REVIEW ARTICLE

LONG-TERM IMPACT OF PERMANENT PACING AFTER MITRAL VALVE SURGERY: A SCOPING REVIEW OF CURRENT LITERATURE

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Abstract

Background: *Conduction disorders after mitral valve surgery (MVS) are frequent with a considerable percentage of patients requiring the implantation of a permanent pacemaker (PPM). This has been associated with prolonged hospital length of stay and increased resource utilization. In this scoping review, we consolidate the current evidence on the impact of PPM on late outcomes after MVS in terms of heart failure and mortality.*

Methods: *A comprehensive electronic literature search was conducted on Medline, EMBASE, Cochrane, ClinicalTrials.gov, and Google Scholar using the keywords ('mitral valve repair', 'mitral valve replacement', 'pacemaker implantation'). The search was performed in November 2023. Studies were included if they involved adults ≥18 years old who underwent MVS, reported the long-term outcomes of PPM implantation, and were observational or randomized control trials. Exclusion criteria included case series, case reports, conference abstracts, and non-English studies.*

Results: *Literature search identified 2263 citations, of which, four studies, with a total of 49,006 patients (of which, 38,063 underwent mitral valve procedures) were ultimately included in this review. The incidence of PPM after MVS ranged between 4.2-11.8%. Factors associated with higher PPM risk, including advanced age, concomitant surgical procedures, pre-existing atrial fibrillation, conduction disorders, and ischemic heart disease, were chosen for their consistent identification across multiple studies. Data was not conclusive on whether there was a correlation between PPM implantation and an increased risk of late congestive heart failure or mortality.*

Conclusions: *We did not find enough evidence to suggest that permanent pacing may have negative impact on late outcomes after mitral valve surgery. This may be explained by the heterogeneity of the included studies and the complex nature and multi-factorial etiology of post-surgical electric conduction disorders.*

INTRODUCTION

Mitral valve surgery (MVS) has been established as the gold-standard treatment for patients presenting with severe mitral valve pathology[1][2]. Given the close anatomical proximity of the mitral annulus to the atrioventricular conduction system, MVS procedures are frequently associated with atrioventricular block or or other conduction disturbances[3].

Preoperative predictors of early PPM include some demographic and clinical factors such as advanced age, prior history of myocardial infarction, pre-existing conduction and rhythm disturbances, left ventricular systolic dysfunction, diabetes mellitus, renal impairment, and active endocarditis[1][2]. Intraoperative factors such as longer cross-clamp and cardiopulmonary times have also been reported to correlate with an increased need for PPM. Postoperatively, electrolyte disturbances may also play an important role in the development of conduction abnormalities[3]. During the early postoperative period, PPM implantation can be associated with significant morbidity, prolonged postoperative total hospital length of stay, and significant resource utilization[4].

