Reoperation for Bioprosthetic Mitral Structural Failure: Risk Assessment

W.R.E. Jamieson, MD; L.H. Burr, MD; R.T. Miyagishima, MD; M.T. Janusz, MD; G.J. Fradet, MD; S.V. Lichtenstein, MD; H. Ling, MD

Background—The predominant complication of bioprostheses is structural valve deterioration and the consequences of reoperation. The purpose of the study was to determine the mortality and risk assessment of that mortality for mitral bioprosthetic failure.

Methods and Results—From 1975 to 1999, 1,973 patients received a heterograft bioprosthesis in 2,152 operations. The procedures were performed with concomitant coronary artery bypass (CAB) in 694 operations and without in 1,458 operations. There were 481 reoperations for structural valve deterioration performed in 463 patients with 34 fatalities (7.1%). Of the 481 re-replacements, 67 had CAB and 414 had isolated replacement; the mortality was 11.9% (8) and 6.3% (26), respectively. Eleven predictive factors inclusive of age, concomitant CAB, urgency status, New York Heart Association (NYHA; reoperation), and year of reoperation (year periods) were considered.

The mortality from 1975 to 1986 was 9.8% (6/61), from 1987 to 1992 it was 10.8% (20/185), and from 1993 to 2000 it was 3.4% (8/235) (I versus III P = 0.0458, II versus III P = 0.0047). The mortality by urgency status was elective/urgent 6.0% (26/436) and emergent 17.8% (8/45) (P = 0.00879). The mortality was NYHA I/II 0.00% (0/37), III 5.1% (14/273), and IV 11.7% (20/171) (P = 0.0069). The predictive risk factors by multivariate regression analysis were age at implant, odds ratio (OR) 0.84 (P = 0.0113); age at explant, OR 1.2 (P = 0.0089); urgency, OR 2.8 (P = 0.0264); NYHA, OR 2.5 (P = 0.015); 1975–1986 versus 1993–2000 of reoperations, OR 5.8 (P = 0.0062); and 1987–1992 versus 1993–2000, OR 4.0 (P = 0.0023). For the period 1993 to 2000 of reoperations, only age at implant and age at explant were significant; NYHA class, urgency status, and concomitant CAB were not significant.

Conclusion—Bioprosthetic mitral reoperative mortality can be lowered by reoperations on an elective/urgent basis in low to medium NYHA functional class. The routine evaluation of patients can achieve earlier low risk reoperative surgery.

Key Words: mitral bioprostheses • reoperative risk assessment • optimal timing of reoperation

The predominant complication of bioprostheses is structural valve deterioration and the consequences of reoperative management. The choice of prostheses for mitral valve replacement surgery—bioprostheses and mechanical prostheses—is influenced predominantly by valve-related complications (mortality and morbidity) of the prosthesis type. The purpose of this study was to determine the mortality and the risk assessment of that mortality for mitral bioprosthetic failure.

The replacement of diseased native valves usually results in satisfactory symptomatic and hemodynamic benefit, which usually remains unaltered until the valve prosthesis commences to fail or fails abruptly. Controversy exists regarding bioprosthetic reoperations, whether there is an incremental effect to mortality compared with the primary operation, and what risk factors are contributing to that mortality. The documented mortality of bioprosthetic re-replacement for structural valve deterioration ranges from 7% to 18% in most series, depending on risk factors and patient status.1–6

The literature provides documentation on the factors that increase the risk of reoperation for all complications, inclusive of structural valve deterioration.1–3,6 The documented factors include age, gender, preoperative New York Heart Association (NYHA) class, indication for reoperation, type of prosthetic valve, position of prosthetic valve, number of previous operations, and timing of reoperations.1,6–8

The choice of prosthesis is determined by the influence of predominant valve-related complications of prosthesis-type on valve-related mortality and morbidity. The utilization of bioprostheses for mitral valve replacement is determined by the risk of failure; that is, the risk of valve failure with time and the risk of reoperation with time.9 The major consideration is the competing risks of death without re-replacement and re-replacement before death.9 As stated, this study

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addresses the reoperative mortality and the risk assessment of that mortality for management of mitral bioprosthetic structural failure from biological tissue deterioration.

