increased by 15% to 40% for each 1 mm further in depth of valve implantation [13]. Currently, the recommended depth of valve implantation is less than 6 mm; (c) Device-related factors: the novel transmission conduction delay is also affected by the type and size of the prosthesis. The self-expanding valve system such as Medtronic CoreValve will expand further after implantation, exerting a higher radial force on left ventricular outflow tract (LVOT) and resulting in higher risk of conduction block [10,14].

Some of the above factors have been proven to be predictors of new conduction block after TAVR, with the prosthesis implantation depth the most relevant risk factor. Other risk factors including the type of valve implanted, overexpansion of native annulus, the occurrence of right bundle branch block (RBBB) at baseline, preexisting LVOT calcification, preexisting first-degree AVB and prolonged baseline QRS duration, previous coronary bypass and female gender [15–17]. The presence of RBBB at baseline was one of the important predictors. Studies have reported significantly higher rate of PPI in patients with preoperative RBBB. Because most of the study end points were identified as new LBBB after TAVR, patients with baseline LBBB were excluded at enrollment, so there are few studies on the association between baseline LBBB and new block. According to the literature review, Mangieri proposed that ventricular depth of the prosthesis (odds ratio [OR] = 1.37 for each increase of 1 mm) and baseline QRS duration (OR = 1.24 for each increase of 4 ms) could be used as predictors of new onset persistent LBBB. No data existed regarding predictors of transient LBBB [18].

3. Incidence, Variation and Timing of New Onset LBBB after TAVR

The incidence of PPI was lower in surgical aortic valve replacement (3.2%) than in TAVR [5]. Rates of PPI after TAVR range between 3.4% and 25.9% according to the European Society of Cardiology (ESC) guidelines for 2021. New-onset LBBB is the most common conduction block following TAVR, with the incidence of 4%–65% [10,14]. Muntané-Carol G analyzed the incidence of LBBB in different valve systems [19]. Due to improvements in structure and materials, the new generation of valve systems has greatly improved the safety of surgery, but the impact on the conduction system has not been significantly improved. So far, the incidence of LBBB in the new generation of valves reported in the literature is as high as 77% [20]. The great variation of incidence is most likely attributed to differences in inclusion electrocardiogram criteria and valve types. Studies reported that incidence of new onset LBBB following the CoreValve prosthesis implantation was higher than the Edwards SAPIEN prosthesis [14]. Another important reason is whether or not the strict diagnostic criteria of LBBB have been adapted in these studies was not specifically addressed. However, no study up until now has evaluated the incidence of LBBB post-TAVR with strict criteria and therefore it is highly possible that from where the bias was derived. Alqarawi *et al*. [21] described the Electrocardiograph (ECG) characteristics of new onset LBBB following TAVR and proposed a new ECG definition of LBBB which consists of two novel criteria: notching/slurring of the R wave in at least one lateral lead and an R wave $\leq$20 ms in V1. A recent Expert Panel suggested that patients with unresolved new onset LBBB on day 2 post-TAVR, which defined as QRS duration $>$150 ms or PR interval $>$240 ms, could be considered for PPI.

Approximately 90% of TAVR related new onset LBBB occurs within 24 h and may be associated with mechanical damage caused by the guide system [22]. The damage may be temporary, some new onset LBBB can recover within hours or days. About 55% of new onset LBBB will persist at hospital discharge. However, nearly 60% of them will persist after discharge. Late-onset LBBB is very rare [23].

4. Clinical Consequences of New Onset LBBB

High degree of AVB after TAVR usually predicts a poor prognosis, resulting in deterioration of cardiac function and a high mortality. However, patients with new onset LBBB often have insidious clinical symptoms and weak intervention indications, while existing prognostic studies mainly include these patients, so the impact of TAVR related new onset LBBB on cardiac function and mortality is also controversial [24].

4.1 Impact of TAVR Related New Onset LBBB on LVEF

Most studies so far have shown a limited left ventricular ejection fraction (LVEF) improvement after TAVR in patients with new onset LBBB [25–28]. Nazif *et al*. [25] described that the LVEF did not elevate significantly post-TAVR in patients with new onset LBBB and remained lower than those patients without LBBB at 1-year follow-up. In Carabba's study, results showed that LVEF increased in the

initial stage after TAVR, while LVEF remained constant in patients without conduction disorder [26]. The results showed that LBBB-related dyssynchrony may offset the improvement of heart function which benefit from TAVR procedure. But Chamandi's team came to a different conclusion that new onset LBBB increased the risk of PPI but negatively impacted left ventricular function in 2019 [29]. It was a multi-center study to evaluate the long-term (3 years) outcomes in new onset LBBB patients. More than 1000 patients without preexisting LBBB were enrolled in the study, of which 20.1% had persistent new onset LBBB. The study included different types of valves (48% balloon and 52% self-expandable). During the follow-up period of 3 years, LVEF improved in non-LBBB patients (Δ 1.9 $\pm$ 0.6%) while decreased in LBBB patients (Δ 1.4 $\pm$ 0.9%, $p < 0.001$). Furthermore, patients with new onset LBBB have higher incidence of PPI at follow-up (15.5% vs 5.4%, $p = 0.002$). In addition to above effects on LVEF, there was no difference between groups regarding rehospitalization for heart failure (new onset LBBB vs control group: 19.8% vs 15.6%, $p = 0.18$).

4.2 Impact of TAVR Related New Onset LBBB on Mortality

The potential impact of TAVR related new onset LBBB on mortality has proved inconclusive so far. Houthuizen *et al.* [30] found that 34% of patients developed new onset LBBB upon discharge, among them, patients with LBBB had an increased mortality and morbidity ($p < 0.01$), while Testa *et al.* [31] found that 27% of patients developed new onset LBBB upon discharge, mortality and morbidity remained statistically insignificant at 1-year follow-up. However, the echocardiographic data of Testa's study were only available in 50% of the patients. Two studies conducted by Nazif *et al.* [25] and Urena *et al.* [27], with a total of 668 and 1151 patients involved respectively, both concluded that new onset LBBB was unrelated to mortality compared to their counterparts. However, only one type of prostheses was implanted in those studies, and the number of patients developing persistent LBBB was significantly lower [79/668 (12%) and 62/1151 (5%)]. Another subgroup analysis of new onset LBBB after TAVR from the PARTNER II [32] showed that 15.2% in this population developed new onset LBBB. During a 2-year follow-up, the results had already shown that new onset LBBB was significantly related to an increased all-cause mortality (19.3% vs 10.8%, $p = 0.002$). However, the low incidence of LBBB in this study (15.2%) makes it difficult to estimate the outcomes. Recently, Regueiro *et al.* [33] reported the results of a meta-analysis regarding the clinical impact of new onset LBBB post-TAVR, which was negative relationship between new onset LBBB and all-cause mortality (RR: 1.21, $p = 0.07$) combining data from 8 studies. But meanwhile, the same authors came to an exact contrary result when the data was limited to 5 studies that provided data on cardiovascular outcomes (RR: 1.39, $p = 0.03$). Nevertheless, due to the differences of sample size and follow-up period, there is heterogeneity in the evaluation of heart failure and mortality among different studies. Investigate its reason, on the one hand, most of the patients receiving TAVR are elderly patients, who may have many underlying diseases, which might be the main causes of death, while new onset LBBB is not directly life-threatening, on the other hand, new onset LBBB may cause ventricular systolic asynchrony or progress to high-degree AVB, leading to a progressive decline of LVEF and an increase of cardiac mortality. Therefore, the impact of TAVR related LBBB on all-cause mortality and cardiovascular mortality needs to be further demonstrated.