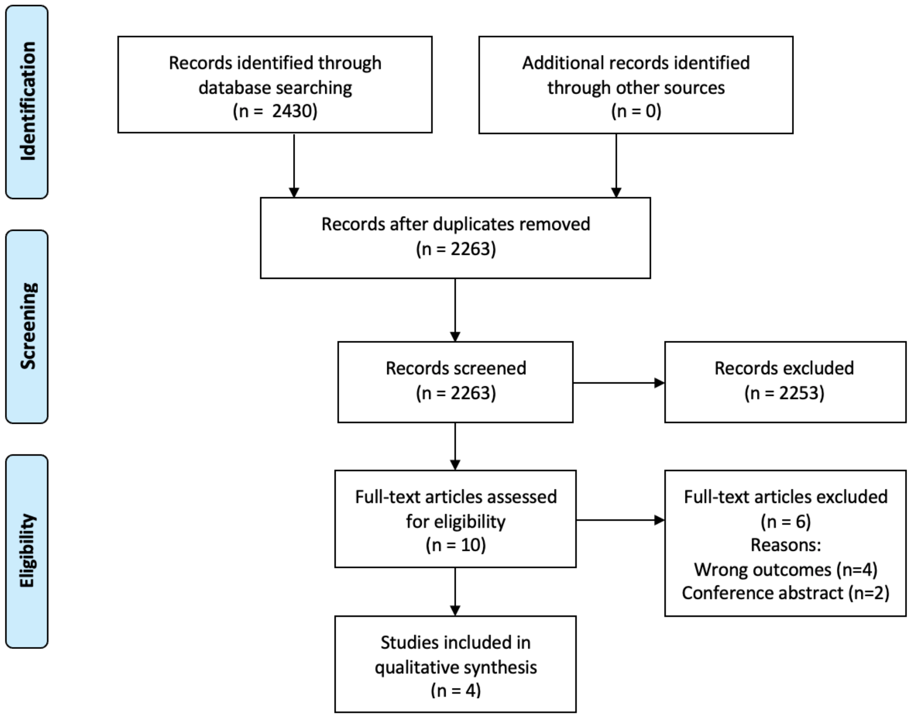

Figure 1 *PRISMA Diagram.*

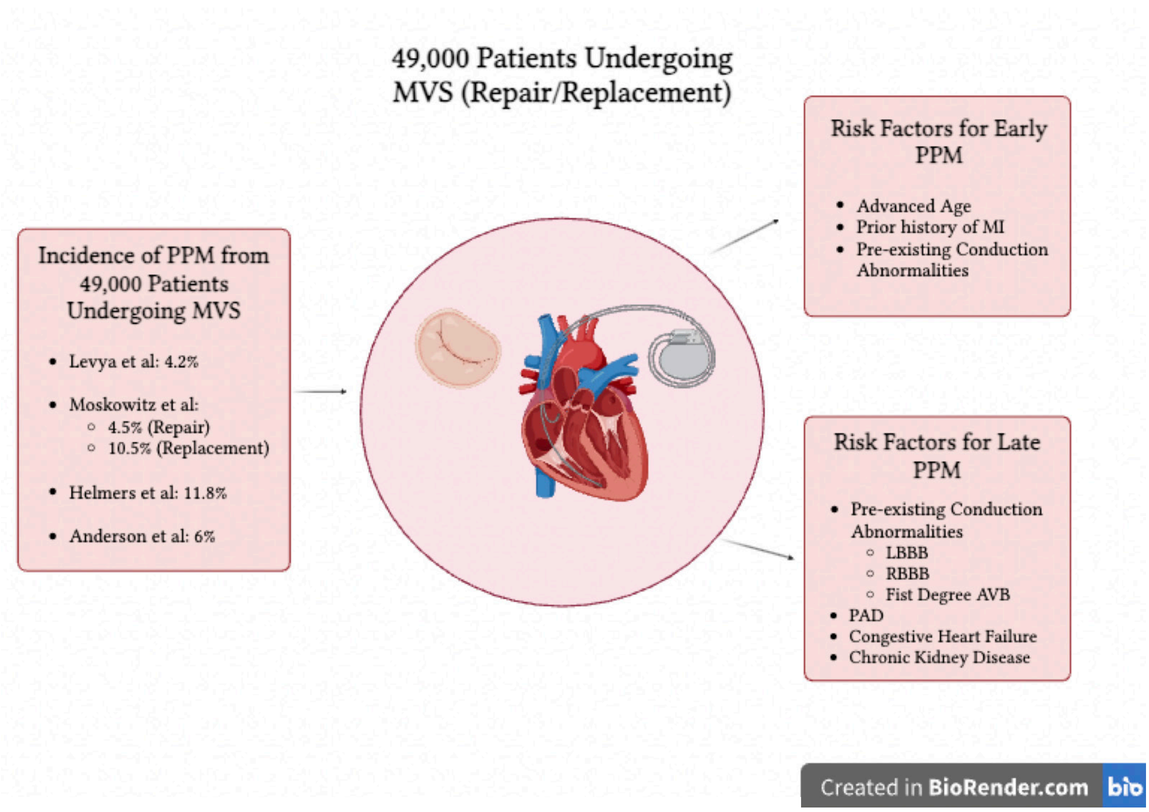

Figure 2 *Central Illustration.*
Abbreviations: Permanent pacemaker implantation (PPM), mitral valve surgery (MVS), left bundle branch block (LBBB), right bundle branch block (RBBB), atrioventricular block (AVB), peripheral artery disease (PAD)

