Chapter

Conduction System Disorders Associated With Valvular Heart Disease and Interventions

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Abstract

The aging population of the Western world will lead to an increase in cardiac pathologies. Valvular disorders include a spectrum of progressive diseases that confers mechanical and functional impairment, including issues with the cardiac conduction system. Pacemakers are a therapeutic standard to reinstate the synchrony of cardiac contraction. Permanent pacemakers are often required for severe, chronic presentations and have been effective in nullifying symptoms and improving cardiac function. Yet, these devices impart new risks and complications that require additional interventions. However, recent advancements in leadless pacemakers and cardiac resynchronization therapy provide a novel approach to applying pacemaker technology and have been shown to reduce associated risks and improve patient outcomes.

Keywords: aortic stenosis (AS), mitral regurgitation (MR), infectious endocarditis (IE), mitral valve, aortic valve, left ventricular hypertrophy

1. Introduction

Amongst all cardiac procedures carried out in the United States, it is estimated that 10–20% were related to Valvular Heart Disease (VHD) [1]. Moreover, given the increasing age of the Western and developed population, the burden of VHD is expected to increase. As VHDs become severe and/or symptomatic, surgery is eventually required. There are invasive and minimally invasive percutaneous interventions for valve repair and surgery, with varying conductive tissue complications. Conversely, treatment for the underlying conductive disease (i.e. pacemakers) has valvular complications. This review will outline these complications.

2. Conduction tissue anatomy

The heart's pumping action is mediated by specialized muscle fibers known as cardiomyocytes. Unlike typical myocytes, they possess the capacity to self-initiate an electrical impulse for muscular contraction. They are regulated by a highly specialized group of cells compacted to form the conduction system (**Figure 1**).

The sinoatrial (SA) node (the pacemaker) is the site of impulse generation and is located between the superior vena cava (SVC) and the right atrium (RA).

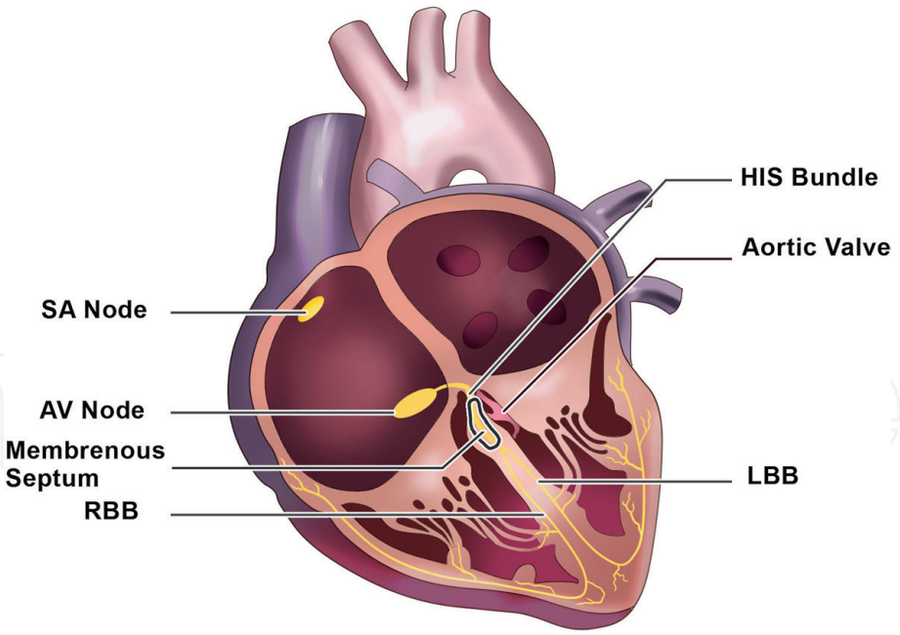

Figure 1.
Normal conduction system of the heart.

The generated electrical pulse propagates from the SA node and travels along the myocardium of the left and right atria, stimulating contraction and propelling blood from the atria into the ventricles. The electrical signal then travels along specialized cardiac muscle fibers to the atrioventricular (AV) node. The specialized cells that guide the signal are collectively known as the internodal pathways; 3 of which originate from the RA and 1 from the left atrium (LA). Upon reaching the AV node (AVN), the electrical impulse slows down, allowing the adequate filling of the ventricles before contraction. The electrical impulse then travels to a group of specialized cardiac cells called the His Bundle, which divides along the septum into left and right branches terminating into the Purkinje fibers. Signal transduction along these fibers results in ventricular contraction to expel the blood from the heart and into pulmonary (from the right ventricle) and systemic (from the left ventricle) circulation.

3. Conduction tissue disease

Cardiac conduction tissue disorders are a group of disorders that impair the above system. They are classified according to the area affected by disease processes as shown in **Figure 2**.

3.1 Sinus node dysfunction

Sinus Node Dysfunction (SND) refers to the ailment in the SA node's ability to generate electrical impulses. SND primarily affects older individuals (over 65 years of age), however, individuals of any age can present with it. As such, the most common pathological mechanism is degenerative fibrosis of the SA node and its subsequent remodeling. Any factors that affect the ionic currents of the pacemaker cells can lead to the presentation of SND. These include beta-blockers, calcium channel blockers and antiarrhythmic medication. SND is often associated with electrolyte imbalances such as hyperkalemia, hypokalemia or hypercalcemia.

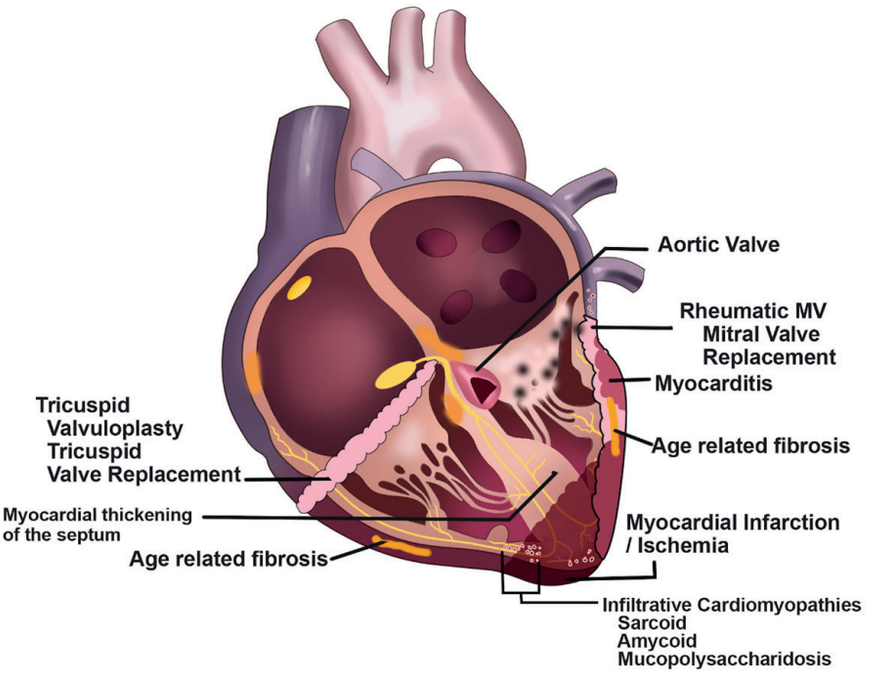

Figure 2.
Conditions associated with conduction system abnormalities.