Although the impact of LBBB on cardiac function and mortality are still controversial and the long-term clinical outcomes are unclear, it is believed that LBBB can affect cardiac function due to ventricular dyssynchrony. Greater sample sizes and a longer follow-up period (>5 years) are required to verify the impact of new onset LBBB on clinical outcomes.

5. Pacing Treatment of New Onset LBBB

Based on all the previous studies, current available data do not recommend a prophylactic pacemaker implantation in patients with TAVR related LBBB. However, pacemaker implantation is recommended in presence of complete AVB. American College of Cardiology updated a guideline in 2020 in which a PPI was recommended in high-degree AVB, and AVB patients at high risk of developing to LBBB, which defined as prolongation of QRS or PR interval >20 ms, or QRS duration $\geq$150 ms or PR interval $\geq$240 ms after TAVR. Whereas the guidelines do not recommend PPI in patients with isolated new onset LBBB after TAVR [34].

There are three questions still needed to be answered to provide the appropriate management of the patients with LBBB after TAVR.

5.1 Whether It Is Necessary to Implant a Pacemaker or Even CRT/D in Patients with TAVR-Related LBBB?

Based on the above research, PPI is recommended in complete heart-block patients. However, permanent right ventricular pacing (RVP) may aggravate heart function damage. As we discussed earlier, evidence so far of the impact of PPI after TAVR on mortality is nonetheless conflicting. CRT or CRTD implantation may be appropriate among these patients with reduced LVEF ($\leq$35%) combined with LBBB. But based on what we discussed previously, new onset LBBB may be caused by transient edema and inflammation which may recover over a period of time, thus a prophylactic CRT/D is not mandatory [35]. Unfortunately, few factor has been currently identified to predict the incidence of LBBB after TAVR. According to the guidelines, pacemaker implantation in patients identified as of high risk is currently the best option. At the same time,

we need more data on whether CRT is beneficial, and we need to explore more cost-effective pacing methods. Studies evaluating the influences and the clinical outcomes of PPI after TAVR so far are listed in the table (Table 1, Ref. [9,32,36–49]).

5.2 At What Time Should These Patients Be Implanted?

The latest recommendations of the 2021 ESC Guidelines provide specific recommendations as to the management of persistent LBBB post TAVR [50]. According to the guideline, there are few patients who indeed meet the pacing indications, such as complete AVB. Besides, part of the conduction block will resume as the edema and inflammation gradually decrease. Thus, "delayed implantation" strategy was recommended, and unnecessary pacing therapy can be avoided. For a more accurate assessment of pacing indications, electrophysiological studies (EP studies) and long-term monitoring of ECG may be considered. During observation and follow-up period, once dynamic progression of conduction disorders (new onset BBB with dynamic prolongation of QRS and/or PR) have been identified, it is considered to be high-risk group, a prolonged monitoring period in hospital of up to 5 days should be recommended. This recommendation is consistent with the 2020 American College of Cardiology (ACC) guidelines.

5.3 What Type of Pacing Method Should Be Performed?

Traditional RVP can prevent some cases of AVB, but it may weaken the improvement of cardiac function brought by TAVR and lead to ventricular systolic asynchrony. RVP does not provide benefit in patients with LBBB after TAVR. Pacing method should be selected as prudent as possible. LBBB related LV dysfunction, biventricular pacing (Traditional CRTP/D [Cardiac resynchronization therapy/Cardiac resynchronization therapy-cardioverter-defibrillator]) may represent an interesting option in this setting. Furthermore, resynchronization therapy should also be considered in patients with high degree AVB, high percentage (predictable >40%) of ventricular pacing, and reduced LVEF (<50%) and with sufficient life expectancy. Nowadays, researches have shown the benefit of biventricular pacing in patients with low LVEF and persistent LBBB after TAVR. In addition to the improvement of LVEF, biventricular pacing seems to be effective in decreasing hospitalizations in heart failure patients. However, most patients undergoing TAVR implantation have preserved LVEF. There has been no previous study on the efficacy of CRT in this population. Therefore, patients with LBBB and cardiac dysfunction are the main target population for biventricular pacing to correct electrical asynchrony. CRTP/D can be systematically implanted in such patients to prevent heart failure promoted by RVP or LBBB electrical activation. But this population did not truly reveal the benefit of CRTP/D in LBBB related heart failure after TAVR. More importantly, TAVR procedure is expensive enough in most countries and regions, CRTP/D will further increase the financial burden of patients.

Nowadays, HPCSP is booming around the world, the anatomy of the conduction system and the most frequently used lead location site of HPCSP are shown in Fig. 1. It can directly capture His bundle or left bundle branch, which is a more physiological pacing mode [51–53]. As the advent of new tools and technologies greatly facilitated HPCSP implantation, a growing number of researchers are coming to a consensus that HPCSP is a more physiological approach than other existing pacing model, especially in patients with LBBB in combination with heart failure or with high percentage of expected pacing needs [54–57]. It is now generally accepted that HPCSP includes two pacing modalities, HBP and LBBP, the main difference between them is the anatomical location of the pacing lead [58,59]. Nonetheless, both of them can capture the conduction system. In the setting of patients with AVB, HBP and LBBP were both successful in achieving stable and low capture thresholds. Although thresholds of HBP upon implantation were higher compared to LBBP (1.2 ± 0.7 V vs 0.6 ± 0.3 V; $p < 0.001$), both remained stable during follow-up [53].

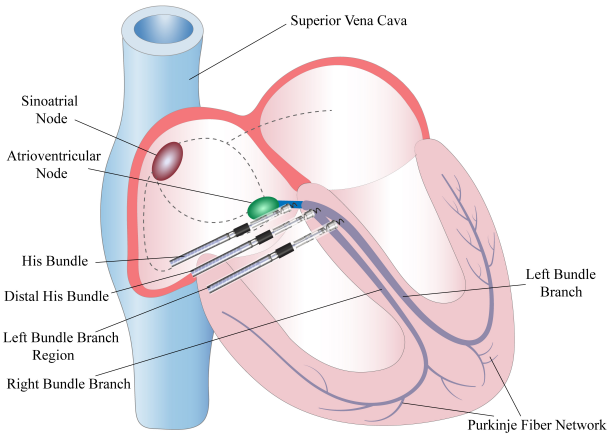

Fig. 1. Diagram of His-purkinje conduction system pacing. Anatomical localization of HPCSP leads. For LBBP, the pacing lead is delivered transvenously into the right ventricle through C315 His-sheath and screwed into the IVS (LBB region). While HBP lead is implanted at His-bundle or distal His bundle (His bundle area). HPCSP, His-purkinje conduction system pacing; LBBP, left bundle branch pacing; IVS, interventricular septum; LBB, left bundle branch.

