Outcome following valve surgery in Australia: development of an enhanced database module

E. Anne Russell, Christopher M Reid, Warren F Walsh, Alex Brown and Graeme P Maguire

Abstract

Background: Valvular heart disease, including rheumatic heart disease (RHD), is an important cause of heart disease globally. Management of advanced disease can include surgery and other interventions to repair or replace affected valves. This article summarises the methodology of a study that will incorporate enhanced data collection systems to provide additional insights into treatment choice and outcome for advanced valvular disease including that due to RHD.

Methods: An enhanced data collection system will be developed linking an existing Australian cardiac surgery registry to more detailed baseline co-morbidity, medication, echocardiographic and hospital separation data to identify predictors of morbidity and mortality outcome following valve surgery.

Discussion: This project aims to collect and incorporate more detailed information regarding pre and postoperative factors and subsequent morbidity. We will use this to provide additional insights into treatment choice and outcome.

Keyword: Indigenous health, Rheumatic heart disease, Valve surgery, Surgery timing, Outcome indicators

Background

Valvular heart disease can be congenital or acquired. Acquired disease can be either a result of aging or due to a disease process that damages valves. Management of valvular heart disease can involve a combination of medication, surgical repair or valve replacement with a mechanical or bioprosthetic valve. There were 9,276 heart valve repair or replacement procedures reported in Australia in the year 2013–14 [1]. From a clinician and patient perspective, the aim is to intervene at a time and in a way that ensures the lowest possible operative complications and mortality with the best short and long-term outcome.

A particular cause of acquired valvular heart disease is rheumatic heart disease (RHD). Whilst now rare in high income countries [2, 3], it remains a condition of global health importance and an important cause of preventable heart disease. In Australia RHD particularly affects Aboriginal and/or Torres Strait Islander peoples (Indigenous Australians) and older non-Indigenous Australians [4, 5].

We have previously analysed data [6] from the Australian and New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS) National Cardiac Surgery Database [7] and have identified differences in surgical management for RHD and non-RHD valve disease and for Aboriginal and/or Torres Strait Islander and non-Indigenous Australian patients [5]. In addition we have been able to identify factors associated with outcomes following valve surgery for RHD and non-RHD related valve disease [5, 6, 8].

The details of the Database have been outlined elsewhere [5]. Briefly it is an Australia-wide database for the collection and analysis of the results of cardiac surgery that collates data from Australian hospitals regarding patients who have undergone cardiac surgery, the type of surgery performed, early complications and 30 day mortality. In addition the Database is linked to the Australian National Death Index [9] to assess longer term survival. The Database commenced in 2001 with six surgical centres and currently encompasses 28 Australian sites.
Clinical registries such as this provide a minimum dataset related to the patient, the procedure and outcome. As such they are a valuable resource for informing clinical care, quality assurance activities and for research hypothesis generation. While the Database collects a range of pre-operative patient demographic, co-morbidity and outcome data it does not include prior medication use, detailed echocardiography measurements and non-lethal complications beyond 30 days post-procedure.

The medical management of advanced valvular disease can include anti-platelet and anti-coagulant medication, diuretics, angiotensin-converting enzyme (ACE) inhibitors [10], and beta blockers but it is unclear if these agents can influence early and longer term outcomes following surgery. In addition while valvular disease can be complicated by cardioembolism (e.g., stroke) [10] the influence of such a history prior to surgery on outcome, and how this may influence surgical choice, remains unclear.

Existing studies highlight the importance of echocardiographic assessment of the severity of valve disease and preoperative valve and heart function. Such data is currently not collected by the existing Database, in particular, left ventricular endsystolic (LVESD) and enddiastolic (LVEDD) diameter and pulmonary arterial systolic pressure (PASP).

Valve morphology has also been shown to predict outcome for those undergoing RHD-related mitral valve repair including the absence of deformity of the mitral valves leaflets and mitral valve prolapse [11] and maintenance of anterior mitral leaflet mobility [12].