A characteristic form of SND is a tachycardia-bradycardia syndrome, whereby tachycardia persists but devolves into severe bradycardia either spontaneously or as an attempt to medically manage tachycardia [2]. SND can also present with varying degrees of severity with differing ECG findings. First-degree SA block is asymptomatic and cannot be detected on the ECG. The second-degree SA block is characterized by a dropped P wave but is not associated with any change in the P–P interval. Third-degree SA block is complete dysfunction of the SA pacemaker cells with no discernable P wave on the ECG (23).

3.2 Atrioventricular block

Atrioventricular block (AVB) refers to disorders whereby the propagation of impulse generated in the SA node is impaired from propagating to the ventricles in varying degrees. AVB can be secondary to defined cardiomyopathy but often is idiopathic. AVB can also be a consequence of intervention for valvular disease. Diagnosis and progression of AVB are determined by the abnormalities in the AV electrical activity and which cardiac structure is affected.

First-degree AVB (AVB I) is associated with a prolonged PR interval, indicating a delay in the AVN, which is typically considered benign due to normal ventricular filling. However, the patient may become symptomatic with increased activity due to deterioration of AVN conduction associated with a faster heart rate. Moreover, cases with marked first-degree AVB (delay greater than 300 ms) can result in shorter diastolic time and produce "pacemaker-like syndrome" symptoms. This is a major mechanism of increased risk of future atrial fibrillation and indicates the need for pacemaker implantation [3].

Second-degree AVB (AVB II) is further sub-classed into Mobitz Type I (Wenckebach) and Mobitz Type II. Mobitz Type I AVB classically presents with progressive prolongation of the PR intervals until there is a non-conducted P wave. Mobitz Type I AVB typically affects the AV node itself and is deemed to be benign and reversible. Mobitz Type II presents with constant PR intervals that are

preceded and followed by a non-conducted P wave. Mobitz Type II AVB is a challenging diagnosis as the PR interval may appear normal and the mere presence of non-conducted P waves is not an automatic indication of Type II AVB. Type II AVB affects the conduction system distal to the AV node in the His Bundle system.

Third-degree AVB (AVB III) is also known as complete AVB in which there is complete dissociation between atrial and ventricular conductive tissue. Thus, any presence of QRS complexes is independent of the generation of P waves. Ventricular contraction is due to intrinsic junctional or ventricular rhythm and poses the greatest risk of hemodynamic instability and fatal cardiac arrhythmias resulting in death.

3.3 Left bundle branch block

Left bundle branch block (LBBB) refers to impaired conduction of branches of the His Bundle system, specifically the narrow anterior fascicle and the broader posterior fascicle. Typically, LBBB presents with prolonged QRS (>120 ms), absent Q wave in V_6 and rS complexes in V_1-V_2 [4]. In isolation, LBBBs are asymptomatic and confer no risk to the patient. However, LBBBs underlying etiology is dilated cardiomyopathy, which itself can be caused by ischemic, infective, infiltrative or valvular cardiac disease [5]. Moreover, it has been shown that individuals with LBBB and incomplete AVB carry a greater risk of progressing to complete AVB [5].

Whilst there is no complete treatment for LBBB, cardiac resynchronization therapy (Section 5.3) has been shown to benefit patients who present with heart failure alongside LBBB (27).

4. Conductive tissue disorders associated with Valvular interventions

Historically, heart surgery has been the only option amongst patients with symptomatic severe valvular heart disease. However, for patients that are not surgical candidates, minimally invasive transcatheter approaches are increasingly employed for valve repair and/or replacement. Each of these interventions can be associated with differing rates of Conductive System Disorders (CSDs). Complete or high-degree AVB is a particular concern, for which guidelines from the American College of Cardiology/American Heart Association recommend permanent pacemakers if there is no resolution after 1-week post-surgical intervention [6]. The conductive tissue complications following invasive and minimally-invasive VHD interventions will be outlined here.

4.1 Aortic valve interventions

Transcatheter aortic valve replacement (TAVR) is a minimally invasive technique for symptomatic severe AS that has gained wide adoption, having been performed in over 400,000 patients worldwide as of 2017 [7]. While initially reserved for patients at high surgical risk, TAVR has shown non-inferior or superiority to SAVR for all-cause mortality, cardiovascular mortality and stroke amongst medium and low surgical risk populations up to 5-year follow-up [8, 9]. However, TAVR has lower valve durability and higher rates of paravalvular leaks and CSD, namely left bundle branch blocks and AVBs requiring pacemaker insertion [8–10]. The rates of pacemaker insertion post-TAVR vary based on type (self-expanding vs. balloon expanding) and generation of valve used. Meta-analyses have reported pacemaker insertion rates of approximately 3.8–6.5% for balloon-expanding vs. 12–25.8% for self-expanding valves [11, 12]. The self-expanding valves do have increased effective orifice area at the cost of worse rates of CSD, though the clinical significance

of better orifice area is not born out in short to medium-term studies done thus far [11]. The mechanism of conductive tissue disruption is thought to be from injury to the AV node while the deployment of the valve into the left ventricular outflow tract; self-expanding valves by their nature exert a greater radial and compressive force on peri-valvular conductive tissue over time which is likely results in the observed outcome of increased pacemaker requirement. There is ongoing research about the predictors of pacemaker requirement following TAVR in either type of valve, but strong associations include male sex, baseline Mobitz type 1, baseline wide QRS, depth of valve implant, and intraprocedural AV block [13–15]. Given the increased risk of LBBB post-TAVR, pre-existing right bundle disease (RBBB or bifascicular block) predisposes to complete AVB requiring pacemaker [13].

Surgical Aortic Valve Replacement (SAVR) is a well-established procedure for the treatment of severe aortic stenosis or regurgitation. An important benefit of SAVR over TAVR is valve durability, particularly with mechanical valves as these are not possible currently with TAVR. SAVR has traditionally been performed using sutured valves, with post-surgical pacemaker requirement in 2–4% of cases [16–18]. However, with the advent of TAVR, sutureless valves (similar in concept to balloon-expanded TAVR valves) are increasingly being used in SAVR as they minimize procedure and hospital time [19]. Given the stent-expanding nature of sutureless SAVR, they result in higher rates of pacemaker requirement compared to conventional SAVR [20, 21]. There are limited trials comparing SAVR to TAVR; many have shown worse rates of pacemaker requirement in TAVR but the TAVR cohorts include both self-expanding and balloon-expanded valves [22–24]. When comparing balloon-expanded TAVR to sutureless SAVR however, the rates of pacemaker requirement were similar over a two-year follow-up [25]. More studies are quired for recommendations between sutureless SAVR and TAVR.

4.2 Mitral valve interventions

The Mitral valve (MV) is significantly more complex than the aortic valve due to the papillary muscles and chordae tendinea that tether leaflets to the left ventricle, as well as its ovoid annulus. The definitive treatment for severe MV stenosis or regurgitation is surgical replacement or repair, but this is limited by surgical risk. The incidence of AVBs following Mitral valve surgical replacement is up to 18% AVB I, 5% AVB II, and 5% AVB III [26–29]. Following mitral valve surgical replacement, a permanent pacemaker is required in approximately 2–11% of cases [30]. Notably, Mitral valve surgical replacement is associated with an approximately 20% higher risk of CSD requiring a permanent pacemaker compared to aortic valve surgical replacement [28]. This is likely related to the proximity of the mitral valve (MV) annulus to the AV node, Specifically, the posterolateral artery which supplies the AV node is adjacent to the mitral annulus and may be damaged intra or post-surgically.

