Long-term requirement for pacemaker implantation after cardiac valve replacement surgery

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BACKGROUND The risk of permanent pacemaker implantation (PPI) after cardiac valve replacement surgery is thought to be highest in the postoperative period. Long-term risks are uncertain.

OBJECTIVE The purpose of this study was to determine rates and timing of PPI after cardiac valve replacement surgery.

METHODS We compared PPI rates of patients undergoing aortic valve replacement (AVR; n = 111,674), mitral valve replacement (MVR; n = 18,402), AVR + MVR (n = 5166), AVR + MVR + tricuspid valve replacement (TVR; n = 114), or coronary artery bypass surgery without valve replacement (n = 249,742).

RESULTS Over a period of 14 years (median 3.9 years; interquartile range 6.3 years), cumulative PPI rates were 3.07–7.6 times higher ($P < .001$ for all) than those after coronary artery bypass surgery, depending on the number of valves replaced. PPI risks after AVR were higher that those after MVR (hazard ratio [HR] 1.22; 95% confidence interval [CI] 1.16–1.28), AVR + MVR (HR 1.52; 95% CI 1.40–1.65), and AVR + MVR + TVR (HR 2.22; 95% CI 1.40–3.53), independent of known confounders. Cumulative PPI hazard rates from the postoperative period to 10 years after surgery increased after AVR (4.22%–14.4%), MVR (4.38%–15.6%), AVR + MVR (5.59%–18.3%), and AVR + MVR + TVR (7.89%–25.9%) ($P < .001$ for all). Age, male sex, emergency admission, and preexisting diabetes mellitus, renal impairment, and heart failure were independent predictors of PPI ($P < .001$ for all).

CONCLUSION Valve replacement surgery was associated with a long-term risk of PPI. This was particularly high after dual and triple valve replacements. Age, male sex, emergency admission, and preexisting diabetes mellitus, heart failure, and renal impairment were independent predictors of PPI.

KEYWORDS Aortic valve replacement; Mitral valve replacement; Tricuspid valve replacement; Permanent pacemaker; Transcatheter aortic valve replacement

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Introduction

The proximity of the conduction system to the cardiac valves renders it susceptible to injury by valve disease and cardiac surgery. In 1935, Yater and Connell[1] described atrioventricular (AV) block in association with calcific aortic valve disease. In 1963, Sellers et al[2] first demonstrated injury to the conduction system during implantation of a mechanical aortic valve. Numerous studies[3–8] have since shown that surgical trauma can lead to permanent AV block requiring permanent pacemaker implantation (PPI).

Currently, a postoperative PPI rate of approximately 5% after valve operations is often quoted.[9,10] Intuitively, the risk of PPI is likely to increase with time after the operation and with increasing complexity of valve surgery. While some studies[6–8] have suggested that bradycardia occurs long after valve surgery, the long-term risk of PPI is uncertain. We hypothesized that the risk of bradycardia continues long after valve surgery and that this risk increases with the number of valves replaced. In this study, we explored rates of PPI after single, dual, and triple valve operations over a 14-year period. The control group consisted of patients undergoing coronary artery bypass surgery (CABG) without valve replacement.

Methods

Data sources

This is a nonrandomized retrospective study exploring conventional PPI practice and long-term survival after valve and CABG operations by using data extracted from the National Health Service Hospital Episode Statistics. This is a data warehouse containing details of all admissions to all National Health Service hospitals in England, including

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patient demographic characteristics, diagnoses, treatments, and services. Patients' unique encrypted identification number links clinical data in individual centers, but no personal identification is disclosed, in order to protect patient confidentiality. Mortality data were cross-linked with mortality data from the Office of National Statistics. As only pseudoanonymized information was used, ethics approval was not required. These data are available to University Hospital Birmingham under a data-sharing agreement (section 251 of the National Health Service Act 2006). The study was approved by the Clinical Audit Department at the Queen Elizabeth Hospital, Birmingham. The study conforms to the Declaration of Helsinki.