Whilst longer-term survival beyond 30 days for the Database is determined from the National Death Index (NDI) [9], other outcomes are currently captured only to 30 days following surgery and only for the surgical site. Non-lethal longer term outcomes relevant to valve surgery include bleeding and thromboembolic complications, heart failure, endocarditis and reoperation.

Thromboembolic events reported in previous studies for follow-up to 7 years following surgery has ranged from none [13] to 5.9% [14] and for up to 10 years, 6% [14] to 24.7% [15] of mechanical valve replacement recipients and 7% [16] to 25% [17] of bioprosthetic valve recipients. Bleeding events have been reported as between 8.8% [17] and 52.6% [18]. The long term risk and burden of heart failure following valve surgery is poorly defined and earlier studies have demonstrated a significant risk of subsequent endocarditis [19].

Reporting of re-operation varies greatly. After a repaired mitral valve, this has ranged from none at 2 years [20] to 90% at 30 years [21], from 1% [22] at 9 years for all mitral valve replacements, 3.4% [14] at 5 years to 12.6% [23] at 25 years for mechanical valve replacement and 3.6% at 5 years [14] to 63% at 25 years [23] for bioprosthetic valve replacements.

### Table 1 Enhanced peri-operative data collection

| Pre-operative history | ICD 10 code [29] |
|-----------------------|------------------|
| Cerebrovascular diseases | I60-69 |
| Haemorrhagic | I60-62 |
| Ischaemic | I63 |
| Transitory ischaemic attack (TIA) | I65-66 |
| Bleeding | Eye: H21.00, H35.6 |
| | Digestive system: K22.11, K22.8, K25.4, K29.00, K29.01, K29.31, K29.41, K29.51, K29.61, K29.71, K29.81, K29.91, K62.5, K92.0, K92.1, K92.2 |
| | Circulatory system: I85.00, I85.01, I85.11, N93.00, N93.0, N93.9, N95.0, R04.0, R04.1 |
| | Genitourinary system: R04.89, R19.5, R58 |
| | Haemorrhagic disorder due to circulating anticoagulants: D68.3 |
| | IS0.9, IS0.0, IS0.1, IS1.5, IS1.0, IS1.9, IS1.30, IS1.32 |
| Heart failure | O74.2, O75.4, I97.1, I97.8, I25.5, O29.1, O89.1, I09.81, I27.89 |
| Endocarditis | B33.21, I01.1, I09.1, I33, I38, I39, I42.9 |
| Cardiac surgery (including type) | CABG: 0210 – 0213; |
| | Valve repair: aortic 02QF, mitral 02QG, pulmonary 02QH, tricuspid 02QJ |
| | Valve replacement: aortic 02RF, mitral 02RG, pulmonary 02RH, tricuspid 02RJ |
| | Percutaneous/trans-catheter valve replacement: 623, 628, 637, 634 |
| | Percutaneous valvuloplasty: 38270-01, 38270-02 |
| Arrhythmia | I44.0-9, I45.0-9, I480-9, I49.0-9, I97.8, I47.0, I48.1-9, M62.8 |
| | Pacemaker and/or defibrillator (insertion but not replacement, removal or adjustment): 38256-00/01, 38368-00, 38390-00/01/02, 38350-00, 90202-00/01/02, 38473-00/01, 38470-00/01, 38353-00, 38393-00 |
| | Pre-operative and discharge |
| Medication | Time period |
| Beta blocker | Pre-operative, on discharge |
| ACE Inhibitors | Pre-operative, on discharge |
| Angiotensin Receptor Blocker | Pre-operative, on discharge |
| Diuretic | Pre-operative, on discharge |
| Digoxin | Pre-operative, on discharge |
| Warfarin | Pre-operative, on discharge |
| NOAC (new oral anticoagulants) | Pre-operative, on discharge |
| Aspirin | Pre-operative, on discharge |
| Clopidogrel/Prasugrel/Ticagrelor | Pre-operative, on discharge |
This multicentre, enhanced surveillance system therefore aims to collect short and longer term outcome data to assist in predicting outcomes and providing evidence to inform the development of guidelines to facilitate consistent practice. Utilizing an enhanced data collection system it will collect and incorporate more detailed information regarding pre and postoperative factors at Australian sites that undertake both non-RHD and RHD-related surgery. It will use these more detailed data to provide additional insights into treatment choice and outcome for valve surgery in general and RHD specifically.