While AVBs are well-document in the surgical intervention of MV, Conductive tissue abnormalities are uncommon following mitral transcatheter edge-to-edge repair (TEER). A case report of a patient with a baseline trifascicular block did show complete AVB following the MitraClip procedure with a proposed mechanism of injury being the instrumentation of MV apparatus during the procedure [31]. Similarly, a case reported the development of Mobitz type II following the Cardioband procedure subsequently degrading into complete AVB. The mechanism of conductive tissue injury was thought to be the deployment of screws into the MV annulus to anchor the Cardioband system. These case reports highlight the significance of MV annulus instrumentation. Nevertheless, transcatheter mitral valve repair is generally not complicated by CSDs.

Transcatheter Mitral Valve Replacement (TMVR) is technically challenging given the complexity of the mitral valve apparatus. Given its infancy, several TMVR systems are undergoing development and research and as of 2020, ACC/AHA guidelines for VHD do not offer any recommendations for TMVR [10]. The TMVR techniques currently in development vary in the approach to valve deployment (transapical vs. transfemoral/transeptal) and mechanism of expansion into valve apparatus (self-expanding vs. balloon-expanding), which theoretically could have implications for CSDs. Yet, AV blocks or bundle branch blocks have not been reported as complications post-valve deployment short-term in feasibility studies thus far [32–35].

4.3 Tricuspid valve interventions

Moderate to severe tricuspid regurgitation is often overlooked as a contributor to mortality, despite its association with increased mortality even after adjusting for LV dysfunction and pulmonary hypertension [36]. It can be categorized as primary (congenital or acquired abnormality of tricuspid apparatus itself) or secondary (abnormality of tricuspid apparatus occurring as a consequence of pulmonary hypertension, right or left ventricular dysfunction). RV damage because of TR can become irreversible, suggesting the benefits of earlier intervention [37]. Surgical intervention is indicated for symptomatic patients with severe primary TR, or in asymptomatic patients with worsening RV dysfunction. Similarly, ESC guidelines recommend early consideration of surgical intervention in patients with symptomatic TR or mildly symptomatic severe TR with RV dilation [38]. However, surgical correction has significant surgery-related morbidity and mortality. Transcatheter Tricuspid Valve Interventions (TTVI) aimed at poor surgical candidates are undoing research and development and include direct annuloplasty, leaflet approximation or valve replacement. TTVIs have shown improvement in RV performance and hemodynamics up to 6 months post-procedure, as well as improvement in HF rehospitalizations and survival up to 1-year post-procedure. An expected complication of TTVIs is heart block, though this has not been a widely report complication in preliminary reports [39, 40]. As the TTVI experience improves, it may become an effective strategy to treat pacemaker-induced TR (Section 5.5).

5. Treatment of conductive tissue disorders

Cardiac CSDs are a major cause of morbidity and mortality. Approximately 1% of the general population has CSDs necessitating permanent pacemakers (PPM), with incident rates continuing to rise each year [41]. The first implantable pacemaker by Senning in Stockholm in 1957, was an extravascular pulse generator with leads implanted into the ventricular myocardium of a patient with complete heart block. Since then, several innovations have made pacemakers more robust. Most modern pacemakers comprise a pulse generator implanted subcutaneously, that is connected to lead(s) that traverse transvenously into the myocardium of the heart chamber(s). Pacing has gained complexity and now includes dual chamber pacing (right atrium and ventricle), continuous resynchronization therapy (CRT), leadless pacing and most recently, conductive tissue pacing as shown in **Figure 3**.

5.1 Single and dual chamber pacemakers

Single chamber pacemakers are the simplest form of pacing: they have a single lead implanted into the myocardium of the right atrium or the right ventricle

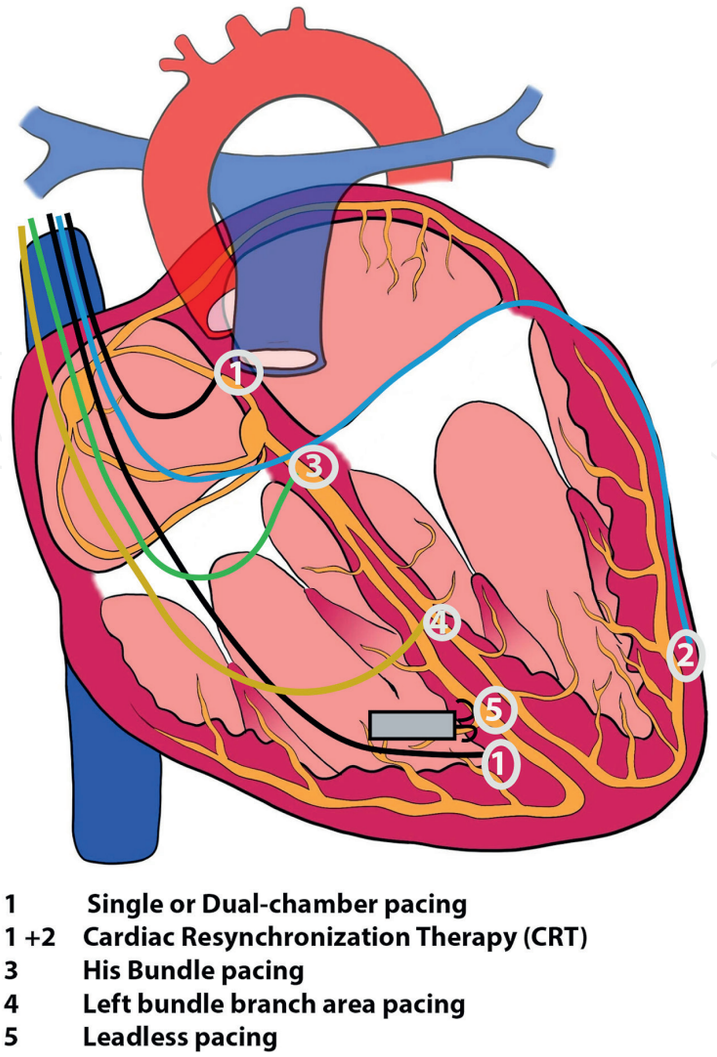

Figure 3.
Treatment of conduction system disease with different types of pacing techniques.

(**Figure 4A**). Single lead pacing is a cure for symptomatic conductive tissue disorders in the short term. However, it was not physiologic as a ventricular contraction occurred irrespective of atrial activity; with loss of synchronized atrial contraction in ventricular single chamber pacing, the ventricular filling would theoretically be diminished. Thus, Ventricular single-chamber pacemakers are now primarily used in patients with poor atrial ejection fraction, namely persistent atrial fibrillation, where the atrial mechanical coupling is compromised. Atrial single-lead pacemakers are theoretically also useful in treating isolated sinus node dysfunction but are rarely used as there is usually concomitant AV and sub-AV node disease.

To preserve atrial and ventricular synchrony, dual-chamber pacemakers were developed, whereby both an atrial and ventricular lead are implanted into the myocardium (**Figure 4B**). Improved synchrony by dual-chamber pacemakers translates to improved outcomes in some but not all populations. A 2004 Cochrane review of 26 studies comparing dual to single-chamber pacemakers revealed a significant reduction in atrial fibrillation and a non-significant reduction in heart failure, stroke and mortality with dual-chamber pacing [42]. Interestingly, amongst elderly patients, there was no difference in clinical outcomes between single and dual chamber pacemakers, likely reflecting higher rates of baseline atrial fibrillation in this age group [43].