### Patients and Methods

In the 25 years from 1975 to 1999 at the University of British Columbia, mitral valve replacement was performed with heterograft bioprostheses in 1,973 patients in 2,152 operations. Of the 2,152 operations performed from 1975 to 1999, there were 1,458 performed without concomitant coronary artery bypass (CAB) and 694 with concomitant CAB. Of the total patients, there were 481 reoperations for structural valve deterioration, 414 without CAB and 67 with concomitant CAB. The incidence of concomitant CAB was unchanged throughout the 25-year evaluation: period I, 11.5% (6/54); period II, 13.0% (24/185); and period III, 15.3% (36/235) (P=0.66). For all patients who had concomitant CAB, the indication for surgery was structural valve deterioration and not ischemic heart disease. The reoperation mortality for the total reoperative procedures extending through 2000 was 7.1%, or 34 patients.

Of the 2,152 operations performed, the age group distribution is detailed in Table 1, ≤40 years, 7.4% (159); 41 to 50 years, 9.9% (213); 51 to 60 years, 18.5% (398); 61 to 70 years, 33.2% (715); and >70 years, 31.0% (667). The prostheses utilized were previous generation porcine bioprostheses (Hancock standard, 79; Carpentier-Edwards standard 497; Medtronic Intact 120; St Jude Medical Bioimplant, 3); pericardial bioprostheses (Mitroflow, 37; Carpentier-Edwards PERIMOUNT 63); and current generation porcine bioprostheses (Carpentier-Edwards SAV, 1,235; Hancock II, 3; and Medtronic Mosaic, 115). The Carpentier-Edwards standard and supraannular porcine bioprostheses comprise 80.5% of the total patient population.

The factors considered as predictors of mortality were gender, age at implant (continuous variable), age at explant (continuous variable), age at explant (<60, 60 to 70, >70 years), age at explant (continuous variable), age at explant (<60, 60 to 70, >70 years), CAB pre-Re-op (reoperation), CAB concomitant with reoperation, urgency status at reoperation, ejection fraction at initial surgery, valve lesion at initial surgery, NYHA function class at reoperation, and year of reoperation surgery (year periods: 1975–1986, 1987–1992, and 1993–2000). The year periods are detailed in Table 2, ≤40 years, 7.4% (159); 41 to 50 years, 9.9% (213); 51 to 60 years, 18.5% (398); 61 to 70 years, 33.2% (715); and >70 years, 31.0% (667). The prostheses utilized were previous generation porcine bioprostheses (Hancock standard, 79; Carpentier-Edwards standard 497; Medtronic Intact 120; St Jude Medical Bioimplant, 3); pericardial bioprostheses (Mitroflow, 37; Carpentier-Edwards PERIMOUNT 63); and current generation porcine bioprostheses (Carpentier-Edwards SAV, 1,235; Hancock II, 3; and Medtronic Mosaic, 115). The Carpentier-Edwards standard and supraannular porcine bioprostheses comprise 80.5% of the total patient population.

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### Statistical Analysis

The project was conducted under the Society of Thoracic Surgeons, American Association for Thoracic Surgery, and European Association of Cardio-Thoracic Surgery “Guidelines for Reporting Morbidity and Mortality After Cardiac Valvular Operations.” The predictive model for early mortality caused by structural valve deterioration was based on multiple logistic regression analysis. Interpretable odds ratios (OR) and 95% confidence intervals to determine significance were determined for the overall population and populations within the reoperating periods 1975 to 1986, 1987 to 1992, and 1993 to 2000.

