Infective Endocarditis, Predictors of Mortality and Morbidity

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Abstract

Objectives:

Infective endocarditis is a disease with high mortality and morbidity. The primary outcome of this study is to assess factors associated with in-hospital mortality in patients undergoing valvular surgery for infective endocarditis. The secondary outcome of this study is to assess the incidence and factors associated with post-operative morbidity; namely post-operative stroke, renal failure and dialysis, complete heart block and return to theatre for bleeding or tamponade.

Methods

Between the years of 2015 to 2019, a total of 89 patients underwent surgery for infective endocarditis at Fiona Stanley Hospital. Data was collected from the Australia and New Zealand Cardiac Surgery Database from 2015 to 2019 as well as patients electronic medical record (EMR). A number of preoperative and perioperative factors were assessed in relation to patient mortality and morbidity. Univariate and multivariate logistical regression analysis was done to assess for the association between factors and in-hospital mortality and morbidity.

Results:

A total of 89 patients underwent surgery for infective endocarditis, affecting 101 valves. The mean age of patients was 53.7. A total of 79 patients had a positive blood culture pre-operatively, with *Staphylococcus Aureus* being the most frequently cultured organism (39%). Fourteen patients (16%) were deemed emergent and underwent surgery within 24 hours of review. A total of five patients died within their hospital stay postoperatively. Variables significantly associated with mortality on univariate analysis were intravenous drug use, emergent surgery, perioperative dialysis, perioperative inotropes, cardiopulmonary bypass (CPB) time and cross clamp time (CCT). Only CBP time was significantly associated with mortality on multivariate analysis. A total of 19 patients (21%) required hemodialysis after surgery, 10 patients sustained a postoperative stroke (11%), 15 patients required to return to theatre (17%) and 11 patients developed a complete heart block post operatively (12%).

Conclusion

There are a number of factors associated with mortality and morbidity in patients undergoing surgery with infective endocarditis. Our study demonstrates a lower mortality rate in these patients than previously quoted in literature. Exposure of prolonged CBP times was the only factor significantly associated with increased mortality on multivariate analysis, although a critical perioperative state was highly significant on univariate analysis.
Introduction

Infective endocarditis is associated with a high mortality and morbidity. The mortality rate in studies has been quoted from 6–25% \(^1\)\(^-\)\(^5\). The risk factors associated with mortality in infective endocarditis have been evaluated. \(^2\)\(^-\)\(^12\). Infective endocarditis is also associated with significant morbidity. Patients can sustain complications such as embolization (either systemic or pulmonary), heart failure and cardiogenic shock, disseminated infection, abscess formation and arrhythmias including complete heart block. Factors associated with these complications have also been assessed in literature, although to a lesser extent\(^2\),\(^11\),\(^13\),\(^14\). Emergent surgery is required in 25–50% of these cases\(^4\),\(^7\). The European Society of Cardiology recently published guidelines outlining the indications for surgery\(^2\). Early or emergent surgery is indicated for patients with infective endocarditis and cardiogenic shock, as well as locally uncontrolled infection. Early surgery is also indicated in patients with high-risk vegetations. Grey areas exist with regards to timing of surgery, especially with respect to surgery in the setting of a pre-operative embolic stroke\(^2\). The concept of a ‘Heart Team’ comprising of various specialties to create management plans for individual cases has been shown to decrease mortality in these cases\(^2\). The primary outcome of this study is to assess factors associated with in-hospital mortality in patients with infective endocarditis undergoing surgery. The secondary outcome of this study is to assess the factors associated with morbidity; namely post-operative stroke, renal failure and dialysis, complete heart block and return to theatre. The identification of prognostic factors will be useful for risk assessment and surgical decision-making.