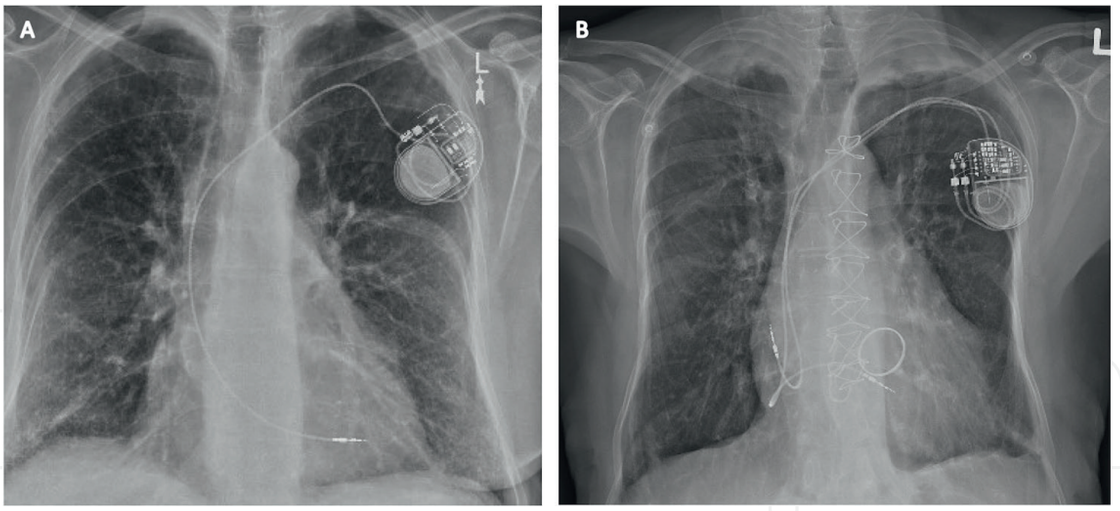

Figure 4.
(A) CXR showing a single chamber pacemaker with pacing lead placed in the RV. (B). CXR showing a dual chamber pacemaker following mitral valve replacement and tricuspid valve annuloplasty.

5.2 Leadless pacemaker

Leadless pacing is a novel therapy whereby an electrical impulse generator is percutaneously implanted directly into the myocardium, obviating the need for leads (**Figure 5**). The lack of leads and subcutaneous pulse generator has the theoretical benefit of avoiding lead-related (ex. lead infections, lead failure, tricuspid regurgitation) and subcutaneous pocket (ex. Pocket infections, hematoma) complications.

At this time, the majority of literature is on two leadless pacemakers: Nanostim (St. Jude Medical, St. Paul, MN,USA) and Micra (Medtronic, Minneapolis, MN). Nanostim had promising results from initial trials but was recalled due to premature battery failure and spontaneous detachment from the myocardium. For these reasons, it did not gain FDA approval and is not currently being implanted. An updated Nansostim system called Aveir VR gained FDA approval in March 2022 but no trials have been completed thus far. As Micra is the only FDA-approved leadless pacemaker with short to medium-term data, it will be the focus of this review. Although there are no clinical trials directly comparing Micra to transvenous

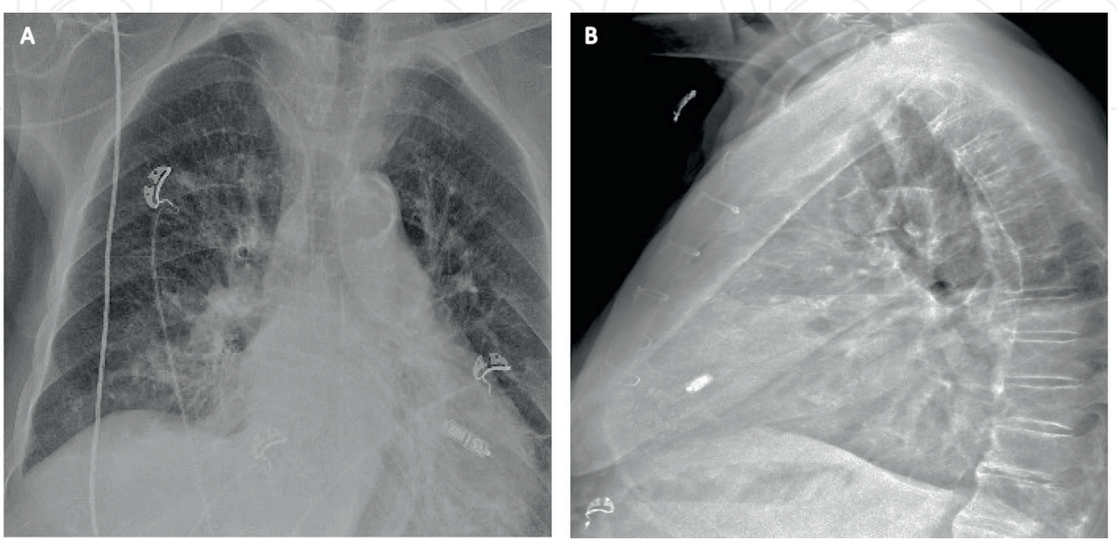

Figure 5.
CXR of a leadless pacemaker. An anteroposterior (A) and a lateral (B) view show the position of the leadless pacemaker.

pacing, observational studies up to 1-year post-implant have shown a significant reduction in the odds of developing infectious complications compared to transvenous pacing, while maintaining electrophysiologic pacing parameters [44–46]. Leadless pacing shows promise in reducing complications, but long-term trials are needed to verify electrophysiologic stability.

5.3 Cardiac resynchronization therapy

CRT is a pacing strategy to improve dyssynchronous left and right ventricular contraction; it involves biventricular pacing (RV and LV lead as shown in **Figure 6**) and can also be achieved in left-sided persistent SVC, congenital heart disease and anomalous coronary sinus veins [47–49]. Cardiac mechanical desynchrony is of particular concern amongst select patients with heart failure with reduced ejection fraction (HFrEF) [50]. Patients with HFrEF undergo cardiac remodeling over time which results in electrical dysregulation and interventricular delays ultimately causing dyssynchronous contraction of the right and left ventricles and poor cardiac function; these interventricular delays can be in the form of left bundle branch block or non-specific electrical conduction delays that increased QRS duration. Indeed, QRS duration correlates with worsening heart failure and sudden cardiac death and death from any cause [50]. CRT is an effective strategy to mitigate interventricular delays as the electrical generator can be programmed to initiate optimal timing of contraction for each ventricle. CRT has been shown to reduce mortality by up to 36% compared to medical therapy alone in patients with interventricular delay [51]. Given the evidence, ACCF/AHA/HRS guidelines suggest CRT for patients with Left Ventricular Ejection Fraction <35%, sinus rhythm, LBBB with QRS > 150 ms and NYHA class 2–4 symptoms on goal-directed medical therapy (class 1) [52].

