

# Trends in Mitral Valve Surgery: A Single Practice Experience

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**Background and aim of the study:** Mitral repair has evolved to a point where three methods can be used to address most pathologies: full ring annuloplasty (RA) for annular disease; Gore-Tex artificial chordal replacement (ACR) for chordal disease; and autologous pericardial augmentation (PA) for leaflet disease. The study aim was to assess the impact of the increasing application of these methods on operative results over time. **Methods:** Of 328 consecutive mitral valve procedures, 34% involved myxomatous prolapse, 23% rheumatic, 13% ischemic, 12% pure annular dilatation, 7% prosthetic dysfunction, 6% endocarditis, 3% hypertrophic obstructive cardiomyopathy (HOCM), and 2% 'other'. All patients underwent RA. Myxomatous prolapse was repaired with ACR, and ischemic and annular dilatation with RA alone. Rheumatic, endocarditis, and HOCM etiologies were repaired with all three methods. Patients were allocated to two-year increments, and also to repair versus replacement groups. Operative outcomes over time were assessed with linear and binomial regression.

The transition to reparative procedures for mitral valve disease has been one of the success stories of cardiac surgery. Historically, mitral surgery was one of the highest risk procedures; for example, in 1970 the operative mortality for valve replacement for mitral regurgitation (MR) approached 20% (1), and valve replacement mortality for ischemic MR was even higher. It was a significant event in 1983 when Carpentier presented his 'French Correction' lecture at the American Association for Thoracic Surgery meeting (2), with operative videos of an organized surgical

**Results:** Overall, 66% of mitral valves were repaired; the average operative mortality was 6% (2% for repair, 7% for replacement), and 18% involved multiple valve procedures (mortality 16%). The extent of repair increased over time, from 55% to 100% of all etiologies. Over the same period, operative mortality fell from 6% in 1994 to 0% over the past six years. Other variables, such as age, presentation status, left ventricular dysfunction and etiology were relatively constant over the period. Reoperation rates after repair have been only 2% over the past 10 years of follow up. **Conclusion:** With recent innovations, most mitral disease can be repaired with combinations of RA, ACR and PA. Today, operative mortality is approaching zero, and one factor may be the increasing application of repair to all mitral pathologies. These data support the trend of expanding valve repair across most mitral disorders.

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approach. This single lecture made a major impression on the cardiac surgical community, and while mitral repair had been investigated for some time, Carpentier's studies initiated intense clinical application. The early techniques consisted of leaflet resection and reconstruction, in addition to ring annuloplasty. However, while these performed well for many pathologies, a number of limitations soon became apparent such that many patients with complex mitral derangements still required valve replacement. Further analyses suggested that the early and late outcomes for repair were generally superior (3-7); consequently, an effort was initiated to increase repair rates for all mitral disease. The advent of Gore-Tex artificial chordal replacement (ACR) and glutaraldehyde-fixed autologous pericardial patches greatly facilitated this effort (8-18). Herein is described the expansion of

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mitral repair techniques over the past 15 years at a single surgical practice, together with an assessment of the impact of this evolution on operative outcomes over time.

## Clinical material and methods

### Patient population

Between July 1993 and November 2008, a total of 328 mitral valve procedures was performed at a single surgical practice. In relation to the etiology of valve disease, 34% of the procedures involved myxomatous prolapse, 23% rheumatic, 13% ischemic, 12% pure annular dilatation, 7% prosthetic dysfunction, 6% endocarditis, 3% hypertrophic cardiomyopathy (HOCM), and 2% 'other' (two calcific valve diseases of dialysis, two viral cardiomyopathies, and one remote atrioventricular canal repair). Each patient was evaluated, operated on, and managed postoperatively by a single surgeon (J.S.R.). Detailed prospective office records were maintained for each patient as part of the clinical process, including baseline and operative characteristics, postoperative complications, and operative mortality, either during hospital admission or within 30 days of surgery. The causes of postoperative death were also recorded. Patients were followed up at approximately yearly intervals, at which time routine transthoracic echocardiography was performed. At these annual visits any echocardiographic recurrence of valve disease was noted, and valve failures requiring reoperation were documented. During late October 2008, all data were collated, and the baseline, procedural, operative mortality and late recurrence rates assessed.