### Results

The overall re-replacement mortality during the years 1979 to 2000, for implants performed from 1975 to 1999, was 7.1% (34). The overall re-replacement mortality by year periods is shown in Figure 1: for the period 1975 to 1986, 9.8% (6); 1987 to 1992, 10.8% (20); and 1993 to 2000, 3.4% (8) (I versus III, P=0.0458; II versus III, P=0.0047). The mortality for the year periods, overall and with and without concomitant coronary bypass, are presented in Figure 2. The mortality for re-replacement with concomitant CAB was, for period I, 0.0% (0/7); for period II, 29.2% (7/24); and for period III, 2.8% (1/36) (II versus III, P=0.0052). The mortality for re-replacement without concomitant CAB was for period I, 11.1% (6/54); for period II, 8.1% (13/161); and for period III, 3.5% (7/199) (I versus III, P=0.0362).

The predictors as risk factors of mortality are detailed in Tables 2 and 3. The univariate analysis of predictive risk factors is presented in Table 2. The significant factors were urgency status, NYHA functional classification, and reoperative period. The reoperative mortality was for urgency – elective/urgent 6.0% (26/436) and emergent 17.8% (8/45) (P=0.00879); NYHA class at reoperation, I/II, 0.0% (0/37); and III, 5.1% (14/273); and IV, 11.7% (20/171) (P=0.00069); and reoperation period: I, 9.8% (6/61); II, 10.8% (20/185); and III 3.4% (8/235) (P=0.0083).

The multivariate analysis predictors of the overall population were age at implant: OR 0.84 (0.73 to 0.96) negative coefficient ($P=0.0113$); age at explant. OR 1.2 (1.05 to 1.37) ($P=0.0089$); urgency, OR 2.8 (1.1 to 7.0) ($P=0.0264$);
reoperative period I versus III, OR 5.8 (1.6 to 20.6) \((P=0.0062)\), II versus III, OR 4.0 (1.6 to 9.8) \((P=0.0023)\). CAB pre-Re-op or CAB at Re-op were not predictive of reoperative mortality.

### TABLE 2. Predictive Risk Factors of Reoperative Mortality (Univariate Analysis)

<table>
<thead>
<tr>
<th>Gender</th>
<th>Male</th>
<th>10.5% (15/143)</th>
<th>(P=\text{NS})</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Female</td>
<td>5.6% (19/338)</td>
<td>(P=\text{NS})</td>
</tr>
<tr>
<td>Age at implant</td>
<td>No</td>
<td>52.6 ± 12.8 years</td>
<td>(P=\text{NS})</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>54.3 ± 12.2 years</td>
<td>(P=\text{NS})</td>
</tr>
<tr>
<td>Age at implant</td>
<td>&lt;60</td>
<td>6.3% (20/316)</td>
<td>(P=\text{NS})</td>
</tr>
<tr>
<td></td>
<td>60–70</td>
<td>9.2% (14/152)</td>
<td>(P=\text{NS})</td>
</tr>
<tr>
<td></td>
<td>&gt;70</td>
<td>0.0% (0/13)</td>
<td>(P=\text{NS})</td>
</tr>
<tr>
<td>Age at explant</td>
<td>No</td>
<td>62.1 ± 13.1 years</td>
<td>(P=\text{NS})</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>64.3 ± 12.5 years</td>
<td>(P=\text{NS})</td>
</tr>
<tr>
<td>Age at explant</td>
<td>&lt;60</td>
<td>5.6% (10/180)</td>
<td>(P=\text{NS})</td>
</tr>
<tr>
<td></td>
<td>60–70</td>
<td>6.3% (10/158)</td>
<td>(P=\text{NS})</td>
</tr>
<tr>
<td></td>
<td>&gt;70</td>
<td>9.8% (14/143)</td>
<td>(P=\text{NS})</td>
</tr>
<tr>
<td>CAB Pre-Re-op</td>
<td>No</td>
<td>6.3% (27/431)</td>
<td>(P=\text{NS})</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>14.0% (7/50)</td>
<td>(P=\text{NS})</td>
</tr>
<tr>
<td>CAB - Re-op</td>
<td>No</td>
<td>6.3% (26/414)</td>
<td>(P=\text{NS})</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>11.9% (8/76)</td>
<td>(P=\text{NS})</td>
</tr>
<tr>
<td>Urgency</td>
<td>elective/urgent</td>
<td>6.0% (26/436)</td>
<td>(P=0.00879)</td>
</tr>
<tr>
<td></td>
<td>emergent</td>
<td>17.8% (8/45)</td>
<td>(P=\text{NS})</td>
</tr>
<tr>
<td>NYHA</td>
<td>I/II</td>
<td>0.0% (0/37)</td>
<td>(P=0.0069)</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>5.1% (14/273)</td>
<td>(P=\text{NS})</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>11.7% (20/171)</td>
<td>(P=\text{NS})</td>
</tr>
<tr>
<td>Reop period</td>
<td>1975–1986</td>
<td>9.8% (6/61)</td>
<td>(P=0.00883)</td>
</tr>
<tr>
<td></td>
<td>1987–1992</td>
<td>10.8% (20/185)</td>
<td>(P=\text{NS})</td>
</tr>
<tr>
<td></td>
<td>1993–2000</td>
<td>3.4% (8/235)</td>
<td>(P=\text{NS})</td>
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</tbody>
</table>