Methods

Variables

Data was retrospectively collected from the Australian and New Zealand Cardiac Surgery database (ANZSCTS). Between the years of 2015 to 2019, a total of 89 patients underwent surgery for infective endocarditis at Fiona Stanley Hospital. This study focused exclusively on patients with endocarditis treated with open heart surgery. Cases of IE related to nonvalvular cardiovascular devices were excluded. Furthermore, cases of infective endocarditis were retrospectively confirmed using the modified Dukes Criteria and patients that did not meet these criteria were excluded\(^15\). A total of 9 patients were excluded. Several preoperative and operative factors were identified and recorded through a combination of the ANZSCTS database and patients electronic medical record. These factors were selected as they are hypothesized to be associated with an increased rate of mortality and morbidity post surgery. Preoperative factors: age, gender, intravenous drug use (IVDU) history, rural status, Aboriginal or Torres Strait Islander (ATSI) status, diabetes, body mass index (BMI), New York Heart Association (NYHA status), positive blood culture, organism, vegetation size, native or prosthetic valve endocarditis, right or left sided endocarditis, preoperative embolic event, cerebral emboli and preoperative creatinine clearance were recorded. Perioperative and operative variables: Presence of Cardiogenic shock, dialysis, respiratory failure, inotrope requirement, urgency, cardiopulmonary bypass (CPB) time, cross clamp time (CCT), red
blood cell use (RBC), non red blood cell use (NRBC) and aortic procedure were also recorded. These are summarized in Table 1 below. The definitions of these factors are in accordance with those set by the ANZSCTS database.
Table 1
Preoperative and Operative variables.

| Preoperative Variable | Operative Variable                        |
|-----------------------|-------------------------------------------|
| Age                   | Perioperative Cardiogenic Shock            |
| 53.7 Years            | Yes 15                                    |
|                       | No 74                                     |
| Gender                | Perioperative Dialysis                     |
| Male 67               | Yes 11                                    |
| female 22             | No 78                                     |
| IVDU history          | Perioperative Respiratory Failure          |
| Yes 28                | Yes 20                                    |
| No 61                 | No 69                                     |
| Location              | Perioperative Inotrope Requirement         |
| Rural 33              | Yes 17                                    |
| Metropolitan 56       | No 72                                     |
| ATSI                  | Urgency                                   |
| Yes 15                | Elective 13                               |
| No 74                 | Urgent 62                                 |
|                       | Emergent 14                               |
| Diabetes              | Cardiopulmonary Bypass Time               |
| Yes 17                | 137 minutes                               |
| No 72                 | Cross Clamp Time                          |
|                       | 102 minutes                               |
| BMI 27.8              | Aortic Procedure                          |
|                       | NYHA Status                               |
|                       | NYHA 1 52                                 |
|                       | Yes 13                                    |
|                       | NYHA 2 11                                 |
|                       | No 76                                     |
|                       | NYHA 3 13                                 |
|                       | NYHA 4 13                                 |
| Preoperative Variable                     | Operative Variable |
|------------------------------------------|--------------------|
| Positive Blood Culture                   |                    |
| Yes 79                                   |                    |
| No 10                                    |                    |
| Organism                                 |                    |
| Staph A                                  |                    |
| Vegetation Size (mm)                     |                    |
| 0–10: 30                                 |                    |
| 10–20: 32                                |                    |
| >20: 27                                  |                    |
| Native or Prosthetic Valve Infection     |                    |
| Native Valve 68                          |                    |
| Prosthetic Valve 21                      |                    |
| R or L sided Disease                     |                    |
| R sided 7                                |                    |
| L sided 82                               |                    |
| Preoperative embolic event               |                    |
| Yes 39                                   |                    |
| No 50                                    |                    |
| Cerebral Emboli                          |                    |
| Yes 23                                   |                    |
| No 66                                    |                    |
| Preoperative Creatinine                  |                    |
| 134 micromol/L                           |                    |

**Surgical Technique**

All operations were performed through a median sternotomy and the use of Cardiopulmonary Bypass. Arrest was achieved using hyperkalemic cold blood cardioplegia. Intraoperative transoesophageal echocardiography was also routinely performed in all cases. The valvular procedure was documented from a combination of the ANZSCTS database and the patients electronic medical record. This includes whether the patient had an aortic procedure, aortic valve, mitral valve, tricuspid valve or pulmonary...
valvular procedure. The number of valves affected was documented, as well as whether the index operation was a valvular replacement or repair. When a prosthesis was used, the prosthesis type was recorded (mechanical or bioprosthetic). In patients who underwent valvular repair, details of the repair were recorded.