Table 1. Studies for evaluating the clinical impact of PPI after TAVR.

Reference	Study Design	Inclusion Period	Region	Vavle Type (%)	Sample Size	Age (y)	Male (%)	PPI Implantation Criteria	PPI at Discharge (%)
D'Ancona *et al*. [36]	Prospective	2008–2011	Germany	ESV (100)	322	81 ± 7	36	High-degree AVB or symptomatic bradycardia	5.9
De Carlo *et al*. [37]	Prospective	2007–2010	Italy	MCRS (100)	275	82 ± 6	47	ESC 2007 Guidelines	24.0
Buellesfeld *et al*. [38]	Prospective	2007–2010	Germany, Switzerland	ESV (10) MCRS (90)	305	83 ± 6	43	High-degree AVB, new left BBB with PR segment ≥300 ms, or atrial fibrillation with inadequate escape rhythm	32.1
Houthuizen *et al*. [9]	Prospective	2005–2010	Netherlands	ESV (43) MCRS (57)	797	N/A	N/A	N/A	14.8
Pereira *et al*. [39]	Retrospective	2007–2011	Portugal	MCRS (100)	58	79 ± 6	46	ESC 2007 Guidelines	33.0
Biner *et al*. [40]	Prospective	2014	Israel	ESV (13) MCRS (87)	230	83 ± 5	38	Pre-TAVR right BBB, post-TAVR high-degree AVB, alternating BBB, or new left-BBB with PR segment ≥280 ms	25.2
Urena *et al*. [41]	Prospective	2005–2013	International	ESV (55) MCRS (45)	1556	80 ± 8	47	ACC/AHA/HRS 2008 Guidelines	15.4
Schymik *et al*. [42]	Retrospective	2008–2012	Germany	ESV (81) MCRS (19)	634	82 ± 4	38	ESC 2013 Guidelines	10.8
Mouillet *et al*. [43]	Prospective	2010–2011	France	MCRS (100)	833	82 ± 7	59	N/A	30.2
Nazif *et al*. [32]	Retrospective	2015	International	ESV (100)	1937	84 ± 7	47	High-degree AVB, sick sinus syndrome, and symptomatic bradycardia	8.8
Kawaguchi *et al*. [44]	Prospective	2010–2012	France	ESV (34) MCRS (66)	160	83 ± 7	55	N/A	17.5
Rampat *et al*. [45]	Retrospective	2013–2015	UK	LOTUS valve (100)	228	81.2 ± 7.7	51	N/A	32
Cresse *et al*. [46]	Retrospective	2008–2017	USA	ESV (76) MCRS (24)	386	83 ± 7.7	53	Symptomatic bradycardia progressing to CHB	6.7
Jilaihawi *et al*. [47]	Prospecive	2016–2018	USA	Evolut R, Evolut Pro, and Evolut 34 XL	248	83.2 ± 6.9	57	Complete heart block, post-TAVR high-degree AVB, left bundle branch block (LBBB)	9.7
Monteiro *et al*. [48]	Retrospective	2008–2015	Brazil	MCRS (74) ESV (26)	670	81.4 ± 6.5	48	The indication for PPI was based on the institutional protocols of each participating hospital.	20.1
Kawsara *et al*. [49]	Retrospective	2012–2017	USA	N/A	77,405	80.3	52	The indication for PPI was based on the institutional protocols of each participating hospital.	8.7 (2012) 13.2 (2015) 9.6 (2017)

ESV, Edwards Sapien valve; MCRS, Medtronic CoreValve revalving system; AVB, Atrial ventricular block; N/A, not available; PPI, permanent pacemaker implantation; TAVR, transcatheter aortic valve replacement; ESC, European society of cardiology; BBB , bundle branch block; ACC/AHA/HRS, American College of Cardiology/American Heart Association/Heart Rhythm Society; CHB, complete heart block.

Table 2. Studies for evaluating HPCSP after TAVR.

Reference	Study Types	Pacing Modality	Year	Region	Sample Size	Main Point
Sen J *et al*. [63]	Case Report	HBP	2018	Australia	1	First report of new LBBB in the setting of TAVR corrected by pacing at the His bundle.
De Pooter *et al*. [64]	Prospective study	HBP	2018–2019	International	16	Permanent HBP is feasible in the majority of patients with TAVR requiring a permanent pacemaker with the potential to correct a TAVR-induced LBBB with acceptable pacing thresholds.
Jincun G *et al*. [66]	Retrospective study	LBBP	2018–2019	China	20 (6)	LBBP was safe and feasible in patients with prosthetic valve (PV) implantation.
Patel S *et al*. [67]	Case Report	HBP	2020	USA	1	HBP might be a feasible option in a portion of complete heart block post-TAVR, and the valve, itself a fluoroscopic marker, can serve as an asset for His localization.
Vijayaraman P *et al*. [68]	Prospective study	HPCSP	2020	USA	65	HPCSP is feasible in the majority of patients requiring pacemakers post-TAVR. Success rates of HBP were lower in patients with Core Valves compared to Sapien valves. LBBAP was associated with higher success rates and lower pacing thresholds compared with HBP.
Zhang *et al*. [69]	Case Report	LBBP	2020	China	1	Rapid reversal of heart failure by correcting left bundle branch block induced by TAVR.
Cano Ó *et al*. [70]	EDITORIAL	HPCSP	2020	USA	N/A	The advent of LBBP provide another option for physiologic pacing in post-TAVR patients with failed HBP attempts. His-Purkinje conduction system pacing has the potential to become a standard pacing modality for these patients.

5.3.1 HBP

In 2000, Deshmukh [60] first described permanent HBP combined with AV node ablation in patients with AF and LV systolic dysfunction. From an electrical and hemodynamic point of view, his bundle is the ideal site for physiological pacing. Current evidence shows that HBP is safe and effective and feasible in practice in these settings. Researchers using HBP, instead of RV pacing, biventricular pacing, or His-optimized CRT (HOT-CRT), which achieves a synergistic effect to improve synchrony [50]. With the accumulation of safety and efficacy data, HBP is likely to play a growing role in pacing therapy in the future. However, the technical challenge and problem with elevated long-term thresholds in LBBB patients had been obstacles to application in routine clinical practice.