No indicates no reoperation; Yes, yes reoperation.

The predictors of mortality by multivariate analysis for the specific reoperative periods are different. For the operative period 1975 to 1986, only gender OR 22.8 (1.8 to 294.8) \((P=0.0168)\) and urgency status at reoperation OR 19.4 (1.0 to 370.6) \((P=0.0492)\) were predictive. In the operative period 1987 to 1992, concomitant CAB at reoperation, OR 4.1 (1.0 to 16.6) \((P=0.0446)\) and NYHA, OR 5.6 (1.8 to 17.9) \((P=0.0033)\) were predictive. Urgency status was not predictive – elective/urgent 9.3% (15/162) and emergent 21.7% (37/176) \((P=\text{NS})\). NYHA was also predictive by univariate analysis: I/II, 0.0% (0/8); III, 4.5% (5/110); and IV, 22.4% (15/67) \((P=0.00022)\). Concomitant CAB was CAB – “No” 8.1% (13/161) and CAB – “Yes” 29.2% (7/24) \((P=0.00642)\).

For the latest operative period (III) 1993 to 2000 only age at implant and age at explant were predictive by multivariate analysis. Age at implant OR was 0.74 (0.58 to 0.95) (negative coefficient) \((P=0.0197)\) and age at explant OR was 1.34 (1.04 to 1.73) \((P=0.025)\). Urgency status was now predictive, elective/urgent 3.2% (7/222) and emergent 7.7% (1/13) \((P=\text{NS})\). NYHA class at reoperation was not predictive: I/II, 0.0% (0/28); III, 2.5% (3/118); and IV, 5.6% (5/89) \((P=\text{NS})\). The total experience revealed that NYHA classification IV and emergent urgency status were the predominant predictors of reoperative mortality. In the final evaluation period (1993–2000), these risk factors were no longer predictive. The assessment of NYHA IV over the time periods, the incidence
of NYHA IV decreased as follows: period I, 24.6% (15/61); period II, 8.1% (15/185); and period III, 2.1% (5/235). (I versus II, P = 0.0014; I versus III, P < 0.0001; II versus III, P = 0.0009). The same frequency of incidence occurred for emergent status: period I, 14.8% (9/61); period II, 12.4% (23/185); and period III, 5.5% (13/235). (I versus II, P = 0.80; I versus III, P = 0.025; and II versus III, P = 0.020).

