Reoperation for Bioprosthetic Mitral Structural Failure: Risk Assessment

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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, 1973 patients received a heterograft bioprosthesis in 2152 operations. The procedures were performed with concomitant coronary artery bypass (CAB) in 694 operations and without in 1458 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 0.0% (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. (Circulation. 2003;108[suppl II]:II-98-II-102.)

Key Words: mitral bioprostheses reoperative risk assessment optimal timing of reoperation
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 1,485 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% (7/61); 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 SAV, 1,235; and Medtronic Mosaic, 115). The Carpentier-Edwards standard and generation 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 1975–1986 (period I), 1987–1992 (period II), and 1993–2000 (period III).

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.”10 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 reoperation 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 reoperation 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, III, 0.0% (0/37); 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 = 0.00883).

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>(No. of Events)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Female</td>
<td>(No. of Events)</td>
<td></td>
</tr>
<tr>
<td>Age at implant</td>
<td>No</td>
<td>10.5% (15/143)</td>
<td>P=NS</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>5.6% (19/338)</td>
<td>P=NS</td>
</tr>
<tr>
<td>Age at implant</td>
<td>&lt;60</td>
<td>52.6 ± 12.8 years</td>
<td>P=NS</td>
</tr>
<tr>
<td></td>
<td>60–70</td>
<td>9.2% (14/152)</td>
<td>P=NS</td>
</tr>
<tr>
<td></td>
<td>&gt;70</td>
<td>0.0% (0/13)</td>
<td>P=NS</td>
</tr>
<tr>
<td>Age at explant</td>
<td>No</td>
<td>62.1 ± 13.1 years</td>
<td>P=NS</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>64.3 ± 12.5 years</td>
<td>P=NS</td>
</tr>
<tr>
<td>Age at explant</td>
<td>&lt;60</td>
<td>5.6% (10/180)</td>
<td>P=NS</td>
</tr>
<tr>
<td></td>
<td>60–70</td>
<td>6.3% (10/158)</td>
<td>P=NS</td>
</tr>
<tr>
<td></td>
<td>&gt;70</td>
<td>9.8% (14/143)</td>
<td>P=NS</td>
</tr>
<tr>
<td>CAB Pre-Re-op</td>
<td>No</td>
<td>6.3% (27/431)</td>
<td>P=NS</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>14.0% (7/50)</td>
<td>P=NS</td>
</tr>
<tr>
<td>CAB Re-op</td>
<td>No</td>
<td>6.3% (26/414)</td>
<td>P=NS</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>11.9% (8/67)</td>
<td></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></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></td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>11.7% (20/171)</td>
<td></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></td>
</tr>
<tr>
<td></td>
<td>1993–2000</td>
<td>3.4% (8/235)</td>
<td></td>
</tr>
</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 marginal) 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 6.0% (26/436) and emergent 17.8% (8/45) (P=0.00879).

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 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=0.00022). 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=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. In 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, \( P=0.0099 \). 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 prosthetic dysfunction. The publications addressing bioprosthetic valve failure are Akins, Bortolotti, Glower, McGiffin, O'Brien, Sundt, Vogt, and Jamieson and colleagues. The publications by Tyers, McGrath, and Sener and their colleagues access both bioprostheses and mechanical prostheses and the publications address re-replacement risk for mitral bioprosthetic structural valve deterioration.

Jamieson and coauthors reported, in 2000, on survival and actual (and actuarial) freedom from structural valve deterioration in 1,582 mitral valve replacements and 2,237 aortic valve replacements. For the mitral replacement in the 61 to 70-year-old age group, the survival at 15 years was 16.0%, and the actual freedom from valve-related reoperation was 71%, whereas for greater than 70 years of age at 15 years survival was only 2.8% and actual freedom from valve-related reoperation was 93.3%. The predictors of freedom from structural valve deterioration for mitral prostheses were advancing age and patients older than 70 years.

The early mortality for mitral reoperation for bioprosthetic valve failure was 6.8% in the series reported by Akins and colleagues. In this series, the early mortality over 25 years was 7.1%, 34 deaths in 481 operations. Bortolotti et al reported a reoperative mortality over 26 years for structural valve deterioration for all valve positions of 9%. Tyers and colleagues reported on the University of British Columbia experience, a bioprosthetic early mortality for all positions of 10.6%, whereas McGrath et al identified an early mortality of 13.2% for failed bioprostheses reoperation. In the series by Sener and coinvestigators, the early mortality for bioprosthetic failure was 6.8%. The remaining publications deal exclusively with aortic reoperative mortality. The reoperative mortality rates are similar to the mortality for the initial surgery.

Several authors have documented the predictors of reoperative mortality. Akins et al identified age greater than 65 years, male gender, renal insufficiency, and nonelective surgery. The study showed that the best results occurred in elective surgery without concurrent cardiac procedures. Bortolotti et al confirmed that mortality was greatly influenced by preoperative clinical status and reduction in operative risk must be attributed to increasing surgical experience, better myocardial protection, and patient management. Tyers et al identified mortality higher for age greater than 75 years and tended 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 echocardiographic 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.

References
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