In addition, pacemaker-related complications, such as insertion site hematoma, skin erosion, pocket infections, and lead displacement can occur in approximately 7% of patients[5]. Lastly, lead endocarditis is a common complication of PPM, especially in patients with additional intra-cardiac prosthesis[4].

Also, there is discrepancy in the reported rates of late PPM dependency after cardiac surgery [6]. This is mainly due to the lack of consensus on the definition and diagnosis of PPM dependency in these patients [7]. Furthermore, non-surgical patients with long-term PPM have been shown to develop multiple adverse effects such as tricuspid regurgitation, right ventricular dysfunction as a complication of right ventricular pacing, device related infections, bi-ventricular dyssynchrony, and congestive heart failure [4][2].

Current literature on the long-term impacts of PPM implantation post-cardiac surgery is heavily focused on patients undergoing surgical or percutaneous aortic valve procedures [5][8]. In addition, most of the studies reporting on PPM implantation post-MVS are mainly focused on presenting the risk factors for requiring PPM implantation without delving into the late outcomes in this group of patients[1][2]. Therefore, in this review, we aimed to consolidate the available evidence on long-term impacts of PPM implantation following MVS in terms of heart failure and mortality.

MATERIALS AND METHODS

Search Strategy

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) [9]. Study characteristics and results were independently extracted into a standardized form. A literature search was conducted by A.H on databases Medline, EMBASE, Cochrane, ClinicalTrials.gov, and Google Scholar for primary studies assessing the long-term impact of PPM following patients that have undergone MVS. The literature search consisted of a combination of relevant keywords, including 'mitral valve repair,' 'mitral valve replacement,' and 'pacemaker implantation.' Additional details on the search strategy can be consulted in supplemental material 1. The search was performed from the inception of the databases to November 31, 2023, and we also conducted backward snowballing by scanning the references included in the retrieved articles and other reviews.

Study selection and Outcomes

Identified papers underwent abstract screening followed by full-text review of potentially relevant articles independently by two (AES and NS) using Covidence® Systematic Review software (Veritas Health Innovation, Melbourne, Australia. Available at www.covidence.org). Discrepancies between reviewers were resolved by the senior author (MED). Eligible studies included: 1) observational studies or randomized control trials; 2) enrolled adults (≥18 years of age); 3) enrolled patients submitted to MVS; 4) reported the long-term outcomes of PPM following MVS, specifically long-term mortality and congestive heart failure. Studies that involved concomitant aortic valve or tricuspid valve procedures were [included/excluded], as these factors may independently affect conduction outcomes. Case series, case reports, conference abstracts, and non-English reports were excluded.

Data Extraction

A.E.S and A.H performed the data extraction, which included the study author, date of publication, study design, incidence of PPM, baseline demographics of the study population, relevant outcomes, and differences in PPM rates between mitral valve repair (MVr) and mitral valve replacement (MVR). This analysis aimed to assess whether the type of procedure influenced the incidence of PPM implantation. A study characteristics table was formed to summarize all the papers (Table 1).