### Valve procedures and perioperative care

During the early years of the study, mechanical valves were employed predominantly for replacement, while tissue valves were used only when anticoagulation was contraindicated. All mitral procedures described were open operations using median sternotomy, and transesophageal echocardiography (TEE) was performed routinely. At the authors' center, a transition to robotic repair has occurred recently, especially in cases of simple myxomatous prolapse managed with ACR; details of these patients are reported elsewhere (19). The present report relates primarily to the evolution of open repair techniques over this period, and the expansion of repair to most mitral pathologies. Throughout the study period, patients with pure annular dilatation and ischemic MR were managed primarily with full rigid ring annuloplasty. In 1993, myxomatous prolapse was approached with leaflet resection/reconstruction, but after 1995 all prolapses were treated with Gore-Tex ACR (without leaflet resec-

tion), together with a full ring annuloplasty (20).

In 2002, glutaraldehyde-fixed autologous pericardial patches were introduced for leaflet augmentation and, after 2004, all rheumatic valves were repaired by inserting pericardial patches into scarred/retracted posterior leaflets, resecting the pathological submitral structures, and reattaching the anterior leaflet to the papillary muscles with ACR (21). This approach routinely achieved full valve competence, good anterior leaflet mobility, and low transvalvar gradients. Similar methods were used to repair valves with endocarditis, and full rings were placed in all cases. During later years, ischemic MR with severe leaflet tethering was treated with posterior leaflet pericardial augmentation (17), and the few with prolapse from elongated papillary muscles were repaired with ACR (22).

Between 1993 and 2000, six patients with severe MR and HOCM were treated with a low-profile mechanical valve replacement; however, during the past three years, three HOCM patients underwent mitral repair combining septal myectomy, resection of the obstructing anterior papillary muscles, and valve repair with Gore-Tex artificial chordal transposition to a posterior papillary muscle (23). In recent periods, patients with congenital and calcific mitral disease (classified as 'other') were managed by the resection of calcified lesions and/or augmentation of leaflets with pericardial patches (24). Tricuspid valves were repaired with a similar pericardial patch and ACR techniques, along with a Carpentier tricuspid ring annuloplasty. Aortic valve repair was performed increasingly with commissural annuloplasty and Schaefer's 'leaflet plication' method (25). In later years, multiple internal mammary artery grafts were favored for concomitant coronary artery bypass grafting (CABG) (26), while after 2003 the Cox-maze IV procedure was performed routinely in patients with preoperative atrial fibrillation (27).

Since 1995, all patients have received routine amiodarone anti-arrhythmic prophylaxis (28). Improved biocompatible bypass systems (using pulsatile pumps) were introduced in 2001, and cold-potassium antero-grade cardioplegia was employed routinely. The Daily hypothermic heart jacket was added for improved myocardial protection after 2003; this change was especially important for increasing safe arrest times in complex repairs. Finally, the management of postoperative immune dysfunction was developed in 2002; the subsequently improved efficacy in managing pulmonary infection/multi-organ failure syndrome led to a significant reduction in mortality (29).

During the past six years, patient selection for mitral repair has been liberal, with only two patients rejected for surgery. The first patient was a 78-year-old man who required a third-time reoperative triple valve procedure in the setting of multiorgan failure; the second

Table I: Sample size and mortality data over time.

Procedure	Study period								Total (average)
	1993-1995 (1994)	1995-1997 (1996)	1997-1999 (1998)	1999-2001 (2000)	2001-2003 (2002)	2003-2005 (2004)	2005-2007 (2006)	2007-2008* (2008)	
Overall (n)	51	64	56	51	33	19	25	29	328
Mortality (n)	3	3	3	6	4	0	0	0	19
Mortality (%)	5.9	4.7	5.4	11.8	12.1	0	0	0	5.8
Isolated repair (n)	24	32	32	25	16	14	20	20	183
Mortality (n)	1	0	2	1	0	0	0	0	4
Mortality (%)	4.2	0	6.3	4.0	0	0	0	0	2.2
Isolated replacement (n)	19	23	18	17	9	2	-	1	89
Mortality (n)	2	2	1	0	1	0	-	0	6
Mortality (%)	10.5	8.7	5.6	0	11.0	0	-	0	6.7
Multiple valves (n)	8	9	6	9	8	3	5	8	56
Mortality (n)	0	1	0	5	3	0	0	0	9
Mortality (%)	0	11.1	0	55.5	37.5	0	0	0	16.1