Outcomes

Two outcomes were considered. Outcome 1, in hospital mortality, was defined as death following surgery during the patients initial hospitalization. This also included on-table mortality. Outcome 2 was defined as the presence of one of four issues post operatively, namely a new cerebrovascular accident (CVA), post-operative hemodialysis, return to theatre (RTT) and new complete heart block (CHB). CVA post op was defined as the occurrence of a stroke or new central neurologic deficit (persisting > 72 hours) post operatively. RTT was defined as patients returning to theatre after the initial index operation, within the patients initial hospitalization period. CHB was defined as the presence of new complete heart block post operatively. The presence/absence of these outcomes was obtained from a combination of the ANZSCTS database and the patients’ electronic medical record.

Statistical analysis

Descriptive statistics including number of events, mean and standard deviation was calculated for each preoperative and operative variable. Univariate analysis was firstly conducted to identify variables significant associated with either in hospital mortality (outcome 1) or morbidity (outcome 2). Categorical variables were assessed using the chi squared ($x^2$) test to ascertain odds ratios. Fishers exact test was conducted when more than 20% of cells on the contingency table had an expected frequency less than five. Continuous variables were first assessed for normality and then with the independent T test to assess for equality of means. Variables that weren’t normally distributed were assessed with the Mann-Whitney U test. P values less than 0.05 were deemed as significant. Preoperative and operative variables that reached significance were then further assessed with multivariate logistic regression analysis using a binary logistic regression model. Statistical analysis was done on IBMM® SPSS statistics version 25.

Results

Preoperative Factors

A total of 89 patients underwent surgery for infective endocarditis, affecting 101 valves. The mean age of patients was 53.7, with a minimum age of 16 and a maximum age of 83. Most of the patients were male (n = 67). A large portion of patients (n = 28) had a history of IVDU. In terms of location, 33 patients were from a rural setting. Eight patients were from the South West region, 5 from the Pilbara and 3 from the Kimberley. Fifteen patients identified as ATSI. Thirteen patients (15%) were NYHA class 4 preoperatively. The majority of patients (52 patients) were NYHA class 1 preoperatively. Twenty-seven patients had vegetations greater than 20mm on echocardiography, 32 patients had vegetations between 10–20mm and 30 were less than 10mm. The majority of patients who underwent surgery had left-sided disease (82
patients) with 7 patients undergoing surgery for right-sided disease. A total of 79 patients had a positive blood culture pre-operatively, with Staphylococcus Aureus being the most commonly cultured organism (39%). Other common organisms include Enterococcus Faecalis (20%) and Streptococcus Mitis (9%). Ten patients (11%) had culture negative endocarditis. These results are summarized in Table 2. Embolic phenomena were present in 39 patients (44%). The most common site of embolization noted was brain, with 23 patients. Other common sites were skin (6 patients), lungs (5 patients) and spine (4 patients). Two patients had concomitant septic arthritis. Ten patients had multiple sites of embolization. These results are summarized in Table 3.

### Table 2
Organisms Isolated

| Organism (N = 79)       | Number (%) |
|------------------------|------------|
| Staphylococcus Aureus  | 35 (29%)   |
| Enterococcus Faecalis  | 18 (20%)   |
| Streptococcus Mitis    | 8 (9%)     |
| Streptococcus Mutans   | 3 (3.3%)   |
| Streptococcus Anginosus| 2 (2.2%)   |
| Streptococcus gordonii | 2 (2.2%)   |
| Escherichia Coli       | 2 (2.2%)   |
| Streptococcus Agalactiae| 2 (2.2%)  |
| Streptococcus Parasanguinis| 1 (1.1%)|
| Streptococcus Sanguinis| 1 (1.1%)   |
| Staphylococcus Hominins| 1 (1.1%)   |
| Capnocytophaga Canimorsus| 1 (1.1%)  |
| Streptococcus Pneumonia| 1 (1.1%)   |
| Staphylococcus Epidermitis | 1 (1.1%)  |
| Streptococcus Oralis   | 1 (1.1%)   |
| Haemophilus Inuenzae   | 1 (1.1%)   |
| Neisseria Gonorhoeae   | 1 (1.1%)   |
| Aerococcus Urinae      | 1 (1.1%)   |
| Culture Negative       | 10 (11%)   |
Table 3
Sites of Embolic Phenomenon