Information demonstrated to be important and relevant will be considered for future inclusion in the existing ANZSCCTS national cardiac surgery database to assist in predicting outcomes and providing evidence to inform the development of guidelines to facilitate consistent and evidence-based practice in the management of valve disease including for that relating to RHD [10].

**Methods**

**Population and method of sampling**

Four Australian cardiothoracic surgical sites with significant RHD and non-RHD surgical caseloads representing cases from two different Australian jurisdictions will be included. A random subset of patients having procedures over the preceding ten years, will be chosen from the existing Database.

**Sample size**

The sample size will be based on the number required to detect a difference in major adverse prosthesis-related events (MAPE) between bioprosthetic and mechanical valve replacements. MAPE will be defined as a composite outcome of any reoperation, major bleeding, thromboembolic event, or endocarditis during late follow-up [24]. A sample size of 600 patients will be recruited based on an anticipated rate of MAPE over ten years of follow-up of 50% for mechanical valve replacements and 35% for bioprosthetic valve replacement [24], a ratio of mechanical to bioprosthetic mitral valve replacements of 2:1 [5], two-sided alpha of 0.05 and power of 80%.

**Instrumentation**

An enhanced baseline dataset with identical definitions for all data points has been created to standardize data collection. Field names and coding have been defined in line with the existing Database data definitions. The enhanced baseline dataset consists of data shown in Table 1. Pre-operative history will be based on linkage with hospital separation data and with reference to the Massive Transfusion Registry (MTR) [25]. Medication and echocardiography data will be ascertained from the index hospital admission for valve surgery including admission history for pre-operative medication, discharge medication and linkage with imaging reporting systems.

In addition to enhanced baseline data collection the project will identify late (more than 30 day) complications potentially associated with valve surgery. In line with pre-surgery morbidity this will be undertaken by using jurisdiction hospital separation data linkage for all hospitalizations and the conditions outlined in Table 1 as well as with reference to the MTR [25]. Outcomes will be recorded and reported according to the Guidelines for reporting mortality and morbidity after cardiac valve interventions [24] with comparisons of major morbidity between mechanical and bioprosthetic valves made using MAPE [26].

Once ethics committee approval is obtained for all sites for the data collection, data will be obtained from surgeon and hospital records for the initial admission and entered onto data collection forms. Permission to access the MTR will be sought to identify all valve surgery patients (≥18 years old) who have received at least 5 units of red blood cells (RBCs) within any 4 h time period.

**Analysis plan**

The data collected will be analysed using multivariable, logistic and Cox proportional hazard models to identify independent factors associated with the outcome previously analysed [5, 6] and short and long term outcome. This will be undertaken using IBM SPSS Statistics 20 (IBM, New York, USA) and STATA Release 14 (StataCorp LP, Texas, USA).
USA). Missing data will be noted and assessed for potential bias. Possible missing data could be specific echocardiographic measurements not performed, which would be missing at random and readmission occurring outside the jurisdiction, which may not be missing at random if they are patients from remote areas. Where the patient's residential address is determined to be outside the jurisdiction of the surgical site access to local hospital separation data will be sought. Echocardiographic continuous variables will be stratified as necessary for analysis, using acknowledged cut off values (e.g., mild, mod, severe). The analysis will be assessed to determine if the new data is useful for future incorporation in the national ANZSCTS database for ongoing prospective collection.

This study has been reported following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations [27].

Discussion
The development of this multicentre, enhanced surveillance systems to collect enhanced baseline and longer term morbidity data will aim to assist in predicting outcomes and providing evidence to inform the development of guidelines to facilitate consistent practice. Added to the existing national cardiac surgery database (Australian and New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS)) these data may assist in deciding the most appropriate choice and timing of surgery.