Amongst HFrEF patients who would otherwise benefit from CRT, the presence of atrial fibrillation (AF) can be problematic. The rapid ventricular response or irregularity of AF can interfere with biventricular pacing capture rendering CRT ineffective in up to 67% of patients with persistent AF [53]. One solution to this dilemma is ablation followed by biventricular pacing. A recent meta-analysis showed worse mortality in AF patients compared to normal sinus patients that underwent CRT [54]. However, when AF patients underwent ablation, all-cause mortality

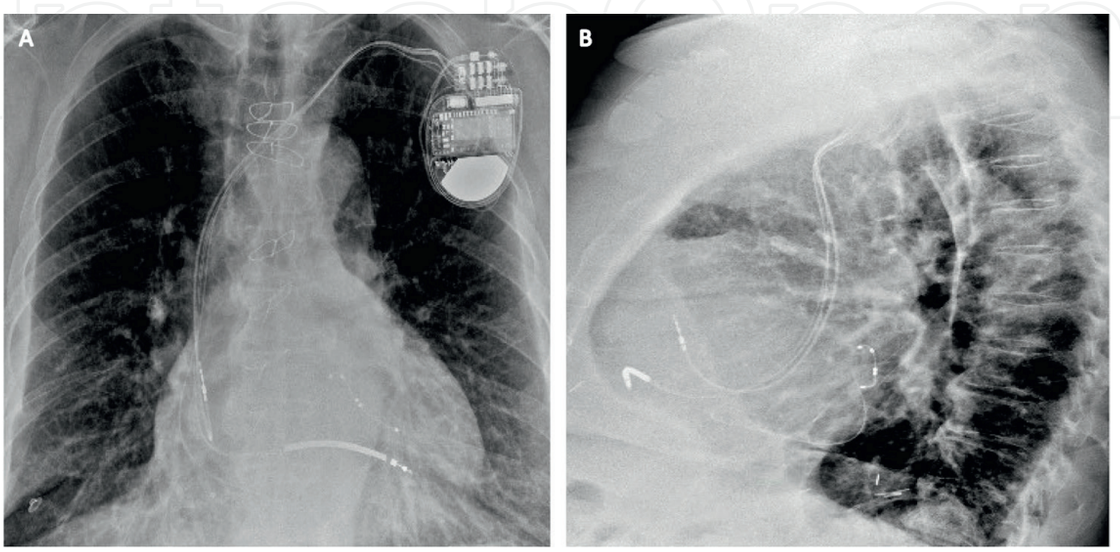

Figure 6.
CXR of CRT. An anteroposterior and lateral view showing the leads in the right atrium, right ventricle and a quadripolar left ventricular pacing lead through the coronary sinus.

was not different between the normal sinus and AF patients undergoing CRT [54]. Most recent ACCF/AHA/HRS guidelines recommend CRT for AF patients that a) otherwise meet CRT criteria as above and b) AV nodal ablation or pharmacologic rate control will achieve near 100% ventricular pacing with CRT (class IIa) [52].

5.4 Conductive system pacing

International guidelines for pacing currently recommend the above conventional myocardial pacing whereby slow-conducting myocytes are activated and therefore only indirectly activate the fast-conductive cardiac tissue (i.e. His-Purkinje network). Direct conduction system pacing (CSP) is emerging as an alternative approach to myocardial pacing; by directly activating conductive tissue, CSP has the theoretical benefit of mitigating electrical and mechanical ventricular desynchrony.

Two methods of CSP that have garnered attention are His Bundle Pacing (HBP) whereby a lead is inserted proximally close to His bundle, and Left Bundle Branch area Pacing (LBBaP) whereby a lead is inserted more distally close to the LBB (**Figure 7**). Wang et al. recently showed that HBP was feasible and safe with improvements in LVEF in patients with persistent AF and HFrEF who indicated implantable cardioverter defibrillator [55]. Abdelrahman et al. showed that patients with HBP had better survival and heart failure hospitalization rates compared to conventional RV pacing [56]. While HBP can be effective, it can be technically challenging given the small target area for lead placement, with longer procedure times even amongst experienced electrophysiologists compared to conventional pacing [57]. Furthermore, HBP has higher rates of lead dislodgement, up to twice as compared to conventional RV pacing [58]. LBBaP may be a better alternative in some patient populations. For instance, in patients requiring AV node ablation LBBaP is technically less challenging and pacing output to correct the left bundle branch block is lower. However, given the relative recency of CSP, there is currently a paucity of data including complications, such that international cardiology societies have yet to make recommendations [59].

One possible advantage of CSP over conventional pacing is the concept of synchrony. While right ventricular pacing is effective for the treatment of bradycardia and syncope, this approach can lead to electrical and mechanical desynchrony (particularly between ventricles) with the remodeling of the heart long-term; the broad consequences are higher rates of atrial fibrillation, heart failure and mortality [60, 61]. As previously described, Cardiac Resynchronization therapy (CRT) can mitigate hemodynamic and structural complications associated with only right ventricular pacing. Clinical trials have demonstrated that CRT reverses remodeling, and improves left ventricular ejection fraction (LVEF) and overall mortality in patients with reduced ejection fraction heart failure (HFrEF) [62, 63]. However, up to 40% of patients eligible for CRT demonstrate "non-response" (i.e. poor improvement in NYHA class, QRS duration, or echocardiographic parameters) [64]. Furthermore, while conventional CRT does improve QRS duration, it does not return it to a range seen in patients with intact conduction tissue, suggesting better therapeutic benefits with shorter QRS [65]. Whether CSP can be used as an alternative to, or as rescue therapy for patients with an indication for CRT remains to be seen. Several centers, including our own, are undergoing trials to address this question.

5.5 Tricuspid regurgitation following pacing

As mentioned in Section 4.3, TR is an independent cause of mortality [66]. Pacemaker-associated TR can be primary TR by direct damage of the tricuspid valve by leads, secondary TR by RV dilation and dysfunction due to pacemaker