RESULTS

General Findings of the Literature Search

The literature search identified 2263 citations, of which ten studies were eligible for full-text evaluation. Ultimately, four studies were included in this review (Figure 1). Across the four studies, a total of 49,006 patients were included. Of these, 38,063 (77.6%) underwent mitral valve procedures, including 29,591 (60.4%) who had mitral valve replacement (MVR) and 8,472 (17.3%) who had mitral valve repair (MVr). The remaining 10,943 patients (22.3%) underwent combined surgeries involving MVR or MVr with other valve procedures, such as aortic or tricuspid valve replacements. Three studies were retrospective: Andersson et al. (n=4072) [10], Leyva et al. (n=18,402) [11], and Moskowitz et al. (n=22,905) [2], while Helmers et al. (n=3391) [4] was prospective. The follow-up period ranged from 1 to 14 years across the studies. In Moskowitz et al., the total cohort included 22,905 patients who underwent various types of valve surgeries, including aortic and combined valve procedures. For this review, only the 14,686 patients who underwent isolated mitral valve procedures (MVR or MVr) were included, while outcomes for patients undergoing other types of valve surgeries were excluded to maintain consistency with the review's inclusion criteria. Detailed characteristics of each study, including population demographics and key findings, are presented in Table 1.

PPM Implantation Rates

The time range for PPM implantation was between 30 days to one year following MVS [10][4][11][2]. The incidence of PPM following MVS was 9.02% (4.2-11.8%)[10][4][11][2]. In Levya et al., which focused primarily on MVR (18,402 patients), PPM rates were reported for additional surgery types to provide comparative context: 4.2% for MVR, 3.5% for AVR, and 7.6% for combined AVR and MVR. However, only outcomes for patients undergoing MVR were included in this

Table 1 **Study characteristics.**

Study	Country and Year	Type of Study (Population)	Sample Size	Follow up (years)	# of patients	Males	PPM Rate (%)	Mortality (%)
Andersson et al. [10]	Denmark 2020	Retrospective (National Hospital Registry)	Total: 4072 MVR: 1743 MVr: 2329	5	4072	2724 (68%)	6.0	30 (PPM) vs. 27 (non-PPM), p=0.72
Helmers et al. [4]	USA 2021	Prospective (Institutional Database)	Total: 3391 MVR: 1227 MVr: 1941	5	3391	1932 (57%)	11.8	No significant difference
Leyva et al. [11]	England 2017	Retrospective (National Hospital Registry)	MVR: 18,402	14	18,402	8960 (49%)	9.3 (10 years)	45.5 (PPM) vs. 50.1 (non-PPM, 10 years)
Moskowitz et al. [2]	United States 1996-2014	Retrospective (New York hospital registry)	Total: 22905 MVR: 8219 MVr: 4202	1	14686	5841 (40%)	10.5	Not reported

MVR: Mitral Valve Replacement, MVr: Mitral Valve Repair

Table 2 **Study findings.**

Study	Risk Factors for PPM	General Conclusion
Andersson et al. 2020 [10]	Increased Age, Concomitant Aortic valve surgery (CAVR), ischemic heart disease, atrial fibrillation	PPM placement did not alter the long-term risks of heart failure and mortality following MV surgery
Helmers et al. 2021 [4]	Increased Age, CAVR, tricuspid valve procedures, history of myocardial infarction	PPM placement was not independent predictor of 5-year mortality post mitral surgery
Levya et al. 2017 [11]	Increased Age, male sex, emergency admission, pre-existing diabetes mellitus, renal impairment, heart failure	Total mortality was higher in MVS than AVR and highest in those with dual and triple valve replacements. Valve replacement surgery was associated with a long-term risk of PPM
Moskowitz et al. 2019 [2]	Increased age, history of arrhythmias, pre-operative conduction disturbances, CAVR, chronic comorbidities beyond 30 days.	1-year PPM rate was 4.5%, MVS was associated with lowest risk of PPM.

