Repeat heart valve surgery: Risk factors for operative mortality

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Background: Patients undergoing repeat heart valve operations are a diverse population. We assessed risk factors for operative mortality in patients undergoing a first heart valve reoperation.

Methods: A retrospective review of hospital records was performed for 671 patients who underwent first repeat heart valve operations between 1969 and 1998. Univariable and multivariable analyses were performed.

Results: Operative mortality was 8.6%. Mortality fell each decade to 4.8% in the most recent period (adjusted χ^2 for linear trend $P < .0005$). Mortality increased from 3.0% for reoperation for a failed repair or reoperation at a new valve site to 10.6% for prosthetic valve dysfunction or periprosthetic leak and to 29.4% for endocarditis or valve thrombosis. Concomitant coronary artery bypass grafting was associated with a mortality of 15.4% compared with 8.2% when it was not required. Mortality for aortic valve replacement was 6.4%, mitral valve replacement 7.4%, aortic and mitral valve replacement 11.5%, tricuspid valve replacement 25.6%, periprosthetic leak repair 9.1%, and isolated valve repair 2.2%. Among 336 patients requiring replacement of prosthetic valves, mortality was 26.1% for replacement of a mechanical valve compared with 8.6% for replacement of a tissue valve ($P < .0005$). Multivariable analyses identified year of reoperation, age, coronary artery bypass grafting, indication, and replacement of a mechanical valve rather than a tissue valve as significant explanatory variables for operative mortality.

Conclusions: Heart valve reoperations can be performed with an acceptable operative mortality. However, we have identified several categories of patients in whom reoperation carries an increased risk.

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The operative mortality associated with repeat heart valve surgery is higher than for the initial valve operation.[1] However, patients requiring heart valve reoperation are diverse in terms of both the initial operation and the reoperation. We reviewed our total experience at a single institution, from 1969 until 1998, of all patients undergoing a first repeat heart valve operation to identify possible risk factors for operative mortality.

TABLE 1. Mortality associated with decade of reoperation

Decade	Age (y; mean and range)*	Mean age at deaths* (y)	Mortality†	Percentage†
1969-1978	46 (17-73)	50	21/130	16.2
1979-1988	53 (16-77)	56	22/226	9.7
1989-1998	60 (18-83)	64	15/315	4.8

*Age and time are positively correlated but there is no statistically significant interaction between them.
†χ^2 for linear trend $P < .0005$ with decreased mortality in recent decades.

TABLE 2. Indication for reoperation

Indication	Mortality	Percentage
Failed repair/new native valve disease	9/299	3.0
Prosthetic valve dysfunction or periprosthetic leak	34/321	10.6*
Endocarditis or thrombosed valve	15/51	29.4*†

*$P < .0005$ compared with "Failed repair/New native valve disease."
†$P < .0005$ compared with "Prosthetic valve dysfunction or periprosthetic leak."

Patients and Methods

Between June 1968 and December 1998, a total of 5720 valve operations (1083 valve repairs, 1195 tissue valve replacements, and 3442 mechanical valve replacements) were performed at the Royal Victoria Hospital. During this period, 671 patients had a first reoperation (11.7% of all valve operations) for a subsequent valve problem, although the first of these reoperations did not occur until 1969. Patients with congenital valve disorders who were 15 years or younger at reoperation were excluded. Hospital records were retrospectively reviewed and a computer database was constructed. The pathologic state of the valve was obtained from operative and pathologic reports. A 5-group classification of indication for reoperation was used, based on an original 4-group classification by Lytle and associates[2]:

1. Failed repair/new native valve disease: All patients who had a failed previous valve repair and patients who at reoperation required repair or replacement of a valve different from that operated on during the initial procedure.
2. Prosthetic valve dysfunction: Valve dysfunction resulting from tissue ingrowth, mechanical dysfunction and calcification, and leaflet tears for bioprostheses. This group excludes patients with active prosthetic valve endocarditis and thrombosed mechanical valves.
3. Periprosthetic leak: Periprosthetic leak and a normally functioning prosthesis. Patients with active endocarditis were excluded.
4. Valve thrombosis: Thrombosis of the mechanical valve to the extent that the thrombosis interfered with valve opening characteristics. This group does not include patients who had embolic phenomena only.
5. Prosthetic valve endocarditis: Patients with organisms or inflammation documented on the valve specimen, or patients who underwent operation while receiving prolonged antibiotic treatment for clinical endocarditis. Patients with a history of endocarditis who underwent surgery for valve dysfunction that was remote from prolonged antibiotic treatment and whose valves showed neither organisms nor active inflammation were considered to have "healed endocarditis" and were placed in other groups.