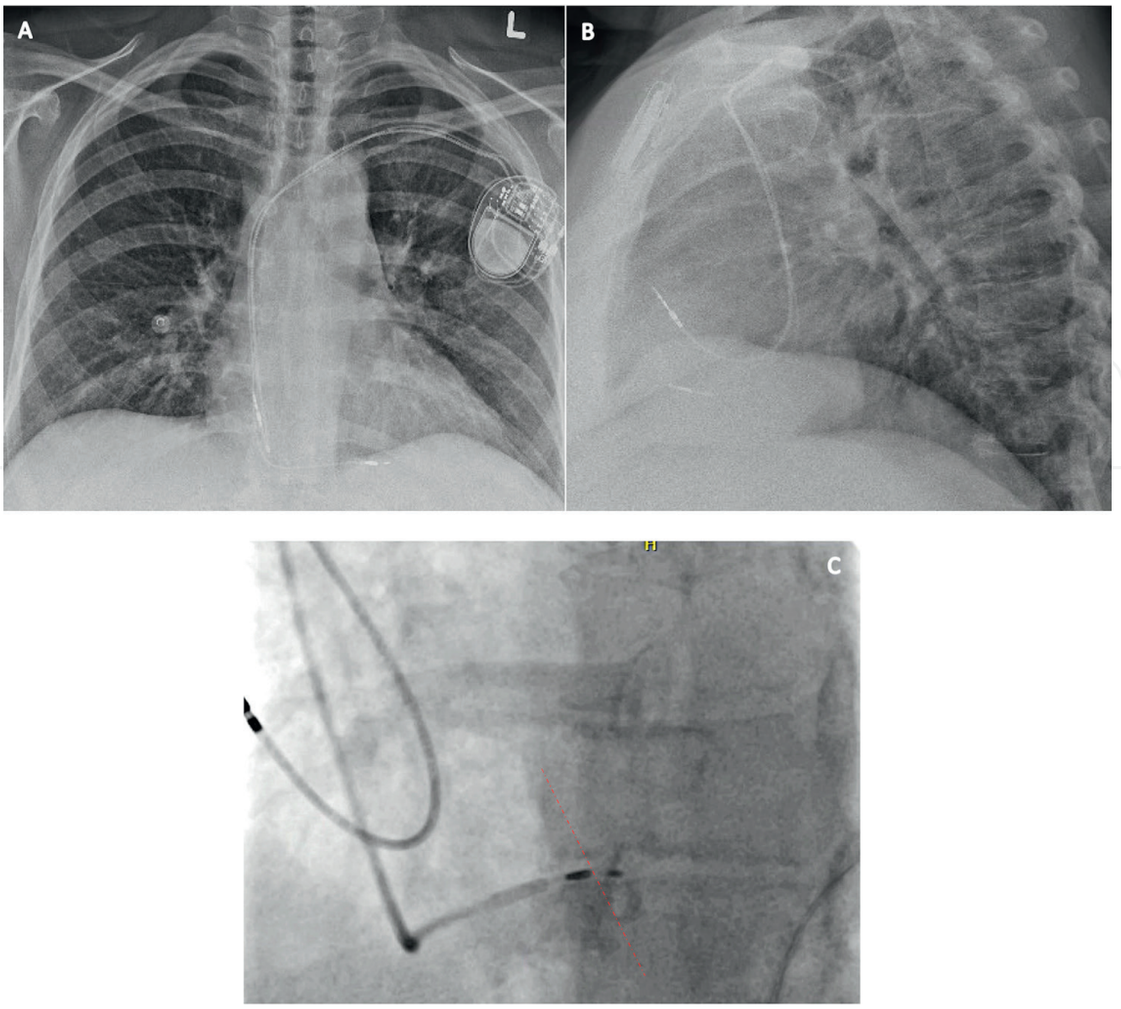

Figure 7.
CXR of dual chamber pacemaker. An anteroposterior and lateral view showing the position of a dual chamber pacemaker. RV lead is placed in the apical position (A) in comparison to placement at the region of LBBAP (B). Contrast injection through the delivery sheath showing the lead penetrating the RV septum to successfully deliver LBBAP.

cardiomyopathy, or a combination of both. As TR is a major complication of pacing, prevention of TR is an important consideration.

Leadless pacemakers (see 5.2) have the theoretical benefit of minimizing primary damage to the tricuspid valve. However, Beurskens et al. showed that 12-month follow-up for leadless pacing had comparable rates of TR to the dual-chamber paced group, suggesting that lead-related damage to the tricuspid valve may not be the primary mechanism of TR following pacing [67]. The TR observed in leadless pacing may be due to RV dysfunction from pacemaker cardiomyopathy or damage to the tricuspid apparatus while crossing the tricuspid valve during implantation [68]. One way to avoid tricuspid apparatus entirely is to implant lead into the left ventricle via the coronary sinus. Schliefer et al. tested this hypothesis in a prospective trial comparing rates of TR at 12 months between pacing at RV-apex vs. RV-septum vs. LV-coronary sinus; coronary sinus pacing failed to achieve a statistically significant reduction of TR [69]. More studies over longer follow-ups are required to verify these findings.

6. Conclusion

Given the aging population of the Western world, the burden of Valvular Heart Diseases is predicted to increase. Advancement and development of new

percutaneous valvular interventions have been a boon for patients, particularly those deemed to be poor surgical candidates. Alongside these percutaneous valvular interventions are increased rates of CSDs, often requiring artificial pacing. Pacing techniques have also seen rapid advancements, with the advent of CRT, leadless pacing and conductive tissue pacing. Each of these has merit and warrants further research, particularly in the need to tailor different pacing modalities to different valvular interventions.

Abbreviations

AF	Atrial Fibrillation
AVN	Atrioventricular Node
AVB	Atrioventricular Block
CRT	cardiac resynchronization therapy
CSD	conduction system disorder
CSP	conduction system pacing
HBP	His Bundle Pacing
HFrEF	heart failure with reduced ejection fraction
LA	Left Atrium
LBBaP	Left Bundle Branch area Pacing
LBBB	Left Bundle Branch Block
LVEF	left ventricular ejection fraction
MV	Mitral valve
NYHA	New York Heart Association
RA	Right Atrium
RBBB	Right Bundle Branch Block
SA	Sinoatrial Node
SAVR	Surgical Aortic Valve Replacement
SND	Sinus Node Dysfunction
SVC	Superior Vena Cava
TAVR	Transcatheter aortic valve replacement
TEER	transcatheter edge-to-edge repair
TMVR	Transcatheter Mitral Valve Replacement
TR	Tricuspid Regurgitation
TTVI	Transcatheter Tricuspid Valve Interventions
VHD	Valvular Heart Disease

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References

[1] Iung B, Vahanian A. Epidemiology of valvular heart disease in the adult. Nature Reviews. Cardiology. 2011;**8**:162-172

[2] Sick Sinus Syndrome: A Review. Available from: https://www.aafp.org/pubs/afp/issues/2013/0515/p691.html. [Accessed: July 17, 2022]

[3] Cheng S, Keyes MJ, Larson MG, McCabe EL, Newton-Cheh C, Levy D, et al. Long-term outcomes in individuals with prolonged PR interval or first-degree atrioventricular block. JAMA. 2009;**301**:2571-2577

[4] Nikoo MH, Aslani A, Jorat MV. LBBB: State-of-the-art criteria. International Cardiovascular Research Journal. 2013;**7**:39

[5] Francia P, Balla C, Paneni F, Volpe M. Left bundle-branch block—Pathophysiology, prognosis, and clinical management. Clinical Cardiology. 2007;**30**:110-115

[6] Gregoratos G, Abrams J, Epstein AE, Freedman RA, Hayes DL, Hlatky MA, et al. ACC/AHA/NASPE 2002 guideline update for implantation of cardiac pacemakers and Antiarrhythmia devices: Summary article. A report of the American College of Cardiology/American Heart Association task force on practice guidelines (ACC/AHA/NASPE committee to update the 1998 pacemaker guidelines). Circulation. 2002;**106**:2145-2161

[7] Kourkoveli P, Spargias K, Hahalis G. Perspective open access • TAVR in 2017-what we know? What to expect? Journal of Geriatric Cardiology. 2018;**15**:55-60

[8] Kolte D, Vlahakes GJ, Palacios IF, Sakhuja R, Passeri JJ, Inglessis I, et al. Transcatheter versus surgical aortic valve replacement in low-risk patients. Journal of the American College of Cardiology. 2019;**74**:1532-1540

[9] Siontis GCM, Overtchouk P, Cahill TJ, Modine T, Prendergast B, Praz F, et al. Transcatheter aortic valve implantation vs. surgical aortic valve replacement for treatment of symptomatic severe aortic stenosis: An updated meta-analysis. European Heart Journal. 2019;**40**:3143-3153

[10] Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin JP, Gentile F, et al. 2020 ACC/AHA guideline for the Management of Patients with Valvular Heart Disease: A report of the American College of Cardiology/American Heart Association joint committee on clinical practice guidelines. Circulation, 2021; 143: E72–E227.