| Embolic Phenomenon (N = 39a) | Number |
|-----------------------------|--------|
| Lungs                       | 5      |
| Spleen                      | 2      |
| Spine                       | 4      |
| Joints (Septic Arthritis)   | 2      |
| Brain                       | 23     |
| Skin                        | 6      |
| Vascular                    | 3      |
| Kidney                      | 1      |
| Other                       | 4      |

a.10 patients had multiple sites of embolization

**Perioperative Factors**

A total of 15 patients (17%) were in cardiogenic shock perioperatively. Eleven patients (12%) required perioperative hemodialysis, 20 patients (22%) were in perioperative respiratory failure and 17 patients (19%) had perioperative inotrope requirements. Fourteen patients (16%) were deemed emergent and underwent surgery within 24 hours of review, whereas the majority of patients (62) underwent urgent surgery. A total of 13 patients (15%) underwent elective surgery after a prolonged period of antibiotic therapy. The mean cardiopulmonary bypass time was 137 minutes and the mean cross clamp time was 102 minutes. The most commonly performed procedure was mechanical valve replacement (total of 42 patients), with 23 patients undergoing mechanical Aortic Valve replacement (AVR) and 18 patients undergoing mechanical Mitral Valve replacement (MVR). One patient underwent a mechanical Tricuspid Valve replacement (TVR). A bioprosthetic valve was used in 40 cases, 29 AVR and 10 MVR. One patient underwent a bioprosthetic Pulmonary Valve replacement. A Bentall’s procedure was done in 11 patients (12%) and one patient underwent an AVR and Hemiarch. Mitral valve disease resulted in MVR in 28 out of 43 cases, and 15 patients underwent a mitral valve repair. No patients underwent an Aortic Valve repair. These results are summarized in Table 4.
Table 4
Valve and Procedure

| Procedure/Prosthesis | Aortic Valve (N = 52) | Mitral Valve (N = 43\(^b\)) | Tricuspid Valve (N = 9) | Pulmonary valve (N = 1) |
|----------------------|-----------------------|-----------------------------|------------------------|------------------------|
| Mechanical           | 23                    | 18                          | 1                      |                        |
| Bioprosthetic        | 29                    | 10                          |                        | 1                      |
| Bentalls             | 11                    |                             |                        |                        |
| Hemiarch             | 1                     |                             |                        |                        |
| Annuloplasty         | 12                    | 5                           |                        |                        |
| Suture Repair        | 5                     | 3                           |                        |                        |
| Neochords            | 8                     |                             |                        |                        |
| Commisuroplasty      | 1                     |                             |                        |                        |
| Other                | 2\(^a\)               |                             |                        |                        |

\(^a\) One patient Aortic root suture repair
\(^b\) One patient: Resection Subaortic Membrane
\(^c\) 11 patients underwent a combination of procedures