Our sample included patients undergoing valve replacement surgery or CABG between January 1, 2002, and January 30, 2016. An interest in this study was to explore whether an increasing number of valves replacements was associated with a higher risk of PPI. We first selected patients who had aortic valve replacement (AVR) or mitral valve replacement (MVR), and from these, we specified 4 groups: single AVR, single MVR, AVR + MVR, and AVR + MVR+ tricuspid valve replacement (TVR). Mitral and/or tricuspid valve annuloplasty and mitral valve repair were excluded. Patients with a preexisting PPI were also excluded. PPIs undertaken before discharge from hospital for the surgical hospitalization were considered "postoperative." Only data relating to the first valve replacement operation were used in analyses. Online Supplemental Appendix 1 lists the codes used according to the *International Statistical Classification of Diseases and Related Health Problems, 10th Revision*.

End points

The primary end point was time to a first PPI after surgery. Total mortality was the secondary end point. Survival times were calculated using linkage to date of death in the Office of National Statistics database.

Statistical analysis

Continuous variables are expressed as mean ± SD and compared using the Student *t* test. Categorical variables were compared using the χ^2 test.

Kaplan-Meier curves and the log-rank test were used to assess survival. Cox proportional hazards models were used to compare PPI risks between the different valve operations and the contribution of candidate predictors to the risk of PPI. Proportionality hypotheses were verified by visual examination of log (survival) graphs to ensure parallel slopes and by plotting Schoenfeld residuals. Statistical analyses were undertaken using Stata 14 (StataCorp LP, College Station, TX). A 2-sided *P* value of ≤.05 was considered statistically significant.

Results

Baseline characteristics

This study included a population of 135,356 patients undergoing their first AVR (n = 111,674), MVR (n = 18,402), AVR + MVR (n = 5166), or AVR + MVR + TVR (n = 114) over a period of 14 years in 176 centers in England. The control group consisted of 249,742 patients undergoing CABG without valve replacement surgery. Compared to other valve replacement groups (Table 1), patients undergoing AVR were older (20.6% were ≥80 years old) and were mostly men (63.4%) ($P < .001$ for group comparisons); they were more likely to be hypertensive (47.9%) and diabetic (14.3%) and less likely to have been hospitalized for surgery as an emergency (8.3%). In addition, they were less likely to have been hospitalized for heart failure (12.2%) ($P < .001$). More patients in the AVR group had concomitant CABG (34.4%; $P < .001$). Renal impairment was less prevalent in patients undergoing MVR (2.52%; $P < .001$).

Rate and timing of PPI

Rates of PPI and total mortality over the follow-up period are presented in Table 2 and Figure 1. Postoperative PPI cumulative rates were similar after AVR (4.22%) and MVR (4.38%) and higher after AVR + MVR (5.59%) and AVR + MVR + TVR (7.89%) ($P < .001$ for group comparisons). One year after surgery (Figure 2), PPI cumulative hazard rates were lowest for AVR (5.9%), followed by MVR (6.2%), AVR + MVR (8.3%), and AVR + MVR + TVR (11.2%) ($P < .001$). By year 10, PPI cumulative hazard rates increased to 14.4% for AVR, 15.6% for MVR, 18.3% for AVR + MVR, and 25.9% for AVR + MVR + TVR ($P < .001$). In contrast, PPI cumulative hazard rates for patients undergoing CABG increased from 0.67% to 5.11% over the same follow-up period.

Mortality

Total mortality was 26.8% for AVR, 30.1% for MVR, 36.8% for AVR + MVR, 39.5% for AVR + MVR + TVR, and 20.5% for CABG ($P < .001$ for group comparisons) (Figure 1 and Table 2).

Risk factors for PPI

In univariable analyses (Table 2), age, male sex, emergency admission, and preexisting diabetes, renal impairment, heart failure, and type of valve replacement (using AVR as reference) emerged as predictors of PPI ($P < .001$ for all). In multivariable analyses, age, male sex, emergency admission, diabetes mellitus, renal impairment, and heart failure emerged as independent predictors of PPI ($P < .001$ for all). There was a higher risk of PPI after MVR (hazard ratio [HR] 1.22; 95% confidence interval [CI] 1.16–1.28), AVR + MVR (HR 1.52; 95% CI 1.40–1.65), and AVR + MVR + TVR (HR 2.22; 95% CI 1.40–3.53) than after AVR, independent of potential confounders. PPI rates for CABG were 3.07–7.60 times higher than those for valve operations (Table 3), independent of potential confounders.

Discussion

This is the largest study of PPI rates after valve replacement surgery to date. Several findings have emerged. First, PPI