Operative mortality was defined as death within 30 days of surgery or during the same hospital admission. The following variables were examined for their relationship with operative mortality:

1. Age in years
2. Sex
3. Year of reoperation
4. Indication for reoperation: Native/failed valve repair, prosthetic valve dysfunction, periprosthetic leak, endocarditis or thrombosed valve
5. Procedure at repeat operation: Aortic valve replacement, mitral valve replacement, combined aortic/mitral valve replacement, tricuspid valve replacement (isolated or part of multiple replacement), valve repair only, or isolated periprosthetic leak repair
6. bypass grafting (CABG) (at initial operation or reoperation) versus no CABG
7. Reoperation for replacement of prosthetic valve: Replacement of a mechanical valve versus replacement of a tissue valve

Statistical Methods

The association between each variable and operative mortality was investigated by means of the χ^2 test or the Fisher exact test depending on the table; classes were combined where necessary. Possible trends in ordinal variables were examined by the χ^2 test for trend. Multivariable analysis of the entire group was based on logistic regression modeling with operative mortality as the outcome variable. Because of the low incidence of operative mortality and the number of events (58), the number of variables in the models considered was limited to approximately 6, as recommended by Peduzzi and coworkers.[3] Variables were selected on the basis of their clinical importance and their significance level ($P < .2$) in the univariable analysis.[2] The contributions of variables and their interactions were assessed for significance by use of differences of log likelihoods. A similar multivariable analysis was performed on the subgroup of patients who underwent replacement of prosthetic valves. There were 45 events in 336 patients. Analyses were performed with the use of SPSS for Windows version 8.0 (SPSS, Inc, Chicago, Ill).

Results

Over a 30-year period, from January 1969 until December 1998, 671 patients (242 men and 429 women) with a mean

TABLE 3. Mortality according to principal valve procedure at reoperation

Principal procedure	Mortality	Percentage
Aortic valve replacement	12/187	6.4
Mitral valve replacement	20/269	7.4
Aortic/mitral valve replacement	12/104	11.5
Tricuspid valve replacement	11/43	25.6
Isolated periprosthetic leak repair	2/22	9.1
Valve repair only	1/46	2.2

TABLE 4. Cause of operative mortality

Cause of death	No. of patients	Percentage
Myocardial failure	30	51.7
Hemorrhage	9	15.5
Endocarditis	6	10.3
Bronchopneumonia	4	6.9
Myocardial infarction	3	5.2
Multiple organ failure	2	3.5
Renal failure	2	3.5
Cerebrovascular accident	1	1.7
Acute abdomen	1	1.7
Total	58	

age of 54.7 years (range 16-83 years) underwent first reoperation on a heart valve with an overall operative mortality of 8.6%. Mortality was 35 of 429 (8.2%) for women and 23 of 242 (9.5%) for men ($P > .2$). The age of those patients who had an operative death was 55.9 years (standard deviation [SD] 10.9) compared with 54.6 years (SD 13.1) for those who survived surgery ($P > .2$).

The approximate halving in mortality (χ^2 for linear trend $P < .0005$), despite the increasing average age of the patients for successive decades during the study period, is shown in Table 1. Analysis of the year of operation as a continuous variable after adjusting for other factors likewise demonstrated that operative deaths occurred with greater incidence earlier in the period ($P < .0005$) (see Table 5).

Reoperation on a previously repaired valve or for new native valve disease was associated with a mortality of 3.0% compared with 13.2% after previous valve replacement ($P < .0005$). Some of the initial repairs were closed mitral valvotomies, but mortality after reoperation on these patients was similar (2.3%) to that after open valve repair.