Outcome 1 – Factors affecting in-hospital mortality

A total of five patients died within their hospital stay postoperatively (6%). Variables significantly associated with mortality on univariate analysis were IVDU (OR 10, P = 0.032), emergent surgery (OR 9.95, P = 0.026), Perioperative dialysis (OR 44, P = 0.001), Perioperative inotropes (OR 21.8, P = 0.004), Cardiopulmonary Bypass time, with 250.8 minutes for non survivors compared to 130.5 minutes for survivors (P < 0.001) and Cross Clamp time, with 175 minutes for non survivors compared to 97.8 minutes for survivors (P = 0.006). These results are summarized in Table 5 below. Multivariate analysis revealed that only CBP time was a significant predictor of operative mortality, with an odds ratio of 1.05 per minute of additional bypass time (95% CI 1.001–1.101, P = 0.046).
| Variable Assessed            | Death (N = 5) | Survivors (N = 84) | Odds Ratio     | P Value |
|------------------------------|---------------|--------------------|----------------|---------|
| Age                          | 52.4          | 53.8               |                | P = 0.852 |
| Gender (Male)                | 4             | 63                 |                | P > 0.900 |
| IVDU                         | 4             | 24                 | 10.0 (1.0–94)  | P = 0.032 |
| Rural patient                | 3             | 30                 |                | P = 0.355 |
| ATSI                         | 2             | 13                 |                | P = 0.196 |
| Hx of Diabetes               | 1             | 16                 |                | P > 0.900 |
| BMI                          | 28.0          | 27.7               |                | P > 0.900 |
| NYHA 4                       | 2             | 11                 |                | P = 0.153 |
| Positive Blood Culture       | 4             | 75                 |                | P = 0.457 |
| Staph A.                     | 3             | 32                 |                | P = 0.378 |
| Vegetation > 20mm            | 3             | 24                 |                | P = 0.161 |
| Prosthetic Valve involved    | 3             | 18                 |                | P = 0.083 |
| Right vs Left Sided          | 5             | 77                 |                | P > 0.900 |
| Embolic Phenomenon           | 2             | 37                 |                | P > 0.900 |
| Cerebral Emboli              | 1             | 22                 |                | P > 0.900 |
| Preoperative Creatinine      | 118           | 135                |                | P = 0.624 |
| Emergent Surgery             | 3             | 11                 | 9.95 (1.49–66.4) | P = 0.026 |
| Perioperative Cardiogenic Shock| 2             | 13                 |                | P = 0.196 |
| Perioperative Respiratory Failure | 3         | 17                 |                | P = 0.073 |
| Perioperative Dialysis       | 4             | 7                  | 44.0 (4.31–449) | P = 0.001 |
| Perioperative Inotropes      | 4             | 13                 | 21.8 (2.26–211) | P = 0.004 |
| Aortic Procedure             | 2             | 11                 |                | P = 0.153 |
| CPB Time                     | 250.8         | 130.5              | 1.02 (1.01–1.03) | P < 0.001 |
| Cross Clamp Time             | 175           | 97.8               | 1.26 (1.01–1.04) | P = 0.006 |
| Variable                      | Postoperative Stroke (N = 10) | Postoperative Dialysis (N = 19) | Return to theatre (N = 10) | Complete Heart Block (N = 11) |
|-------------------------------|-------------------------------|-------------------------------|---------------------------|-----------------------------|
| NYHA 4                        | N = 7                         | OR 6.22 (1.8–22)              |                           |                             |
|                               |                               | P = 0.005                     |                           |                             |
| Preoperative Emboli           | N = 8                         | OR 6.19 (1.23–31)             |                           |                             |
|                               |                               | P = 0.019                     |                           |                             |
| Cerebral Emboli               | N = 6                         | OR 5.47 (1.38–22)             |                           |                             |
|                               |                               | P = 0.017                     |                           |                             |
| Preoperative Creatinine       | 207 vs 125                    |                               |                           |                             |
|                               |                               | P 0.036                       |                           |                             |
| Perioperative Cardiogenic Shock| N = 5                         | OR 6.90 (1.7–28)              | OR 14.4 (4.0–52)          |                             |
|                               |                               | P = 0.011                     | P < 0.001                 |                             |
| Perioperative Respiratory Failure| N = 5                       | OR 4.26 (1.1–16)              | OR 6.67 (2.2–20)          |                             |
|                               |                               | P = 0.042                     | P = 0.001                 |                             |
| Perioperative Ionotropes       | N = 5                         | OR 5.58 (1.4–22)              | OR 14.7 (4.3–51)          |                             |
|                               |                               | P = 0.020                     | P < 0.001                 |                             |
| Perioperative Dialysis        | N = 9                         | OR 30.6 (5.8–162)             |                           |                             |
|                               |                               | P < 0.001                     |                           |                             |
Outcome 2 - Factors affecting postoperative morbidity