[11] Lee HA, Chou AH, Wu VCC, Chen DY, Lee HF, Lee KT, et al. Balloon-expandable versus self-expanding transcatheter aortic valve replacement for bioprosthetic dysfunction: A systematic review and meta-analysis. PLoS One. 2020;**15**:e0233894

[12] van Belle E, Vincent F, Labreuche J, Auffret V, Debry N, Lefèvre T, et al. Balloon-expandable versus self-expanding Transcatheter aortic valve replacement. Circulation. 2020;**141**:243-259

[13] Ullah W, Zahid S, Zaidi SR, Sarvepalli D, Haq S, Roomi S, et al. Predictors of permanent pacemaker implantation in patients undergoing Transcatheter aortic valve replacement - a systematic review and meta-analysis. Journal of the American Heart Association. 2021;**10**:20906

[14] Nazif TM, Dizon JM, Hahn RT, Xu K, Babaliaros V, Douglas PS, et al. 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

[15] Kiani S, Kamioka N, Black GB, Lu MLR, Lisko JC, Rao B, et al. Development of a risk score to predict new pacemaker implantation after Transcatheter aortic valve replacement. JACC. Cardiovascular Interventions. 2019;**12**:2133-2142

[16] Limongelli G, Ducceschi V, D'Andrea A, Renzulli A, Sarubbi B, de Feo M, et al. Risk factors for pacemaker implantation following aortic valve replacement: A single Centre experience. Heart. 2003;**89**:901-904

[17] Bagur R, Manazzoni JM, Dumont É, Doyle D, Perron J, Dagenais F, et al. Permanent pacemaker implantation following isolated aortic valve replacement in a large cohort of elderly patients with severe aortic stenosis. Heart. 2011;**97**:1687-1694

[18] van Mieghem NM, Head SJ, de Jong W, van Domburg RT, Serruys PW, de Jaegere PP, et al. Persistent annual permanent pacemaker implantation rate after surgical aortic valve replacement in patients with severe aortic stenosis. The Annals of Thoracic Surgery. 2012;**94**:1143-1149

[19] Meco M, Montisci A, Miceli A, Panisi P, Donatelli F, Cirri S, et al. Sutureless perceval aortic valve versus conventional stented bioprostheses: Meta-analysis of postoperative and midterm results in isolated aortic valve replacement. Journal of the American Heart Association. 2018;**7**:e006091. DOI: 10.1161/JAHA.117.006091

[20] Hurley ET, O'Sullivan KE, Segurado R, Hurley JP. A meta-analysis examining differences in short-term outcomes between Sutureless and conventional aortic valve prostheses. Innovations (Phila). 2015;**10**:375-382

[21] Phan K, Tsai Y-C, Niranjan N, Bouchard D, Carrel TP, Dapunt OE, et al. Sutureless aortic valve replacement: A systematic review and meta-analysis. Annals of Cardiothoracic Surgery. 2015;**4**:e46

[22] Muneretto C, Solinas M, Folliguet T, di Bartolomeo R, Repossini A, Laborde F, et al. Sutureless versus transcatheter aortic valves in elderly patients with aortic stenosis at intermediate risk: A multi-institutional study. The Journal of Thoracic and Cardiovascular Surgery. 2022;**163**:925-935.e5

[23] Muneretto C, Alfieri O, Cesana BM, Bisleri G, de Bonis M, di Bartolomeo R, et al. A comparison of conventional surgery, transcatheter aortic valve replacement, and sutureless valves in "real-world" patients with aortic stenosis and intermediate- to high-risk profile. The Journal of Thoracic and Cardiovascular Surgery. 2015;**150**:1570-1579

[24] Abdel-Wahab M, Fujita B, Frerker C, Bauer T, Beckmann A, Bekeredjian R, et al. Transcatheter versus rapid-deployment aortic valve replacement: A propensity-matched analysis from the German aortic valve registry. Cardiovascular Interventions. 2020;**13**:2642-2654

[25] Leon MB, Mack MJ, Hahn RT, Thourani VH, Makkar R, Kodali SK, et al. Outcomes 2 years after Transcatheter aortic valve replacement in patients at low surgical risk. Journal of the American College of Cardiology. 2021;**77**:1149-1161

[26] Berdajs D, Schurr UP, Wagner A, Seifert B, Turina MI, Genoni M. Incidence and pathophysiology of atrioventricular block following mitral valve replacement and ring annuloplasty. European Journal of Cardio-Thoracic Surgery. 2008;**34**(1):55-61. DOI: 10.1016/j.ejcts.2008.03.051

[27] Meimoun P, Zeghdi R, D'Attelis N, Berrebi A, Braunberger E, Deloche A, et al. Frequency, predictors, and consequences of atrioventricular block after mitral valve repair. The American Journal of Cardiology. 2002;**89**:1062-1066

[28] Leyva F, Qiu T, Mcnulty D, Evison F, Marshall H, Gasparini M. Long-term requirement for pacemaker implantation after cardiac valve replacement surgery. Heart Rhythm. 2017;**14, 4**:529-534. DOI: 10.1016/j.hrthm.2016.11.029

[29] Merin O, Ilan M, Oren A, Fink D, Deeb M, Bitran D, et al. Permanent pacemaker implantation following cardiac surgery: Indications and long-term follow-up. Pacing and Clinical Electrophysiology. 2009;**32**:7-12

[30] Ghauri H, Iqbal R, Ahmed S, Ashraf A, Khan MSQ, Malik J, et al. Predictors of permanent pacemaker insertion after mitral valve replacement: A systematic review. PACE - Pacing and Clinical Electrophysiology. 2022;**45**:681-687

[31] Erinne I, Theertham AK, Maleki K, Chen C, Russo M, Hakeem A. Complete atrioventricular block: A rare complication of MitraClip implantation. JACC Case Reports. 2021;**3**:772-777

[32] Alkhouli M, Alqahtani F, Aljohani S. Transcatheter mitral valve replacement: An evolution of a revolution. Journal of Thoracic Disease. 2017;**9**:S668-S672

[33] Bapat V, Rajagopal V, Meduri C, Farivar RS, Walton A, Duffy SJ, et al. Early experience with new Transcatheter mitral valve replacement. Journal of the American College of Cardiology. 2018;**71**:12-21

[34] Webb JG, Murdoch DJ, Boone RH, Moss R, Attinger-Toller A, Blanke P, et al. Percutaneous Transcatheter mitral valve replacement: First-in-human experience with a new Transseptal system. Journal of the American College of Cardiology. 2019;**73**:1239-1246

[35] Makkar R, O'Neill W, Whisenant B, Guerrero M, Feldman T, Rihal C, et al. TCT-8 updated 30-day outcomes for the U.S. early feasibility study of the SAPIEN M3 transcatheter mitral valve replacement system. Journal of the American College of Cardiology. 2019;**74**:B8

[36] Nath J, Foster E, Heidenreich PA. Impact of tricuspid regurgitation on long-term survival. Journal of the American College of Cardiology. 2004;**43**:405-409

[37] Dreyfus J, Ghalem N, Garbarz E, Cimadevilla C, Nataf P, Vahanian A, et al. Timing of referral of patients with severe isolated tricuspid valve regurgitation to surgeons (from a French Nationwide database). The American Journal of Cardiology. 2018;**122**:323-326

[38] Riesenhuber M, Spannbauer A, Gwechenberger M, Pezawas T, Schukro C, Stix G, et al. Pacemaker lead-associated tricuspid regurgitation in patients with or without pre-existing right ventricular dilatation. Clinical Research in Cardiology. 2021;**110**:884-894

[39] Hahn RT, Kodali S, Fam N, Bapat V, Bartus K, Rodés-Cabau J, et al. Early multinational experience of Transcatheter tricuspid valve replacement for treating severe tricuspid regurgitation. JACC. Cardiovascular Interventions. 2020;**13**:2482-2493

[40] Kar S, Noureddin N, Aboulhosn J, Mahmzi Y, Coluzzi A, Tobis J, et al. Rapid pacing using the guidewire during Transcatheter tricuspid valve in valve implantation. Journal of Structural Heart Disease. 2017;**3**:157-162

[41] Bradshaw PJ, Stobie P, Knuiman MW, Briffa TG, Hobbs MST. Trends in the incidence and prevalence of cardiac pacemaker insertions in an ageing population. Open Heart. 2014;**1**:e000177. DOI: 10.1136/openhrt-2014-000177