5.3.2 LBBP

Left bundle branch pacing (LBBP) was first reported by Huang in 2017, according to Huang, LBBP avoids further deterioration of the proximal His bundle or AV node due to delayed progression of AV conduction, and also provides more space for AV nodal ablation [61]. LBBP generates a narrow paced QRS duration and fast LV activation time as HBP and the site of LBBP lead bypasses the vulnerable region which was more distal and deeper, makes it easier to fix. As an alternative physiological pacing therapy for HBP, LBBP has a benefit that avoids many of the limitations of HBP or RV pacing [62]. Compared to HBP, LBBP has a lower and more stable capture threshold because the pacing site is located in the ventricular septal tissue, improving long-term safety and the device longevity. Besides, LBBP technique is relatively simpler than HBP which makes it easier to learn and promotion, because of wide spread of fascicules of left bundle branch in the subendocardium of the left side of the interventricular septum (IVS).

5.3.3 HPCSP in TAVR Related LBBB

For the special population of new onset LBBB after TAVR, according to etiological mechanism, the electrical dyssynchrony is caused by direct conduction injury. If irreversible mechanical dyssynchrony eventually occurs, it may be an ideal indication for HPCSP [63–67]. In 2018, Sen J *et al*. [63] reported the first case of LBBB in the setting of TAVR corrected by pacing at the His bundle. Then, De Pooter reported the inspiring results of a prospective, multi-center study regarding the feasibility and safety of HBP to correct a TAVR-induced LBBB, though the study included only 16 patients [64]. In the post-TAVR LBBB setting, the correction of LBBB by HBP usually requires a higher pacing output, which depends on the relative location of HBP lead and TAVR valve. The damage caused by mechanical injury during valve replacement might be beyond His bundle or even distal, HBP may or may not correct LBBB. Therefore, in addition to the threshold problem, HBP also has the problem of uncertain success rate [55]. Sen *et al*. [63] reported a case of TAVR-induced new onset LBBB failed to be corrected by HBP, meanwhile De Pooter *et al*. [64] reported a correction rate of 69% (11 of 16) with HBP in patients with post-TAVR LBBB. However, higher pacing output negatively impacts on the therapeutic effectiveness and device longevity. Hence, LBBP could offer an alternative in post-TAVR patients with unsuccessful HBP. Vijayaraman *et al*. [68] reported the feasibility and success rates of HPCSP post-TAVR. In the study, 65 consecutive patients requiring pacemakers after TAVR was attempted at 5 centers, which included 18 LBBB patients. The success rate of LBBP was significantly higher than HBP (93% vs 63%), while the success rate of HBP distinctly varied among different valve types (69% in the Edward Sapien valve compared with 44% in patients with CoreValve; $p < 0.05$). Zhang *et al*. [69] reported a LBBP case with heart failure by correcting TAVR induced LBBB with a stable capture and correction threshold, which failed to be corrected by HBP during the procedure. This is because LBBP is delivered by bypassing the pathologic region. In addition, Vijayaraman also confirmed the effectiveness and safety of HPCSP in TAVR-related conduction block, with significantly shortened QRS duration and stable pacing threshold during follow-up. Studies to evaluate HPCSP after TAVR are listed as follows (Table 2, Ref. [63,64,66–70]). Although the sample size of the above studies is small, the results are basically consistent. Therefore, different modalities can be selected according to the type, size, and implantation depth of TAVR valve. Fig. 2 summarizes the mechanism of physiological pacing after TAVR induced new onset LBBB by two kinds of commercially available prosthetic valves. Fig. 3 illustrates the electrocardiogram and imaging characteristics of HPCSP post-TAVR.

Up to now, there is no guidelines particularly for pacemaker or CRTP/D implantation in TAVR induced new onset LBBB patients with cardiac insufficiency. Ventricular electrical activity dyssynchrony caused by LBBB can counteract the positive effect of TAVR on cardiac function, leading to poor recovery of LVEF. It's difficult to estimate how much LBBB contributes to a patient's ejection fraction decline. Further data of prospective studies are needed to evaluate the clinical outcome of pacing with biventricular or His-purkinje conduction system in patients requiring PPI after TAVR.

6. Other Prevention and Treatment Strategies

In the study of Urena [71], 8.1% of patients with new onset LBBB post TAVR had intermittent LBBB during preoperative ECG monitoring, and 31.4% of patients with PPI had high degree AVB, severe bradycardia or other indications of pacemaker implantation before TAVR. This suggests that there are many unrecognized baseline conduction abnormalities in TAVR patients and that the true in-

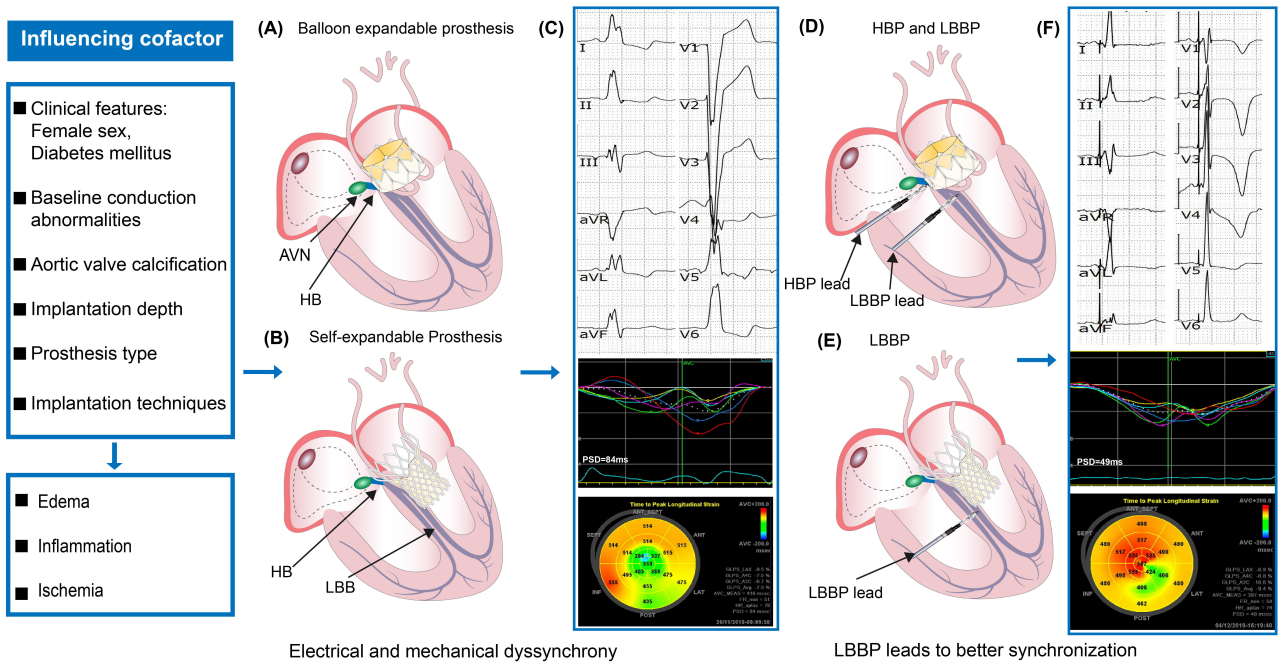

Fig. 2. Summary of the concept: Mechanism of new onset LBBB after TAVR by two prosthetic aortic valves, and LBBB were corrected by two physiological pacing modes respectively. (A, B) The different location and depth of the mechanical damage caused by two different prostheses leading to different incidence of LBBB ((A) balloon expandable prostheses, (B) self-expandable prostheses). (C) Postoperative electrocardiogram showed LBBB and electrical dyssynchrony leads to mechanical dyssynchrony indicated by Phase standard deviation (PSD) on echocardiogram. (D, E) Due to the different length of the lesion, the correction rate of LBBB by HBP is also different (self-expandable valves are much higher), when the conduction disorders extend beyond His bundle or even further, HBP is unable to correct LBBB or requires a higher threshold. LBBP that bypasses the pathologic region, which is deeper and more distal, showed a higher success rate. (F) Electrocardiogram showed LBBB was corrected by LBBP, presented a typical pattern of RBBB and mechanical asynchrony improved with electrical synchronization, with a lower PSD.