A total of 19 patients (21%) requiring hemodialysis after surgery. On univariate analysis, factors associated with the need for dialyses were NYHA class 4 symptoms (OR 6.22, P = 0.005), perioperative cardiogenic shock (OR 14.4, P < 0.001), perioperative respiratory failure (OR 6.67, P = 0.001), perioperative dialysis (OR 30.6, P < 0.001), emergent procedure (OR 7.76, P = 0.001) and RBC transfusion (OR 7.16, P = 0.007). On multivariate analysis, perioperative cardiogenic shock and perioperative dialysis were significantly associated with post-operative dialysis, with an odds ratio of 9.35 (95% CI 1.47–58.8, P = 0.018) and 20 (95% CI 2.24–167, P = 0.007) respectively.

A total of 10 patients sustained a postoperative CVA (11%). On univariate analysis, factors associated with the development of a postoperative CVA were preoperative embolic phenomenon (OR 6.19, P = 0.019), Cerebral emboli (OR 5.47, P = 0.017), preoperative creatinine of 207 vs. 125µmol/L for CVA/non CVA respectively (P = 0.036), perioperative cardiogenic shock (OR 6.90 P = 0.011), perioperative respiratory failure (OR 4.26, P = 0.011), perioperative inotrope requirement (OR 5.58, P = 0.02) and emergent procedure (OR 4.60, P = 0.047). None of these factors reached significance on multivariate analysis.

Fifteen patients required to return to theatre after the index operation. Five patients were taken back to theatre for tamponade, 8 patients for bleeding, one patient for hemodynamic instability and one for a
deep sternal wound infection. On univariate analysis, only RBC transfusion was associated with RTT. None of the patients who returned to theatre died during their hospital stay.

Eleven patients developed a CHB post operatively. All these patients required a pacemaker insertion. Factors associated with the development of CHB were cross clamp time (130 minutes vs 98 minutes P = 0.036) and whether the patient had an aortic procedure (OR 4.38, P = 0.05). None of these factors reached significance on multivariate analysis.

Discussion

Surgical treatment for infective endocarditis is associated with a high mortality rate, quoted between 6–25%. Risk factors associated with mortality including older age, emergent surgery, septic shock, congestive heart failure, cardiogenic shock, high risk organisms, prosthetic valve infection and stroke.

The European Society of Cardiology (ESC) provide guidelines for the management of infective endocarditis. The guidelines advocate for early surgery in patients with heart failure, uncontrolled infection and high-risk lesions to prevent embolization. Of all factors, congestive cardiac failure is the most consistent predictor of mortality. These studies advocate for early surgery in patients presenting in heart failure. Early surgery for high risk lesions is also supported by literature. Of these, a randomized control trial by Kang et al demonstrated that early surgery in patients with large left sided lesions (>10mm) significantly reduced morbidity and embolic events. Therefore, the ESC guidelines provide a class 1 indication for early surgery in vegetations greater than 10mm with ongoing embolic phenomena. Uncontrolled infection is a further indication for early surgery. This is supported by evidence, primarily consisting of retrospective cohort studies, demonstrating that locally aggressive infection is associated with a higher mortality rate. Of these, a retrospective study by Revilla et al demonstrated that persistent infection is an independent predictor of mortality, where patients who undergo urgent surgery with persistent infection are four-fold as likely to die as patients without persistent infection. At Fiona Stanley hospital, we adopted these guidelines to help with decision making regarding operative timing.

In the current study, the in-hospital mortality rate was 5.6% or 5 out of 89 patients. This is at the lower end of the spectrum of mortality figures quoted by other studies. A similar study conducted by Rivas de Oliveira assessed 88 surgical patients between 2005 and 2015, and reported an in-hospital mortality rate of 17%. A study by Dunne et al in a similar Western Australian population with infective endocarditis, treated surgically, reported a mortality rate then of 13%.