Among patients with previous valve replacements, mortality was higher when the indication was endocarditis or thrombosed valve (29.4%) compared with prosthetic valve dysfunction or periprosthetic leak (10.6%), as indicated in Table 2 ($P < .0005$). Valve thrombosis occurred only in mechanical valves. Mortality was 2 of 4 in the aortic position, 4 of 17 in the mitral position, and 2 of 2 in the tricuspid position. Mortality after surgery for periprosthetic leak was similar for repair of leak (4/31) and valve replacement for leak (3/33). There was little difference between repair and replacement at either the aortic or mitral positions (1/3 vs 1/11, aortic position; 3/25 vs 1/16, mitral position).

The mortality according to the procedures performed at reoperation is shown in Table 3. Mortality of aortic valve replacement at the first reoperation was 6.4% and remained low in the most recent decade (5.0%, 5/101). Mortality was 33.3% (2/6) if a concomitant ascending aortic graft was required ($P = .059$). Mortality of mitral valve replacement at the first reoperation was 7.4% and fell slightly in the most recent decade (4.7%, 6/127). Concomitant repairs to other valves were associated with a mortality of 11.4% (4/35) compared with 6.8% (16/234) for isolated mitral valve replacement ($P > .2$). Mortality was 11.5% (14/122) after previous valve replacement compared with 4.1% (6/147) after repair ($P = .019$). Mortality of combined aortic and mitral valve replacement at first reoperation was 11.5% (12/104), and this fell in the most recent decade (3.5%, 2/57). Concomitant tricuspid valve repair was associated with a mortality of 13.3% (2/15) compared with 11.2% (10/89) when it was not required. Mortality was 19.0% (11/58) after previous valve replacement compared with 2.2% (1/46) after repair ($P = .011$). Mortality was not related to the initial site of valve replacement: 16.7% (3/18) after initial combined aortic and mitral valve replacements, 25% (5/20) after aortic valve replacement, and 15% (3/20) after mitral valve replacement. Few patients required tricuspid valve replacement, but the mortality was high (25.6%, 11/43). There was no significant difference between isolated tricuspid valve replacement and tricuspid valve replacement as part of a multiple valve replacement. Although the numbers were small, tricuspid valve replacement remains an operation with a high mortality of 40% (2/5) in the most recent decade. Valve repair was associated with a mortality of 2.0%, the only death occurring in an isolated tricuspid valve repair.

Concomitant CABG at either the initial or repeat valve procedure was associated with a mortality of 15.4% (6/39) compared with 8.2% (52/632) when CABG was not required ($P = .14$).

The causes of operative mortality are shown in Table 4. Nine patients died on the operating table. The cause of death was myocardial failure in 5, left ventricular rupture in 2, and acute myocardial infarction and acute endocarditis in 1 each. A further 8 patients died later on the day of the operation. Heart failure was responsible in 6 patients and uncontrollable hemorrhage in 2 patients, due to left ventricular rupture in 1 of them. One other patient died of left ventricular rupture on the first postoperative day. The 4 patients who had

TABLE 5. Logistic regression analysis for 671 patients undergoing heart valve reoperation

Explanatory variable	Estimated regression coefficient	OR	CL	*P* value
Age (y)	0.04	1.04	1.01-1.07	.009
Time (y)	–0.09	0.91	0.87-0.95	<.0005
CABG	1.23	3.41	1.24-9.37	.017
Indication*				
Prosthetic dysfunction or periprosthetic leak	1.17	3.22	1.50-6.94	.003
Valve thrombosis or prosthetic valve endocarditis	2.55	12.84	5.04-32.71	<.0005
Constant	–4.13			

OR, Odds ratio; *CL,* confidence limits; *CABG,* coronary artery bypass grafting.
*The reference category for *indication* is "Failed repair/new native valve disease."

TABLE 6. Logistic regression analysis for 336 patients undergoing replacement of a prosthetic valve

Explanatory variable	Estimated regression coefficient	OR	CL	*P* value
Age (y)	0.02	1.02	0.99-1.05	.143
Time (y)	–0.07	0.93	0.89-0.98	.004
Mechanical valve	0.81	2.25	1.09-4.63	.028
Valve thrombosis or prosthetic valve endocarditis*	1.09	2.97	1.32-6.66	.008
Constant	–2.73			

OR, Odds ratio; *CL,* confidence limits.
*The indication category "Valve thrombosis or prosthetic valve endocarditis" is compared with "Prosthetic valve dysfunction or periprosthetic leak."

left ventricular rupture had mitral valve replacements at reoperation. Of the 58 patients who died in the hospital, 26 (49.1%) patients had a postmortem examination performed.