Abbreviations: PPM: Permanent Pacemaker, MVS: Mitral Valve Surgery, MV: Mitral Valve, MVR: Mitral Valve Replacement, MVr: Mitral Valve Repair, CAVR: Concomitant Aortic Valve Replacement, AVR: Aortic Valve Replacement.

review, consistent with the inclusion criteria."[11]. Similarly, in the study by Moskowitz et al., the PPM rate was 4.5% after mitral valve repair, 6.6% after AVR, 9.3% after AVR plus mitral valve repair, 10.5% after mitral valve replacement, and 13.3% after AVR plus mitral valve replacement [2]. The majority of PPM implantations occurred during the index hospitalization. In the studies by Helmers et al. and Anderson et al., up to 11.8% and 6% of MVS patients received post-operative PPM, respectively. Predictors of PPM implantation that were described in these studies can be found in Table 2[10][4].

MORTALITY

In their study, Helmers et al reported that five-year survival rates were similar between the PPM and non-PPM group (p=0.25) [4]. Similarly, Andersson et al. reported 5-year mortality rates (30% in the PPM group vs. 27% in the non-PPM group, p=0.72) [10]. In Leyva et al., mortality rates were higher in patients requiring PPM post-surgery, with 30-day mortality at 2.6% for those with PPM compared to 1.7% without PPM; however, this difference was not statistically significant (p=.72).[11]. Mortality was not reported in Moskowitz et al. [2].

Long-Term Survival

Long-term survival outcomes varied across the included studies. Leyva et al. reported that long-term survival was lower in the PPM group compared to the non-PPM group, with survival rates of 72.7% at 5 years and 45.5% at 10 years versus 76.1% at 5 years and 50.1% at 10 years, respectively [11]. In contrast, Helmers et al., the only prospective study included in this review (n=3,391), provided more robust findings. The study reported that long-term survival rates were similar between PPM and non-PPM groups, with PPM implantation not independently predicting mortality (p>0.05)[4]. These discrepancies in survival outcomes may reflect differences in study design, population characteristics, or evolving surgical and postoperative management practices.

Heart Failure

In their study, Andersson et al. did not observe an overall increased risk of long-term heart failure in patients with versus without PPM implantation[10]. However, a subgroup analysis revealed that patients who had a PPM implanted more than 30 days post-surgery exhibited a greater risk of developing heart failure compared to patients without PPM. This finding suggests that the timing of PPM implantation may influence outcomes, with late PPM implantation potentially reflecting more severe baseline conduction disorders or progressive cardiac dysfunction. Similarly, Leyva et al., the largest study included in this review (n=18,402) and retrospective in design, reported no significant difference in readmission rates due to heart failure between PPM and non-PPM groups [11]. Among patients who received a postoperative PPM, those who underwent MVR showed higher rates of heart failure compared to those who underwent MVr (p≤.02), as reported in multiple studies

Mitral Valve Repair vs Replacement

Helmers et al. found that in the PPM cohort, mitral valve replacements were notably more common (35.4% vs 63.3%, P<0.001), with valve replacement identified as a significant risk factor for PPM implantation in this populations[4]. Similarly, Anderson et al. reported that patients with PPM were more likely to undergo mitral valve replacement than repair. In addition, patients who underwent valve replacement showed higher rates of heart failure and mortality compared to those who underwent mitral valve repair (P≤.02) [10].

DISCUSSION

The final patient number included in this review is substantial, with 49,006 patients analyzed across four studies. Given that the incidence of PPM following MVS reaches up to 10% in some studies, this large sample size provides a robust dataset to identify trends and draw meaningful conclusions about PPM incidence and its associated outcomes. This extensive dataset strengthens the generalizability of the findings, despite the variability in study designs and populations.

Conduction abnormalities after MVS are common and can happen in up to 23.7% of the patients [12]. Across the four studies included in this review, risk factors for early PPM insertion included advanced age as well as a prior history of myocardial infarction or conduction abnormalities [10][4][11][2]. This can potentially be explained by the advanced degree of fibrosis, calcification, and ischemia in the conduction systems of these patients which may predispose to postoperative conduction abnormalities. Also, PPM rates were higher in patients who underwent multiple valve procedures, which can be explained by the wider extent of surgical trauma to the aorto-mitral curtain area, the direct conduction tissue damage, and longer ischemia and aortic cross-clamp times [10][4][11][2].