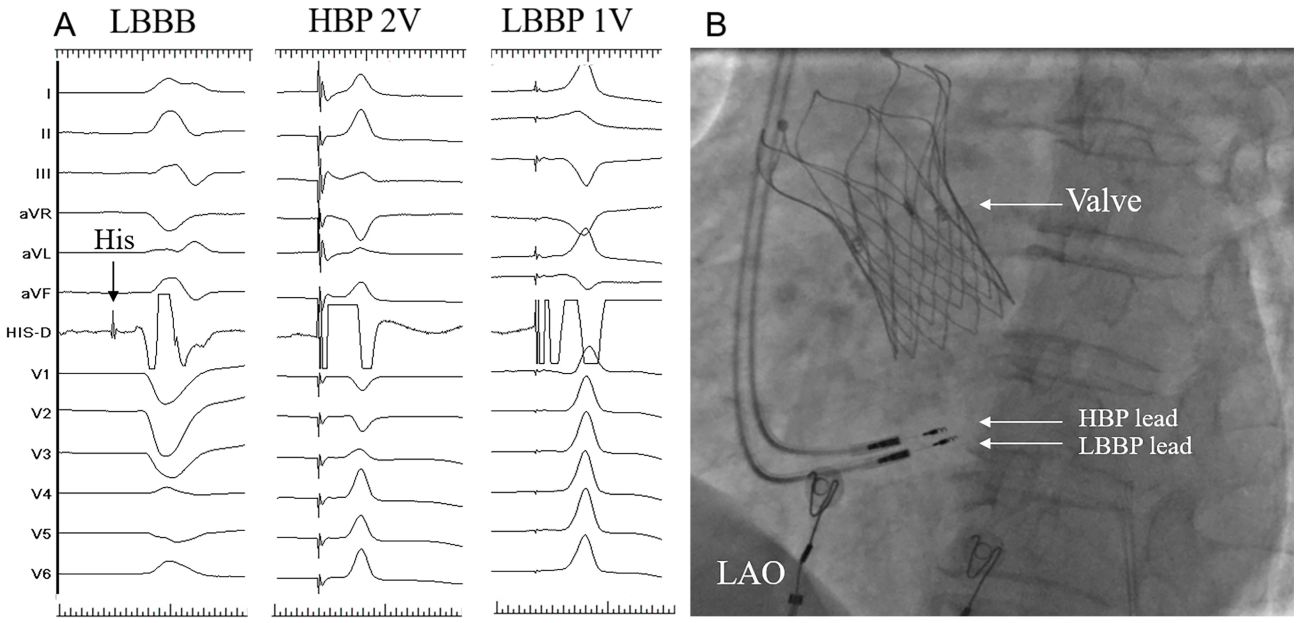

Fig. 3. Electrocardiogram and imaging characteristics of His-purkinje conduction system pacing post-TAVR. (A) The 12-lead ECG shows LBBB and His potential at baseline, as shown by the arrows, followed by bipolar pacing from the HBP (2V) and LBBP (1V), LBBB were both corrected. (B) Left anterior oblique (LAO) view of the HBP/LBBP lead and the relative location of the prosthesis.

cidence of conduction abnormalities derived from TAVR may be lower than published results so far. As we described above, it is recommended to monitor patients to receive TAVR using a long preoperative ECG to identify pre-existed arrhythmias, to accurately predict the risk of intraoperative and postoperative conduction block, and perform drug or pacing interventions in advance if necessary. At present, routine continuous ECG monitoring and implantation of the temporary pacemakers during TAVR can help identification of intraoperative and early postoperative conduction block timely, and rapid pacing can be used when necessary to avoid serious conduction block related to procedure. Postoperative monitoring of 12-lead electrocardiogram also showed a certain predictive value. The sensitivity and specificity of newly diagnosed cardiac conduction disorders (first-degree AVB, LBBB, RBBB, *etc*.) were 99% and 39%, respectively. However, patients with no postoperative ECG conduction disorder and who are stable within 48 hours do not develop delayed high AVB within 8 days after TAVR [72]. After discharge, electrocardiogram changes should be regularly followed up, and the monitoring frequency can be appropriately increased for high-risk patients.

7. Discussion

New onset LBBB remains the most common complication of TAVR procedure. The most relevant contributing factor has been identified as the depth of artificial valve implantation. New onset LBBB may have potential adverse effect on LVEF and poor prognosis, although current data regarding for LVEF and mortality have shown conflicting findings. To date, there is no indication for prophylactic PPI in new onset LBBB patients. However, a subgroup of patients with very long PR interval (>240 ms) or QRS duration (>150–160 ms) may benefit from PPI. To avoid the deterioration of cardiac function and economic burden caused by PPI, the application of HPCSP in TAVR related LBBB or in even other conduction system disorders has shown a promising prospect. The PARTNER 3 trial initiates the era of applying TAVR in patients of low surgical risk [72]. With the expansion of TAVR indications, more people may face TAVR-related conduction block in the future. The rising incidence of post-discharge conduction abnormalities including new onset LBBB requiring a pacemaker after TAVR suggests the need for careful monitoring. The pacing decision should be carefully made according to the different clinical characteristics of patients and the severity of conduction block. Among them, new onset LBBB after TAVR with high risk factors should be treated with PPI as early as possible. It is necessary to evaluate the appropriate pacing mode before pacing procedure. Physiological pacing provides an alternative once the pacing indication is explicit. The strongest indication for LBBP/HBP, other than conventional CRT, in patients with heart failure is still unclear. The physiological pacing research team is still searching for patients who may benefit from HPCSP. Actually, patients with normal QRS duration who develop LBBB immediately post TAVR, especially those combined with cardiac insufficiency, provide an excellent model to restudy the mechanism of LBBB and the indication for CRT implantation.

8. Conclusions

As the rapid development of TAVR procedures, the occurrence of conduction disturbances, particularly of new onset LBBB after TAVR remains an important issue. Patients who develop new onset LBBB should be closely monitored for progression of heart failure, and LBBB correction using physiological pacing serves as an effective alternative strategy. Further studies are warranted to elucidate the clinical impact of new onset LBBB, the pathophysiological basis of new onset LBBB, the factors that influence its outcome, the optimal timing and indication for pacing, and long-term clinical outcomes and safety of physiological pacing in this setting.