[42] Verma N, Dandamudi S, Goldberger JJ, Lip GYH, Huffman MD. Dual chamber versus single chamber ventricular pacemakers for sick sinus syndrome and atrioventricular block. Cochrane Database of Systematic Reviews. 2004;**2004**:CD003710. DOI: 10.1002/14651858.CD003710.PUB2

[43] Toff WD, Camm AJ, Douglas J, Skehan MB. Single-chamber versus dual-chamber pacing for high-grade atrioventricular block. The New England Journal of Medicine. 2005;**353**:145-155. DOI: 101056/NEJMoa042283

[44] Vaidya VR, Dai M, Asirvatham SJ, Rea RF, Thome TM, Srivathsan K, et al. Real-world experience with leadless cardiac pacing. Pacing and Clinical Electrophysiology. 2019;**42**:366-373

[45] Ngo L, Nour D, Denman RA, Walters TE, Haqqani HM, Woodman RJ, et al. Safety and efficacy of leadless pacemakers: A systematic review and meta-analysis. Journal of the American Heart Association. 2021;**10**:19212

[46] Duray GZ, Ritter P, El-Chami M, Narasimhan C, Omar R, Tolosana JM, et al. Long-term performance of a transcatheter pacing system: 12-month results from the Micra Transcatheter pacing study. Heart Rhythm. 2017;**14**:702-709

[47] McIntosh RA, Ansari MI, Moon J, Khan HR. Delivery of cardiac resynchronization therapy via the left inferior phrenic vein: A case report. European Heart Journal - Case Reports. 2019:3, ytz144. DOI: 10.1093/ehjcr/ytz144

[48] Kuo-Wei Chiang C, Ka-Bo Chan W, So A, Yee R, Khan H. Utilizing preprocedural imaging and active fixation lead in cardiac resynchronization therapy device upgrade for persistent left superior vena cava. Heart Rhythm Case Reports. 2021;**8**:50-53

[49] Kanawati J, Kanawati AJ, Rowe MK, Khan H, Chan WK, Yee R. Utility of 3-D printing for cardiac resynchronization device implantation in congenital heart disease. Heart Rhythm Case Reports. 2020;**6**:754-756

[50] Bleeker GB, Schalij MJ, Molhoek SG, Verwey HF, Holman ER, Boersma E, et al. Relationship between QRS duration and left ventricular dyssynchrony in patients with end-stage heart failure. Journal of Cardiovascular Electrophysiology. 2004;**15**:544-549

[51] Cleland JGF, Daubert J-C, Erdmann E, Freemantle N, Gras D, Kappenberger L, et al. The effect of cardiac resynchronization on morbidity and mortality in heart failure. The New England Journal of Medicine. 2009;**352**:1539-1549. DOI: 101056/NEJMoa050496

[52] Nam EFT Jr, Tracy CM, Epstein AE, Chair V, Darbar D, et al. ACCF/AHA/HRS focused update ACCF/AHA/HRS focused update of the 2008 guidelines for device-based therapy of cardiac rhythm abnormalities a report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines and the Heart Rhythm Society. Journal of the American College of Cardiology. 2012;**126**:1784-1800

[53] Ousdigian KT, Borek PP, Koehler JL, Heywood JT, Ziegler PD, Wilkoff BL. The epidemic of inadequate biventricular pacing in patients with persistent or permanent atrial fibrillation and its association with

mortality. Circulation. Arrhythmia and Electrophysiology. 2014;**7**:370-376

[54] Mustafa U, Atkins J, Mina G, Dawson D, Vanchiere C, Duddyala N, et al. Outcomes of cardiac resynchronisation therapy in patients with heart failure with atrial fibrillation: A systematic review and meta-analysis of observational studies. Open Heart. 2019;**6**:e000937

[55] Lin J, Dai Y, Wang H, Li Y, Chen K, Zhang S. A comparison of left bundle branch pacing with his bundle pacing in a patient with heart failure and left bundle branch block. Heart Rhythm Case Reports. 2020;**6**:293

[56] Abdelrahman M, Subzposh FA, Beer D, Durr B, Naperkowski A, Sun H, et al. Clinical outcomes of his bundle pacing compared to right ventricular pacing. Journal of the American College of Cardiology. 2018;**71**:2319-2330

[57] Lewis AJM, Foley P, Whinnett Z, Keene D, Chandrasekaran B. His bundle pacing: A new strategy for physiological ventricular activation. Journal of the American Heart Association. 2019;**8**:10972

[58] Keene D, Arnold AD, Jastrzębski M, Burri H, Zweibel S, Crespo E, et al. His bundle pacing, learning curve, procedure characteristics, safety, and feasibility: Insights from a large international observational study. Journal of Cardiovascular Electrophysiology. 2019;**30**:1984-1993

[59] Glikson M, Nielsen JC, Kronborg MB, Michowitz Y, Auricchio A, Barbash IM, et al. 2021 ESC guidelines on cardiac pacing and cardiac resynchronization therapy. European Heart Journal. 2021;**42**(35):3427-3520. DOI: 10.1093/EURHEARTJ/EHAB364

[60] Brenyo A, Goldenberg I, Barsheshet A. The downside of right ventricular apical pacing. Indian Pacing and Electrophysiology Journal. 2012;**12**:102

[61] Lamas GA, Lee KL, Sweeney MO, Silverman R, Leon A, Yee R, et al. Ventricular pacing or dual-chamber pacing for sinus-node dysfunction. The New England Journal of Medicine. 2002;**346**:1854-1862

[62] Tang ASL, Wells GA, Talajic M, Arnold MO, Sheldon R, Connolly S, et al. Cardiac-resynchronization therapy for mild-to-moderate. Heart Failure. 2010;**363**:2385-2395. DOI: 101056/NEJMoa1009540

[63] Goldenberg I, Kutyifa V, Klein HU, Cannom DS, Brown MW, Dan A, et al. Survival with cardiac-resynchronization therapy in mild heart failure. New England Journal of Medicine. 2014;**370**:1694-1701

[64] Daubert C, Behar N, Martins RP, Mabo P, Leclercq C. Avoiding non-responders to cardiac resynchronization therapy: A practical guide. European Heart Journal. 2017;**38**:1463-1472

[65] Ali N, Shin MS, Whinnett Z. The emerging role of cardiac conduction system pacing as a treatment for heart failure. Current Heart Failure Reports. 2020;**17**:288

[66] Kanawati J, Ng ACC, Khan H, Yu C, Hyun K, Abed H, et al. Long-term follow-up of mortality and heart failure hospitalisation in patients with Intracardiac device-related tricuspid regurgitation. Heart, Lung & Circulation. 2021;**30**:692-697

[67] Beurskens NEG, Tjong FVY, de Bruin-Bon RHA, Dasselaar KJ, Kuijt WJ, Wilde AAM, et al. Impact of leadless pacemaker therapy on cardiac and atrioventricular valve function through 12 months of follow-up. Circulation. Arrhythmia and Electrophysiology.

2019;**12**:e007124. DOI: 10.1161/CIRCEP.118.007124

[68] Chang JD, Manning WJ, Ebrille E, Zimetbaum PJ. Tricuspid valve dysfunction following pacemaker or cardioverter-defibrillator implantation. Journal of the American College of Cardiology. 2017;**69**:2331-2341

[69] Schleifer JW, Pislaru SV, Lin G, Powell BD, Espinosa R, Koestler C, et al. Effect of ventricular pacing lead position on tricuspid regurgitation: A randomized prospective trial. Heart Rhythm. 2018;**15**:1009-1016