\*All periods shown are two years' duration (1st July - 30th June), except for 2008, which is 16 months.

reoperative patient had active methicillin-resistant *Staphylococcus aureus* mitral endocarditis associated with septic cerebral infarcts, multiorgan failure, and minimal MR. Nonetheless, patient selection is important, and in recent periods there has been a reluctance to operate during active endocarditis, especially in the setting of chronic dialysis (30). Instead, a prolonged antibiotic therapy and conversion to 'treated' status was favored whenever possible. In realizing that the subject of endocarditis was controversial, this philosophical change may have biased the results by producing fewer of these referrals, and thus less mortality for the recent series. At least five of the early deaths were among the 'active endocarditis' category, while two patients (one of whom died) had viral cardiomyopathy, which now is better treated with bridge-to-transplant techniques.

#### Data analysis

Trends in baseline characteristics, operative procedures, and outcomes were evaluated by grouping procedures into two-year periods, beginning from 1st July 1993 to 30th June 1995, through until late 2008. Trends in baseline characteristics, pathologic etiologies and the operative mortalities of individual procedures were evaluated using linear regression. Trends in overall mitral repair rates versus each two-year period, and in overall mortality over time, were both evaluated with binomial regression. A multivariable analysis was not attempted because improvements over time reduced death to zero, which is a difficult number to evaluate statistically.

An exemption status for this retrospective review was provided by the Western Institutional Review Board for Centennial Medical Center, Nashville, TN, USA.

#### Results

Among the 328 mitral procedures (Table I), 183 (56%) were isolated mitral repairs ( $\pm$  CABG), 89 (27%) were isolated mitral replacements ( $\pm$  CABG) and 56 (17%) were multiple valve procedures involving the mitral valve ( $\pm$  CABG). Of the 56 multiple valves, 33 (59%) involved mitral repair and 23 (41%) mitral replacement. Of the 54 double valve procedures, 35 (65%) were combined with aortic valve operations and 19 (35%) were coupled with tricuspid surgery. Triple valve procedures (aortic/mitral/tricuspid) were performed in two patients (4%). Two of the multiple valve patients also had ascending aortic replacement. Among the 36 concomitant aortic valves, 21 (58%) were repaired, and 19 of the 20 concomitant tricuspid valves (95%) were repaired. Aortic valve repair was increased from 12/26 (46%) during the first five periods, to 9/10 (90%) in the last three periods. The overall operative mortalities for individual procedures are listed in Table I.

#### Baseline characteristics

The baseline characteristics were relatively stable over the 15-year period (Fig. 1). While the incidence of advanced age, left ventricular (LV) dysfunction (ejection fraction  $<0.35$ ) and multiple valve procedures increased slightly, the acute presentation and CABG

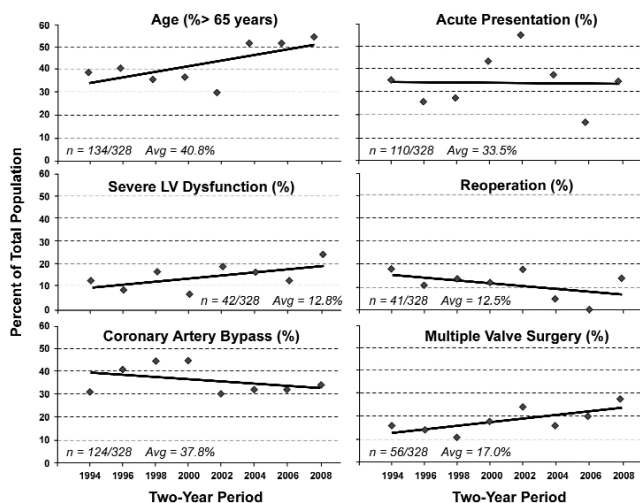


Figure 1: Trends in risk factors for mitral surgery.

usage were relatively constant. The incidence of reoperative surgery seemed to decline modestly. Baseline risk factors for the 19 deaths were: acute presentation (n = 13), age >65 years (n = 12), multiple valves (n = 9), severe LV dysfunction (n = 6), reoperation (n = 5) and CABG (n = 4) (patients often had multiple risk factors). Univariable death rates as related to baseline risk factors were: age >65 years (9%; 12/134), acute presentation (12%; 13/110), severe LV dysfunction (14%; 6/42), concomitant CABG (3%; 4/124), multiple valve surgery (16%; 9/56), and reoperation (12%; 5/41).