One major change reported amongst hospitals during the last decade is the establishment of a dedicated “heart team”. This team comprises of Cardiac Surgeons, Cardiologists and Infectious Diseases physicians. A dedicated “heart team” was established at Fiona Stanley Hospital since its initiation in
2015 is potentially responsible for the low mortality rate. Studies have reported a decline in mortality as a result of a multidisciplinary team (MDT) approach to endocarditis\(^{24,25}\). A retrospective study by Chirillo F et al demonstrated that after the implementation of an MDT, in-hospital mortality reduced from 28% to 13%, as well as surgical mortality from 47–13\%\(^{24}\). Similarly, a retrospective study conducted by Botelho-Nevers E. et al identified that a MDT approach to endocarditis yielded a significant decrease in one year mortality, from 18.5–8.2\%\(^{25}\). There was also a statistically significant increase in compliance to antimicrobial therapy. The 2015 ESC guidelines (class 2 evidence) recommend the timing of surgical intervention via the consensus of an MDT team\(^2\). Our practice at Fiona Stanley Hospital is to conduct weekly MDT meetings to discuss cases of endocarditis.

Our study identified that IVDU, emergent surgery, perioperative dialysis; perioperative Inotropes, prolonged CPB time and prolonged CCT were significantly associated with in-hospital mortality on univariate analysis. This finding is consistent with previous studies\(^{1,3,6,11}\). CPB time was the only factor to be significantly associated with death on multivariate analysis, with a mean CBP time of 250.8 vs 130.5 minutes for non-survivors and survivors respectively. Prolonged CPB time is a reflection of operative complexity, predisposes patients to end organ dysfunction, coagulation disorders and is therefore understandably associated with mortality.

In this study, factors associated with a critical perioperative state were strongly associated with post-operative mortality. Of these, perioperative dialysis was one of the major predictors of post-operative mortality, with an in-hospital mortality rate of 57% in this cohort. None of these patients required dialysis prior to their presentation with endocarditis. Studies of patients requiring perioperative dialysis, although chronic, reported a mortality rate of 40\%\(^{26}\). Elevated peri-operative creatinine clearance is also associated with increased post-operative mortality however did not reach significance in this study\(^3\). Likewise, perioperative inotrope requirement was also associated with mortality post operatively, and reflects the challenges associated with operating on patients in shock.

Embolic phenomena occurred 39 patients (43.8%). The most common site of emboli was the brain (22 patients) followed by skin and lungs. Other studies have also quoted equally high rates of embolic events\(^{10,27}\). Likewise, in these studies, the brain was the most common site of embolism\(^{10,27}\). Pre-operative stroke is a highly relevant complication of infective endocarditis due to the risk of hemorrhagic transformation and postoperative neurological deterioration. Guidelines provide class 2A evidence to delay surgery by a month in the presence of intracranial haemorrhage\(^2\). As a result, we adopted a low threshold to conduct a CT brain, explaining the higher rate of cerebral emboli compared to other sites in this study. Embolic phenomena and cerebral emboli were linked to the incidence of preoperative stroke on univariate analysis, however was not associated with in-hospital mortality.

In terms of organism, *Staphylococcus Aureus* was most commonly cultured and present in 39% of patients. This was followed by *Enterococcus Faecalis* and *Streptococcus Mitis* in 20% and 9% of patients respectively. Eleven percent of patients had culture negative infective endocarditis. The prevalence of
Staphylococcus Aureus is a feature in other studies also. There has been a reported shift in the epidemiology of infective endocarditis, away from Streptococcus species and HACEK (Haemophilus species, Aggregatibacter species, Cardiobacterium hominis, Eikenella corrodens and Kingella) organisms towards Staphylococcus Aureus. This was also evident in our study, with only 15 patients culturing Viridians Streptococci. There was one case of HACEK endocarditis. Staphylococcus Aureus has been linked to a higher mortality rate in surgically treated endocarditis. It is also linked to locally aggressive infection, higher rates of embolization and septic shock. Other studies do not demonstrate a relationship between Staphylococcus Aureus and mortality or morbidity. Our study also did not demonstrate a relationship between Staphylococcus Aureus and in-hospital mortality as well as post-operative complications. Our institution favors early surgery for patients with Staphylococcus Aureus endocarditis.