Multivariable Analysis

The final logistic regression model shown in Table 5 is based on the explanatory variables age, time of reoperation (in years from the start of the study period, ie, 1969), both considered as continuous variables, and the categorical variables CABG and one representing the various indication categories. The interaction effects of these variables were examined and found to be nonsignificant except for the age × indication and CABG × indication effects. However, both interaction models showed signs of overfitting and were rejected. Increased risk of mortality was associated with older age, decreasing time (or earlier year of reoperation), concomitant CABG at either the initial or repeat valve operation, and the indication categories compared with the reference category (failed repair/new native valve disease). In addition, time of reoperation (expressed in decades) has an odds ratio of 0.39 (95% confidence intervals [CI] 0.25 to 0.60).

Replacement of Prosthetic Valves

We reviewed the 336 patients who required replacement of a prosthetic valve at reoperation. Patients who required replacement of a tissue valve at reoperation had a mortality of 8.6% (21/244) compared with 26.1% (24/92) if replacement of a mechanical valve was required ($P < .0005$). The increased mortality after replacement of a mechanical valve occurred with aortic valve replacements ($P = .002$), mitral valve replacements ($P = .061$), combined aortic and mitral valve replacements ($P = .13$), and tricuspid valve replacements ($P > .2$), as shown in Figure 1.

Logistic regression modeling was carried out on the explanatory variables age, time of reoperation (in years from the start of the study period, ie, 1969), type of valve explanted (mechanical vs tissue), and indication (endocarditis or thrombosed valve compared with prosthetic dysfunction or periprosthetic leak). No interaction effects were found to be significant. The final model is given in Table 6. Increased risk of mortality was associated with earlier year of reoperation, replacement of a mechanical valve compared with a tissue valve, and the indication category endocarditis or thrombosed valve compared with prosthetic dysfunction or periprosthetic leak.

Discussion

Mortality at heart valve reoperations is higher than at primary valve procedures.[1] However, patients undergoing heart valve reoperations are a heterogeneous group. Patients differ in terms of their initial valve operation, as well as in factors relating to the reoperation. The aim of this study was to identify the risk factors for operative mortality among patients undergoing first heart valve reoperation.

Overall mortality for those undergoing first heart valve reoperation was only 8.6%, which is similar to the results published by Lytle[2] (10.9%), Cohn[4] (10.1%), Akins[5] (7.3%), Pansini[6] (9.6%), Tyers[7] (11.0%), and their associates.

The risk at reoperation for those patients who had an initial reparative procedure or who were undergoing surgery for new native valve disease was extremely low (3.0%). Such patients were probably not as severely compromised as those requiring surgery on a prosthetic valve. The extent of surgical dissection within the heart would have been less in those who did not require explantation of a previously inserted prosthetic valve. The majority of these patients had a previous mitral valve repair. Although some of these operations were closed mitral valvotomies, the operative mortality was similar after an open or a closed procedure. This encourages the use of valve repair where possible because the risk at reoperation is not increased. Gillinov,[8] Niederhauser,[9] and their associates found an operative mortality of 8.6% and 8.8%, respectively, after reoperation for failed mitral valve repair, which contrasts with our findings.

Mortality was higher for those patients requiring reoperation on a prosthetic valve. The risk at reoperation for periprosthetic leak was not influenced by whether the reoperation was a repair of the leak or a valve replacement. Operative mortality was similar for repair of leaks and replacement in both the aortic and mitral positions. Reoperation for thrombosed valves and endocarditis were both associated with a high operative mortality.