Author Contributions

JFZ and YWP designed and performed the research study. JFZ and YWP reviewed literature and wrote the manuscript. BW and GSF provided help and advice on the manuscript. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

References

[1] Reardon MJ, Van Mieghem NM, Popma JJ, Kleiman NS, Søndergaard L, Mumtaz M, *et al*. SURTAVI Investigators. Surgical or Transcatheter Aortic-Valve Replacement in Intermediate-Risk Patients. New England Journal of Medicine. 2017; 376: 1321–1331.

[2] Braghiroli J, Kapoor K, Thielhelm TP, Ferreira T, Cohen MG. Transcatheter aortic valve replacement in low risk patients: a review of PARTNER 3 and Evolut low risk trials. Cardiovascular Diagnosis and Therapy. 2020; 10: 59–71.

[3] Massoullié G, Bordachar P, Ellenbogen KA, Souteyrand G, Jean F, Combaret N, *et al*. New-Onset Left Bundle Branch Block Induced by Transcutaneous Aortic Valve Implantation. American Journal of Cardiology. 2016; 117: 867–873.

[4] Katsanos S, van Rosendael P, Kamperidis V, van der Kley F, Joyce E, Debonnaire P, *et al*. Insights into new-onset rhythm

conduction disorders detected by multi-detector row computed tomography after transcatheter aortic valve implantation. American Journal of Cardiology. 2014; 114: 1556–1561.
[5] van der Boon RM, Nuis RJ, Van Mieghem NM, Jordaens L, Rodés-Cabau J, van Domburg RT, *et al*. New conduction abnormalities after TAVI–frequency and causes. Nature Reviews Cardiology. 2012; 9: 454–463.
[6] Vijayaraman P, Bordachar P, Ellenbogen KA. The Continued Search for Physiological Pacing: Where Are We Now? Journal of the American College of Cardiology. 2017; 69: 3099–3114.
[7] Moreno R, Dobarro D, López de Sá E, Prieto M, Morales C, Calvo Orbe L, *et al*. Cause of complete atrioventricular block after percutaneous aortic valve implantation: insights from a necropsy study. Circulation. 2009; 120: e29–e30.
[8] Brinkert M, Wolfrum M, Moccetti F, Bossard M, Berte B, Cuculi F, *et al*. Relevance of New Conduction Disorders after Implantation of the ACURATE Neo Transcatheter Heart Valve in the Aortic Valve Position. The American Journal of Cardiology. 2020; 125: 783–787.
[9] Houthuizen P, Van Garsse LA, Poels TT, de Jaegere P, van der Boon RM, Swinkels BM, *et al*. Left Bundle-Branch Block Induced by Transcatheter Aortic Valve Implantation Increases Risk of Death. Circulation. 2012; 126: 720–728.
[10] Auffret V, Puri R, Urena M, Chamandi C, Rodriguez-Gabella T, Philippon F, *et al*. Conduction Disturbances After Transcatheter Aortic Valve Replacement: Current Status and Future Perspectives. Circulation. 2017; 136: 1049–1069.
[11] Auffret V, Webb JG, Eltchaninoff H, Muñoz-García AJ, Himbert D, Tamburino C, *et al*. Clinical Impact of Baseline Right Bundle Branch Block in Patients Undergoing Transcatheter Aortic Valve Replacement. JACC: Cardiovascular Interventions. 2017; 10: 1564–1574.
[12] Saint Croix GR, Lacy SC, Hrachian H, Beohar N. Clinical Impact of Preexisting Right Bundle Branch Block after Transcatheter Aortic Valve Replacement: A Systematic Review and Meta-Analysis. Journal of Interventional Cardiology. 2020; 2020: 1789516.
[13] Aktug Ö, Dohmen G, Brehmer K, Koos R, Altiok E, Deserno V, H, *et al*. Incidence and predictors of left bundle branch block after transcatheter aortic valve implantation. International Journal of Cardiology. 2012; 160: 26–30.
[14] Panchal HB, Barry N, Bhatheja S, Albalbissi K, Mukherjee D, Paul T. Mortality and major adverse cardiovascular events after transcatheter aortic valve replacement using Edwards valve versus CoreValve: a meta-analysis. Cardiovascular Revascularization Medicine. 2016; 17: 24–33.
[15] Phan DQ, Goitia J, Lee M, Gupta N, Aharonian V, Mansukhani P, *et al*. Predictors of conduction recovery after permanent pacemaker implantation following transcatheter aortic valve replacement. Journal of Interventional Cardiac Electrophysiology. 2021; 61: 365–374.
[16] Sharma E, Chu AF. Predictors of right ventricular pacing and pacemaker dependence in transcatheter aortic valve replacement patients. Journal of Interventional Cardiac Electrophysiology. 2018; 51: 77–86.
[17] Elzeneini M, Assaf Y, Aalaei-Andabili SH, Mahmoud A, Hamburger R, Goel R, *et al*. Predictors of ventricular pacing burden after permanent pacemaker implantation following transcatheter aortic valve replacement. Clinical Cardiology. 2020; 43: 1334–1342.
[18] Mangieri A, Montalto C, Pagnesi M, Lanzillo G, Demir O, Testa L, *et al*. TAVI and Post Procedural Cardiac Conduction Abnormalities. Frontiers in Cardiovascular Medicine. 2018; 5: 85.
[19] Muntané-Carol G, Philippon F, Rodés-Cabau J. New-Onset Left Bundle Branch Block Post-TAVI: No More an Innocent Bystander. Canadian Journal of Cardiology. 2019; 35: 1286–1288.
[20] Zaman S, McCormick L, Gooley R, Rashid H, Ramkumar S, Jackson D, *et al*. Incidence and predictors of permanent pacemaker implantation following treatment with the repositionable Lotus™ transcatheter aortic valve. Catheterization and Cardiovascular Interventions. 2017; 90: 147–154.
[21] Alqarawi W, Sadek MM, Golian M, Hibbert B, Redpath CJ, Nair GM, *et al*. A new electrocardiographic definition of left bundle branch block (LBBB) in patients after transcatheter aortic valve replacement (TAVR). Journal of Electrocardiology. 2020; 63: 167–172.
[22] Rodés-Cabau J, Ellenbogen KA, Krahn AD, Latib A, Mack M, Mittal S, *et al*. Management of Conduction Disturbances Associated with Transcatheter Aortic Valve Replacement: JACC Scientific Expert Panel. Journal of the American College of Cardiology. 2019; 74: 1086–1106.
[23] Ream K, Sandhu A, Valle J, Weber R, Kaizer A, Wiktor DM, *et al*. Ambulatory Rhythm Monitoring to Detect Late High-Grade Atrioventricular Block Following Transcatheter Aortic Valve Replacement. Journal of the American College of Cardiology. 2019; 73: 2538–2547.
[24] Muntané-Carol G, Guimaraes L, Ferreira-Neto AN, Wintzer-Wehekind J, Junquera L, Del Val D, *et al*. How does new-onset left bundle branch block affect the outcomes of transcatheter aortic valve repair? Expert Review of Medical Devices. 2019; 16: 589–602.
[25] Nazif TM, Williams MR, Hahn RT, Kapadia S, Babaliaros V, Rodés-Cabau J, *et al*. Clinical implications of new-onset left bundle branch block after transcatheter aortic valve replacement: analysis of the PARTNER experience. European Heart Journal. 2014; 35: 1599–1607.
[26] Carrabba N, Valenti R, Migliorini A, Marrani M, Cantini G, Parodi G, *et al*. Impact on Left Ventricular Function and Remodeling and on 1-Year Outcome in Patients with Left Bundle Branch Block after Transcatheter Aortic Valve Implantation. The American Journal of Cardiology. 2015; 116: 125–131.
[27] Urena M, Webb JG, Cheema A, Serra V, Toggweiler S, Barbanti M, *et al*. Impact of new-onset persistent left bundle branch block on late clinical outcomes in patients undergoing transcatheter aortic valve implantation with a balloon-expandable valve. JACC: Cardiovascular Interventions. 2014; 7: 128–136.
[28] Hoffmann R, Herpertz R, Lotfipour S, Aktug, Brehmer K, Lehmacher W, *et al*. Impact of a New Conduction Defect after Transcatheter Aortic Valve Implantation on Left Ventricular Function. JACC: Cardiovascular Interventions. 2012; 5: 1257–1263.
[29] Chamandi C, Barbanti M, Munoz-Garcia A, Latib A, Nombela-Franco L, Gutiérrez-Ibanez E, *et al*. Long-Term Outcomes in Patients with New-Onset Persistent Left Bundle Branch Block Following TAVR. JACC: Cardiovascular Interventions. 2019; 12: 1175–1184.
[30] Houthuizen P, van der Boon RM, Urena M, Van Mieghem N, Brueren GB, Poels TT, *et al*. Occurrence, fate and consequences of ventricular conduction abnormalities after transcatheter aortic valve implantation. EuroIntervention. 2014; 9: 1142–1150.
[31] Testa L, Latib A, De Marco F, De Carlo M, Agnifili M, Latini RA, P, *et al*. Clinical impact of persistent left bundle-branch block after transcatheter aortic valve implantation with CoreValve Revalving System. Circulation. 2013; 127: 1300–1307.
[32] Nazif TM, Dizon JM, Hahn RT, Xu K, Babaliaros V, Douglas PS, *et al*. PARTNER Publications Office. Predictors and clinical outcomes of permanent pacemaker implantation after transcatheter aortic valve replacement: the PARTNER (Placement of AoRtic TraNscathetER Valves) trial and registry. JACC: Cardiovascular Interventions. 2015; 8: 60–69.
[33] Regueiro A, Abdul-Jawad Altisent O, Del Trigo M, Campelo-