Our analysis of the current database [6] has challenged the findings of earlier studies of surgical outcome in other settings. The finding that neither prior nor near post-operative AF was found to be an independent predictor of survival in RHD versus non-RHD valve surgery highlights the importance of considering these conditions as separate entities in the setting of valve surgery [28].

Our earlier finding that poorer preoperative clinical status, based on NYHA class, was also not independently associated with longer term survival requires further investigation with the addition of other cardiac and non-cardiac factors that influence NYHA-measured function to assess an independent effect on survival [6]. The addition of medications, echocardiography results and longer-term follow-up will also assist in strengthening the understanding regarding how pre-operative comorbidities and medication use influence outcome with the ultimate aim of enhancing the timing and management of patient with advanced valvular heart disease.

Conclusion
This article summarises the methodology of a project that aims to collect and incorporate more detailed information regarding pre and postoperative factors and non-lethal outcomes at Australian sites that undertake a significant proportion of RHD and non-RHD surgery. We will use these more detailed data to provide additional insights into treatment choice, timing and outcome.

Information demonstrated to be important and relevant will be considered for future inclusion in an ongoing Australia cardiac surgery registry to assist in predicting outcomes and providing evidence to inform the development of guidelines to facilitate consistent and evidence-based practice in the surgical management of valve disease.

Such data will also be integral to informing future national and international guidelines for the management of advanced valvular heart disease including for RHD as part of the Australian guideline for prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease [10].

Abbreviations
ACE: Angiotensin-converting enzyme inhibitors; ANZSCTS: Australian and New Zealand Society of Cardiac and Thoracic Surgeons; LVEDD: Left ventricular enddiastolic diameter; LVEDS: Left ventricular endsystolic diameter; MAPE: Major adverse prosthesis-related events; MHRREC: Monash University Human Research Ethics Committee; ND1: National Death Index; PASP: Pulmonary arterial systolic pressure; RBC: Red blood cell; RHD: Rheumatic heart disease; STROBE: Strengthening the Reporting of Observational Studies in Epidemiology

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Availability of data and materials
The data that support the findings of this study are available from Australian and New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS) National Cardiac Surgery Database, Monash Centre of Cardiovascular Research and Education in Therapeutics School of Public Health and Preventive Medicine, Monash University but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of ANZSCTS Research Committee.

Authors’ contributions
EAR drafted the manuscript and will collect the data and perform the statistical analysis. AB helped with revision of the manuscript. CMR helped with revision of the manuscript and will assist with acquisition of data. WW helped with revision of the manuscript. GPM conceived of the study participated in the design of the study, helped to draft the manuscript and will assist with the statistical analysis and interpretation. All authors read and approved the final manuscript.

Competing interests
The authors declare that they have no competing interests.
Consent for publication
Permission was obtained from the ANZSCTS National Cardiac Surgery Database Program, managed by The School of Public Health and Preventive Medicine, to use and analyse the data included in the surveillance system.

Ethics approval and consent to participate
Approval to undertake this study has been provided by the Monash University Human Research Ethics Committee (MUHREC) (CF13/2737 – 2013001472), Central Adelaide Local Health Network Human Research Ethics Committee (CALHNHREC) (R20161023 HREC/16/RAH/435) and Sir Charles Gairdner Hospital Research Ethics Committee (SCGH-HREC) (HREC Ref: 2016-165).

Author details
1Clinical Research Domain, Baker Heart and Diabetes Institute, 75 Commercial Road, Melbourne, VIC 3004, Australia. 2School of Population Medicine, Monash University, Melbourne, VIC, Australia. 3School of Public Health, Curtin University, Perth, WA, Australia. 4Prince of Wales Hospital, Randwick, NSW, Australia. 5Wardliparinga Aboriginal Research Unit, Public Health, Curtin University, Perth, WA, Australia. 4Prince of Wales Hospital, Randwick, NSW, Australia. 5Wardliparinga Aboriginal Research Unit, Public Health, Curtin University, Perth, WA, Australia.

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