Operative mortality was higher at all valve positions for those patients who required replacement of a mechanical valve compared with a tissue valve. This agrees with the findings of Tyers,[7] Magilligan,[10] Bortolotti,[11] and their colleagues but is in contrast to the results published by others who found no difference.[2,12] The multivariable model retained removal of a mechanical valve, year of reoperation, and the indication for reoperation as significant explanatory variables suggesting that, for all indications and years, patients with mechanical valves in situ at reoperation have a higher operative mortality. A possible explanation may be that valve function deteriorates abruptly (eg, thrombosis) in some patients, with consequent decompensation before a relatively urgent operation. An example of this within our series was the group of patients who required reoperation for thrombosed mechanical valves. Cohn and coworkers[13] found that New York Health Association class IV and emergency operation were significant factors in raising the mortality of reoperation. Otherwise, they found no difference in the mortality of reoperation and primary heart valve replacement. We did not review the preoperative New York Heart Association class or urgency of the operation because of an inability to ascertain this information from the patient records without possible bias in a retrospective study.

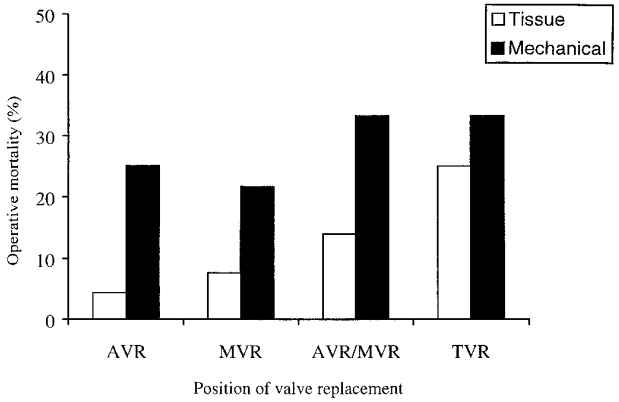

Figure 1. Operative mortality associated with replacement of mechanical and tissue prosthetic valves according to site of operation. *AVR,* Aortic valve replacement; *MVR,* mitral valve replacement; *AVR/MVR,* combined aortic and mitral valve replacements; *TVR,* tricuspid valve replacement.

However, despite greater numbers of mechanical valves being inserted in this unit, fewer patients required replacement of mechanical valves than tissue valves, and thus these figures cannot be used to influence the choice of prosthesis to be inserted at the initial operation.

Mortality in the group of patients who required a tricuspid valve replacement at reoperation was high. This risk at reoperation, however, compares favorably with other series.[14,15] Such patients represent a sick population with severely compromised right ventricular function.

Coronary artery disease had a detrimental effect on the outcome after repeat valve surgery, which was significant in the multivariable model. Others have found the presence of CABG to be of borderline significance.[2,4] Again, this is an indication of compromised status with multiple pathologic conditions.

Sex had no effect on the outcome, an observation that agrees with the conclusions of Cohn and associates.[4] This contrasts with the conflicting findings of Lytle and colleagues,[2] who found that women undergoing reoperation on the aortic valve had an increased risk, and Akins and colleagues,[5] who found that men undergoing valve reoperation at any site had an increased operative mortality.

Age was not a risk factor in the univariable analysis, but it was significant in the multivariable model. Again, reported series differ, with some finding age to be associated with increased risk[2,5] whereas others have found no such association.[4]

Mortality was lowest in the most recent decade (4.8%). The reason for the falling mortality is most likely due to improvements in intraoperative and perioperative care. In particular, the improvements in myocardial protection with

multidose cardioplegia would have had a major role in reducing the mortality in the mid-1970s. Improved monitoring facilities in intensive care units would also have contributed to a reduction in operative mortality despite an older population.

The majority of deaths were due to cardiac causes, especially myocardial failure, which indicates the severely compromised state of these patients. Nine patients died of uncontrollable bleeding. In 4 of these patients the reason was left ventricular rupture after mitral valve replacement. This problem persisted despite awareness of the risk, with 2 deaths in each of the periods 1979-1988 and 1989-1998.

In conclusion, we have shown in this large series that repeat heart valve surgery can be performed with an acceptable operative mortality that compares favorably with results in other published series. We have confirmed that the risk has fallen with the passage of time. However, several categories of patients have an increased risk of death at reoperation. These include older patients and those who had CABG at the time of their previous valve operation or who require concurrent CABG at valve reoperation. In addition, the indication for reoperation, especially thrombosed valves or prosthetic valve endocarditis, carries an increased risk, and greater caution should be exercised in patients who require replacement of a mechanical valve than a tissue valve.

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