Parada F, Puri R, Urena M, *et al*. Impact of new-onset left bundle branch block and periprocedural permanent pacemaker implantation on clinical outcomes in patients undergoing transcatheter aortic valve replacement: a systematic review and meta-analysis. Circulation: Cardiovascular Interventions. 2016; 9: e003635.

[34] Lilly SM, Deshmukh AJ, Epstein AE, Ricciardi MJ, Shreenivas S, Velagapudi P, *et al*. 2020 ACC Expert Consensus Decision Pathway on Management of Conduction Disturbances in Patients Undergoing Transcatheter Aortic Valve Replacement: A Report of the American College of Cardiology Solution Set Oversight Committee. Journal of the American College of Cardiology. 2020; 76: 2391–2411.

[35] Tovia-Brodie O, Letourneau-Shesaf S, Hochstadt A, Steinvil A, Rosso R, Finkelstein A, *et al*. The Utility of Prophylactic Pacemaker Implantation in Right Bundle Branch Block Patients Pre-Transcatheter Aortic Valve Implantation. Israel Medical Association Journal. 2019; 21: 790–795.

[36] D'Ancona G, Pasic M, Unbehaun A, Hetzer R. Permanent pacemaker implantation after transapical transcatheter aortic valve implantation. Interactive CardioVascular and Thoracic Surgery. 2011; 13: 373–376.

[37] De Carlo M, Giannini C, Bedogni F, Klugmann S, Brambilla N, De Marco F, *et al*. Safety of a conservative strategy of permanent pacemaker implantation after transcatheter aortic CoreValve implantation. American Heart Journal. 2012; 163: 492–499.

[38] Buellesfeld L, Stortecky S, Heg D, Hausen S, Mueller R, Wenaweser P, *et al*. Impact of permanent pacemaker implantation on clinical outcome among patients undergoing transcatheter aortic valve implantation. Journal of the American College of Cardiology. 2012; 60: 493–501.

[39] Pereira E, Ferreira N, Caeiro D, Primo J, Adão L, Oliveira M, *et al*. Transcatheter Aortic Valve Implantation and Requirements of Pacing over Time. Pacing and Clinical Electrophysiology. 2013; 36: 559–569.

[40] Biner S, Michowitz Y, Leshem-Rubinow E, Topilsky Y, Ben-Assa E, Shimiaie J, *et al*. Hemodynamic Impact and Outcome of Permanent Pacemaker Implantation Following Transcatheter Aortic Valve Implantation. The American Journal of Cardiology. 2014; 113: 132–137.

[41] Urena M, Webb JG, Tamburino C, Muñoz-García AJ, Cheema A, Dager AE, *et al*. Permanent Pacemaker Implantation after Transcatheter Aortic Valve Implantation: impact on late clinical outcomes and left ventricular function. Circulation. 2014; 129: 1233–1243.

[42] Schymik G, Tzamalis P, Bramlage P, Heimeshoff M, Würth A, Wondraschek R, *et al*. Clinical impact of a new left bundle branch block following TAVI implantation: 1-year results of the TAVIK cohort. Clinical Research in Cardiology. 2015; 104: 351–362.

[43] Mouillet G, Lellouche N, Yamamoto M, Oguri A, Dubois-Rande JL, Van Belle E, *et al*. Outcomes following pacemaker implantation after transcatheter aortic valve implantation with CoreValve (®) devices: Results from the FRANCE 2 Registry. Catheterization and Cardiovascular Interventions. 2015; 86: E158–E166.

[44] Kawaguchi AT, D'Allessandro C, Collet JP, Cluzel P, Makri R, Leprince P. Ventricular Conduction Defects after Transcatheter Aortic Valve Implantation: A Single-Institute Analysis. Artificial Organs. 2015; 39: 409–415.

[45] Rampat R, Khawaja MZ, Hilling-Smith R, Byrne J, MacCarthy P, Blackman DJ, *et al*. Conduction Abnormalities and Permanent Pacemaker Implantation after Transcatheter Aortic Valve Replacement Using the Repositionable LOTUS Device: The United Kingdom Experience. JACC: Cardiovascular Interventions. 2017; 10: 1247–1253.