Discussion

The predominant complication of bioprostheses is structural valve deterioration and the consequences of reoperative management. The major consideration, as stated by McGiffin and colleagues, is the competing risks of death without re-replacement and re-replacement before death. The documentation on risk assessment for valvular prosthesis dysfunction is limited and deals with prosthetic dysfunction for bioprostheses and mechanical prostheses and for all positions. The majority of publications document the risk assessment for re-replacement for aortic prosthesis dysfunction. Akins et al identified mortality higher for age greater than 75 years and trended higher with concomitant procedures and increasing numbers of reoperations. Lytle and coinvestigators, reporting in 1986, identified advanced age as the most predominant predictor of risk, others being concomitant coronary artery bypass and second multiple replacements, but not second replacements for aortic or mitral replacements.

O’Brien and Bortolotti and colleagues have recommended more accurate patient follow-up, closer patient-surgeon relationship and possibly earlier and more optimal timing for re-operation. O’Brien et al have recommended knowledge of the most important risk factors and adherence to specific technical steps at explantation.

The cardiac valve database at the University of British Columbia incorporates the changing patterns of practice over the 25-year observation time, in which longitudinal patient evaluation was conducted. It is for this reason that the 25-year timeframe was divided into three time periods. During the years 1975 to 1986 (first time period), the majority of patients had bioprostheses implanted in both the aortic and mitral positions. Beginning in 1987 (second time period), the use of bioprostheses became more selective as to age indications for both aortic and mitral implantations. In the latest time period, bioprostheses have been recommended for patients more than 65 years of age for aortic valve replacement and more than 70 years of age for mitral valve replacement. These indications obviously would be altered based on comorbidity factors that would potentially alter life expectancy in relation to the anticipated durability of the implanted prostheses.

In the 25-year timeframe, only age at implant, age at explant, urgency status, and NYHA functional class, as well as the earlier time intervals, were predictive of mortality. The mortality for elective/urgent status was 6.0%, whereas for emergent status it was 17.8%. The mortality for NYHA class III was 5.1% and class IV was 11.7%. The odds ratio for emergency status was 2.8 and NYHA class IV was 2.5. In the intermediate time period, the odds ratio for NYHA class IV was 5.6. The mortality for elective/urgent was 9.3% and for emergent status 21.7%. The NYHA class mortality for the intermediate time interval was 4.5% for class III and 22.4% for class IV.

In the latest reoperative time period (1993–2000), the overall mortality decreased to 3.4%; 2.8% with concomitant coronary artery bypass and 3.5% without concomitant coronary artery bypass; urgency status and NYHA functional class were not predictors of mortality. The age at implant 2.7% for age group 60 to 70 years, and 0.0% for age group greater than 70 years was predictive as a negative coefficient with odds ratio of 0.74, whereas the age at explant 5.7% for age group 60 to 70 years and 2.5% for age group greater than 70 years with odds ratio 1.34.

The mortality for age at explant was higher for the earlier time periods for the age group greater than 70 years, 17.9% for period 1987 to 1992 and 28.6% for period 1975 to 1986. This finding can be related to the large number of patients less than 65 years receiving mitral bioprostheses prior to 1986. For the patients who were greater than 70 years at implant,
there were no mortalities in the 25 years, but only 13 patients
had reoperative surgery. For the age at implant 60 to 70 years,
the mortality decreased to 2.7% for 1993 to 2000 from 15.6%
for 1987 to 1992 and 13.3% for 1975 to 1986. This latter
finding can be attributed to surveillance of patients at risk of
structural valve deterioration, and explantation experience.

The mortality for reoperative surgery for mitral structural
failure can be reduced significantly by optimizing timing of
surgery before development of advanced functional class and
emergency status. From 1993 to 2000 mortality was also
reduced for NYHA class IV and emergency status likely
contributed to myocardial protection, operative experience
and optimal patient management. The opportunity for echo-
cardiographic surveillance of patients after 7 to 8 years since
implantation can achieve the opportunity for re-replacement
surgery before advanced ventricular and functional disease.
O’Brien and colleagues16 have recommended that the optimal
timing for reoperation can be achieved by the opportunity for
closer patient-surgeon-cardiologist relationship. Reoperative
mortality can be lowered by performing surgery at lower
elective urgency status and at low/medium NYHA functional
class by the recommended routine evaluation.

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