Complications after surgery for infective endocarditis were not uncommon. Ten patients (11%) had a postoperative stroke. Identifiable risk factors were cerebral emboli, pre-operative creatinine, perioperative cardiogenic shock, perioperative respiratory failure, perioperative ionotropic requirement and emergent procedure. Other studies have demonstrated a similar incidence of post-operative stroke. Only one other study investigated risk factors associated with post-operative stroke. Post-operative stroke is a debilitating issue, and some centers advocate for delaying surgery to minimize the risk of hemorrhagic transformation. Others demonstrate that the overall mortality benefit from early surgery outweighs this risk. The practice at Fiona Stanley Hospital was to delay surgery by a month if feasible if there is a significant risk of hemorrhagic transformation. A total of 19 patients (21%) required dialysis postoperatively. On multivariate analysis, cardiogenic shock and pre-operative dialysis were independently associated with the incidence of post-operative dialysis. Post-operative renal failure is linked to a critical perioperative state and is associated with an increased risk of mortality. Conduction abnormalities are an early indication of an infectious process expanding to involve the membranous interventricular septum, often in cases with aortic valve endocarditis. A total of 11 patients (12%) had complete heart block, all of whom received a pacemaker. The incidence of which is comparable to that published in other studies.

This is a retrospective observational study with inherent biases in data collection. A larger prospective study may enable us to explore more factors associated with mortality and morbidity. Our small patient numbers and the small number of in-hospital deaths have limited the use of multivariate analysis to evaluate risk factors for in-hospital mortality. Fiona Stanley Hospital is a new institution, and data is available over a period of 4 years. As a result, long term morbidity and survival data was not explored by this study and therefore Kaplan-Meier survival data was not conducted. A long term follow up of our patients would be beneficial to assess whether the low in-hospital mortality rate is also translated into long term survival.

Conclusion
This study reports the morbidity and in-hospital mortality of 89 patients undergoing valvular surgery for infective endocarditis at a single institution. It demonstrates that our in-hospital mortality rate fares well compared to other published data. We adopt a MDT approach to the management of infective endocarditis, which is attributable to the lower mortality rate. A number of factors were associated with mortality: IVDU, emergent surgery, perioperative dialysis; perioperative Inotropes, prolonged CPB time and prolonged CCT, with prolonged CPB times reaching significance on multivariate analysis. Of these factors, a perioperative hemodialysis requirement was strongly associated with post-operative mortality. A prolonged CPB time reached significance on multivariate analysis. Post-operative complications were not uncommon, with 11% of patients sustaining a post-operative CVA, 21% requiring post-operative dialysis, 11% requiring return to theatre and 12% demonstrating a complete heart block. A larger prospective study may enable us to explore more factors associated with mortality and morbidity.

**Abbreviations**

- **EMR**: Electronic medical record
- **CCT**: Cross clamp time
- **CPB**: Cardiopulmonary bypass
- **ANZSCTS**: Australia and New Zealand Cardiac Surgery
- **IVDU**: Intravenous drug use
- **ATSI**: Aboriginal and Torres Straight Islander
- **BMI**: Body mass index
- **NYHA**: New York Heart Association
- **RBC**: Red blood cell
- **NRBC**: Non red blood cell
- **CVA**: Cerebrovascular accident
- **RTT**: Return to theatre
- **AVR**: Aortic valve replacement
MVR
Mitral valve replacement

TVR
Tricuspid valve replacement

ESC
European Society of Cardiology

MDT
Multidisciplinary team

Declarations

Ethics:

Ethics approval was granted from the Hospitals review board (approval number 33939)

Consent for Publication

Not applicable. There was no personalised patient information.

Availability of data

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Author Contributions

The corresponding author AE was involved with data collection, analysis and writing of the paper, the authors AS, UA and KS were involved in the subsequent editorial process.

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