[46] Cresse S, Eisenberg T, Alfonso C, Cohen MG, DeMarchena E, Williams D, *et al*. Cardiac conduction abnormalities associated with pacemaker implantation after transcatheter aortic valve replacement. Pacing and Clinical Electrophysiology. 2019; 42: 846–852.

[47] Jilaihawi H, Zhao Z, Du R, Staniloae C, Saric M, Neuburger PJ, *et al*. Minimizing Permanent Pacemaker Following Repositionable Self-Expanding Transcatheter Aortic Valve Replacement. JACC: Cardiovascular Interventions. 2019; 12: 1796–1807.

[48] Monteiro C, Ferrari ADL, Caramori PRA, Carvalho LAF, Siqueira DADA, Thiago LEKS, *et al*. Permanent Pacing after Transcatheter Aortic Valve Implantation: Incidence, Predictors and Evolution of Left Ventricular Function. Arquivos Brasileiros De Cardiologia. 2017; 109: 550–559.

[49] Kawsara A, Sulaiman S, Alqahtani F, Eleid MF, Deshmukh AJ, Cha YM, *et al*. Temporal Trends in the Incidence and Outcomes of Pacemaker Implantation after Transcatheter Aortic Valve Replacement in the United States (2012–2017). Journal of the American Heart Association. 2020; 9: e016685.

[50] Glikson M, Nielsen JC, Kronborg MB, Michowitz Y, Auricchio A, Barbash IM, *et al*. ESC Scientific Document Group. 2021 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy. Europace. 2022; 24: 71–164.

[51] Vijayaraman P, Bordachar P, Ellenbogen KA. The Continued Search for Physiological Pacing: Where Are We Now? Journal of the American College of Cardiology. 2017; 69: 3099–3114.

[52] Muthumala A, Vijayaraman P. Clinical outcomes of his-Purkinje conduction system pacing. Pacing and Clinical Electrophysiology. 2021; 44: 5–14.

[53] Vijayaraman P, Patel N, Colburn S, Beer D, Naperkowski A, Subzposh FA. His-Purkinje Conduction System Pacing in Atrioventricular Block: New Insights into Site of Conduction Block. JACC: Clinical Electrophysiology. 2022; 8: 73–85.

[54] Sharma PS, Naperkowski A, Bauch TD, Chan JYS, Arnold AD, Whinnett ZI, *et al*. Permanent his Bundle Pacing for Cardiac Resynchronization Therapy in Patients with Heart Failure and Right Bundle Branch Block. Circulation: Arrhythmia and Electrophysiology. 2018; 11: e006613.

[55] Wu S, Su L, Vijayaraman P, Zheng R, Cai M, Xu L, *et al*. Left Bundle Branch Pacing for Cardiac Resynchronization Therapy: Nonrandomized on-Treatment Comparison with his Bundle Pacing and Biventricular Pacing and Biventricular Pacing. Canadian Journal of Cardiology. 2021; 37: 319–328.

[56] Arnold AD, Shun-Shin MJ, Keene D, Howard JP, Sohaib SMA, Wright IJ, *et al*. His Resynchronization Versus Biventricular Pacing in Patients with Heart Failure and Left Bundle Branch Block. Journal of the American College of Cardiology. 2018; 72: 3112–3122.

[57] Huang W, Wu S, Vijayaraman P, Su L, Chen X, Cai B, *et al*. Cardiac Resynchronization Therapy in Patients with Nonischemic Cardiomyopathy Using Left Bundle Branch Pacing. JACC: Clinical Electrophysiology. 2020; 6: 849–858.

[58] Chen X, Jin Q, Li B, Jia J, Sharma PS, Huang W, *et al*. Electrophysiological parameters and anatomical evaluation of left bundle branch pacing in an in vivo canine model. Journal of Cardiovascular Electrophysiology. 2020; 31: 214–219.

[59] Zhang J, Pan Y, Sun Y, Fu G. Anatomical and histological assessment of left bundle branch area pacing in human heart with refractory heart failure. ESC heart failure. 2022. (in press)

[60] Deshmukh P, Casavant DA, Romanyshyn M, Anderson K. Permanent, direct His-bundle pacing: a novel approach to cardiac pacing in patients with normal His-Purkinje activation. Circulation. 2000; 101: 869–877.

[61] Huang W, Su L, Wu S, Xu L, Xiao F, Zhou X, *et al*. A Novel Pacing Strategy with Low and Stable Output: Pacing the Left Bundle Branch Immediately beyond the Conduction Block. Canadian Journal of Cardiology. 2017; 33: 1736.e1–1736.e3.

[62] Zhang S, Zhou X, Gold MR. Left Bundle Branch Pacing: JACC Review Topic of the Week. Journal of the American College of Cardiology. 2019; 74: 3039–3049.
[63] Sen J, Mok M, Perrin M. His-Bundle Pacing in a Patient with Transcatheter Aortic Valve Implantation-Induced Left Bundle Branch Block. Case Reports in Cardiology. 2018; 2018: 4606271.
[64] De Pooter J, Gauthey A, Calle S, Noel A, Kefer J, Marchandise S, *et al*. Feasibility of his-bundle pacing in patients with conduction disorders following transcatheter aortic valve replacement. Journal of Cardiovascular Electrophysiology. 2020; 31: 813–821.
[65] Sharma PS, Subzposh FA, Ellenbogen KA, Vijayaraman P. Permanent his-bundle pacing in patients with prosthetic cardiac valves. Heart Rhythm. 2017; 14: 59–64.
[66] Guo J, Li L, Xiao G, Huang X, Li Q, Wang Y, *et al*. Feasibility and stability of left bundle branch pacing in patients after prosthetic valve implantation. Clinical Cardiology. 2020; 43: 1110–1118.
[67] Patel S, Jamoor K, Khan A, Maskoun W. Late onset complete heart block after transcatheter aortic valve replacement treated with permanent his-bundle pacing. Pacing and Clinical Electrophysiology. 2021; 44: 194–198.
[68] Vijayaraman P, Cano Ó, Koruth JS, Subzposh FA, Nanda S, Pugliese J, *et al*. His-Purkinje Conduction System Pacing Following Transcatheter Aortic Valve Replacement: Feasibility and Safety. JACC: Clinical Electrophysiology. 2020; 6: 649–657.
[69] Zhang J, Yu F, Wang B, Fu G. Rapid reversal of heart failure by correcting left bundle branch block induced by transcatheter aortic valve replacement. Pacing and Clinical Electrophysiology. 2021; 44: 203–207.
[70] Cano Ó, Vijayaraman P. The search for physiologic pacing post-TAVR. Journal of Cardiovascular Electrophysiology. 2020; 31: 822–824.
[71] Urena M, Hayek S, Cheema AN, Serra V, Amat-Santos IJ, Nombela-Franco L, *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: 469–477.
[72] Toggweiler S, Stortecky S, Holy E, Zuk K, Cuculi F, Nietlispach F, *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: Cardiovascular Interventions. 2016; 9: 1269–1276.