Helmers et al.[4] reported the highest rate of PPM implantation (11.8%) among the studies included in this review, despite being the only prospective study. Notably, this study also found no significant difference in mortality between PPM and non-PPM groups. This discrepancy may be explained by several factors.

First, Helmers et al.[4] included a relatively higher proportion of patients undergoing concomitant valve procedures, such as aortic and tricuspid valve surgeries, which are known to increase the risk of conduction disturbances and subsequent PPM implantation. Second, as a more recent study, it may reflect advancements in surgical techniques and postoperative management. For example, the study showed a higher proportion of mitral valve repair (MVr) compared to replacement (MVR), which is associated with lower mortality and better long-term outcomes. This shift toward MVr may contribute to the lack of observed mortality difference in this cohort [4].

The prospective nature of Helmers et al.[4] also allows for better control of confounders and more accurate outcome tracking compared to retrospective designs, potentially offering a more reliable assessment of the true relationship between PPM implantation and mortality. Nonetheless, the higher PPM rate warrants further investigation to determine whether it reflects differences in patient population, procedural complexity, or evolving surgical preferences.

In addition, there is an incremental yearly risk for requiring PPM after MVS beyond the initial surgical phase with baseline conduction anomalies, such as left bundle branch block, right bundle branch block, or first-degree atrioventricular (AV) block, being reported as important predictors for late conduction disorders[13][14]. High percentages of ventricular pacing, especially with right ventricular pacing, are strongly associated with pacing-induced dyssynchrony, which can exacerbate left ventricular dysfunction and increase the risk of heart failure. For example, studies have demonstrated that patients with persistent pacing reliance, especially those with over 40% ventricular pacing, exhibit higher rates of heart failure progression due to reduced cardiac efficiency and mechanical dyssynchrony. This underscores the importance of adopting strategies such as left bundle branch area pacing, which minimizes dyssynchrony, or resynchronization therapy in high-risk patients [15]. Other risk factors for late PPM implantation, reported as PPM implanted between 31 days and one year after hospitalization, were identified in the study by Moskowitz et al., and included peripheral artery disease, congestive heart failure, chronic kidney disease, and history of cardiac arrhythmias [2].

However, it is generally accepted that not all patients who received a PPM will continue to be pacing-dependent in the future and it is challenging to know the exact percentage due to several reasons [6]. For instance, there is substantial variability in the existing literature concerning definitions of PPM dependency. This includes differences in the criteria used to define PPM dependency, such as the absence of an underlying escape rhythm after cessation of ventricular pacing, symptoms despite an escape rhythm, or quantifying a minimum percentage of paced ventricular events over a preceding interval during device interrogation[6]. Also, the length of the follow-up period in studies varies considerably, influencing the reported rates of pacemaker dependency. In addition, a significant proportion of patients who received PPM for postoperative bradyarrhythmias have been observed to spontaneously recover native conduction, which eliminates the need for continued pacing, however, it remains unclear what proportion of patients with recovered native conduction undergo pacemaker and lead extraction versus continuing to live with the device implanted, even when it is no longer necessary[6].

Many reports have described long-term infectious complications of permanent pacing such as lead-related endocarditis or PPM pocket/device infection[15]. Also, there are multiple long-term pacing-related complications that may develop independently of the initial indication for PPM and may be associated with a higher risk for late morbidity and mortality[16]. These complications include pacemaker lead-related tricuspid valve regurgitation, right ventricular (RV) dilatation and dysfunction, mitral regurgitation, and LV dilatation and dysfunction [17][18][19]. Biventricular dyssynchrony is another important clinical condition that results from the non-physiological pattern of ventricular pacing and it can result in exacerbation of biventricular failure and subsequent mortality[20]. Finally, late-onset congestive heart failure was described as a significant risk factor for increased mortality after PPM implantation in the cardiac surgical population[21].

To mitigate the negative impact of chronic RV pacing, LV/RV re-synchronization therapy may be indicated to enhance cardiac function, improve heart failure symptoms, and lower the risk of mortality in this group of patients [22]. Additionally, physiological pacing is becoming an increasingly popular approach, with left bundle branch area pacing now more commonly adopted than His bundle pacing, as it offers improved feasibility and outcomes while still targeting the His-Purkinje system [23]. This technique has shown promising results in terms of improved cardiac function, lesser LV dyssynchrony, and lower risk for congestive heart failure [23].

Also, it is important to highlight that PPM recipients already had higher baseline comorbidities, making it unclear whether PPM is a true risk factor for adverse outcomes or it is merely a marker that reflects the higher comorbidity index in these patients [10][4][11][2]. Nonetheless, none of the studies in our review reported PPM to be associated with significantly increased mortality. This may suggest that the underlying comorbidities and post-surgical complications may be the primary drivers of long-term postoperative mortality after MVS rather that the implantation of PPM[24].

In terms of cost, the need for PPM can add a significant burden on available resources due to 1) the added cost of the pacing device, 2) the extended periods of hospital stay while awaiting the PPM implantation procedure, and 3) the cost of the operative procedure and staffing[4][25]. In the study by Yamamura et. al, PPM implantation in the operating room was associated with an added cost of $5,464 per patient [25]. Finally, complications related to PPM implantation, such as bleeding or infection, may result in a substantial prolongation in hospital stay and increased resource utilization, including the cost of the implantation procedure [25].

According to the 2021 guidelines by the European Society of Cardiology, a clinical observation period of at least 5 days is recommended in post-surgical patients to assess whether the rhythm disturbance is transient and resolves. However, in cases of complete atrioventricular block (AVB) with a low or absent escape rhythm where resolution is unlikely, this observation period can be shortened[26]. This duration may allow for the potential recovery of adequate rhythm. However, in patients who develop complete AV block in the first 24 hours after surgery that lasts for more than 48 hours, the likelihood of rhythm recovery over the following 1-2 weeks remains very low, therefore early implantation of PPM in these patients may be considered to reduce hospital stay and overall cost [26].

STUDY LIMITATIONS

Despite our review comprises data from more than 49,000 patients, only four studies were included. Three out of the four studies were retrospective studies which are subject to selection bias, misclassification of outcome bias, and loss to follow-up. Another limitation of our review is the reliance of the included studies on data collected from administrative databases therefore allowing for the possibility of inaccurate coding. In addition, since the implantation of defibrillators were not reported in these studies, patients who had dual indications for both defibrillation (either for primary or secondary prevention) and pacing were not captured. However, an important limitation of the included studies is the lack of detailed follow-up data. While all studies provided a general follow-up period ranging from 1 to 14 years, specifics on how many patients reached critical milestones (e.g., 5 years) and how many were lost to follow-up were not consistently reported. This variability in follow-up completeness could bias the long-term outcomes reported, particularly for mortality and heart failure rates. Future research should ensure comprehensive reporting of follow-up durations and patient retention to allow for more accurate comparisons and robust conclusions. Finally, we were unable to perform any meaningful statistical analysis between the studies due to the heterogeneity of the study design, the varying patient population, the type of mitral valve surgery (repair vs. replacement), and the inconsistencies in reporting studies outcomes.

CONCLUSIONS

We did not find enough evidence to suggest that permanent pacing may have negative impact on late outcomes after mitral valve surgery. This may be explained by the complex nature and multi-factorial etiology of post-surgical electric conduction disorders. Finally, the need for permanent pacing may reflect the co-morbid profile of these patients rather than being a predictor of mortality perse.

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