### Pathologic etiologies

The pathologic etiologies of mitral valve disorders also remained relatively constant, varying by less than 15% over the 15 year period (Fig. 2) Univariable death rates were: endocarditis (25%; 5/20), prosthetic dysfunction (15%; 1/7), rheumatic (7%; 5/74), pure annular dilatation (5%; 2/40), ischemic MR (5%; 2/43) and myxomatous prolapse (3%; 3/112). It should be noted that 'prosthetic dysfunction' patients having mitral repair were re-repairs, after a previous failed repair.

By combining the techniques of ACR, pericardial leaflet augmentation and full ring annuloplasty, the incidence of mitral repair was increased from 50-60% during the 1990s to 100% in recent years (Fig. 3A). Since adopting routine ACR in 1995, all patients with myxomatous prolapse were repaired, including Barlow's valves with generalized prolapse. All nine rheumatic patients and five with endocarditis over the past four years were repaired, and three patients with HOCM and severe mitral anomalies during the last period underwent repair. Finally, mitral valves were repaired in all multiple valve procedures over the past six years. The aortic cross-clamp times for complex repair could be long, perhaps averaging 3 h for rheu-

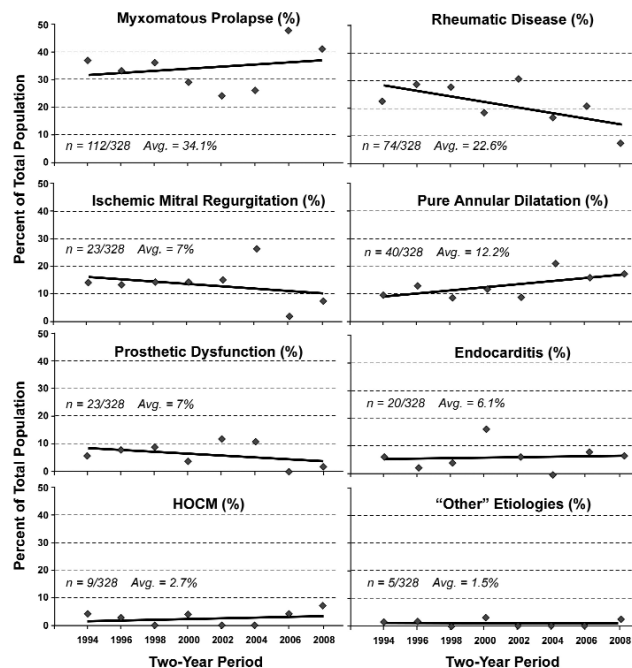


Figure 2: Trends in etiologies of mitral valve disease.

matic cases (21), although most of these patients also underwent concomitant procedures. This type of complex repair required extra attention for myocardial protection, such as use of the Daily heart jacket. Coincident with increasing repair rates, and also certainly due to improved care, the operative mortality fell to zero for all isolated and multiple valve procedures involving the mitral valve over the last six years of the series (Fig. 3B). Consequently, no patient left the operating room with more than mild residual MR, and over 90% had no residual leak.

The individual operative mortalities over time for the various procedures are shown in Figure 4. Of the prostheses used for mitral replacement, 96% (108/112) were mechanical valves. The operative mortality for replacement was consistently higher than for repair, although in the last two periods replacement was performed only for one failing bioprosthetic valve that could not have been repaired. Mortality for isolated mitral repair ( $\pm$  CABG) was 0% for the last half of the series across all pathologies, and this correlated with the fall in overall mortality. The spike in multiple valve mortality over the middle period was due largely to increased pneumonia rates, before the immune intervention was devised. Of the 19 deaths over the whole period, nine were due to postoperative pneumonia/multiorgan failure, three experienced low cardiac output, two each had sepsis (after endocarditis surgery) and stroke; and one patient each involved ventricular arrhythmias, perioperative myocardial infarction, and generalized circulatory thrombosis



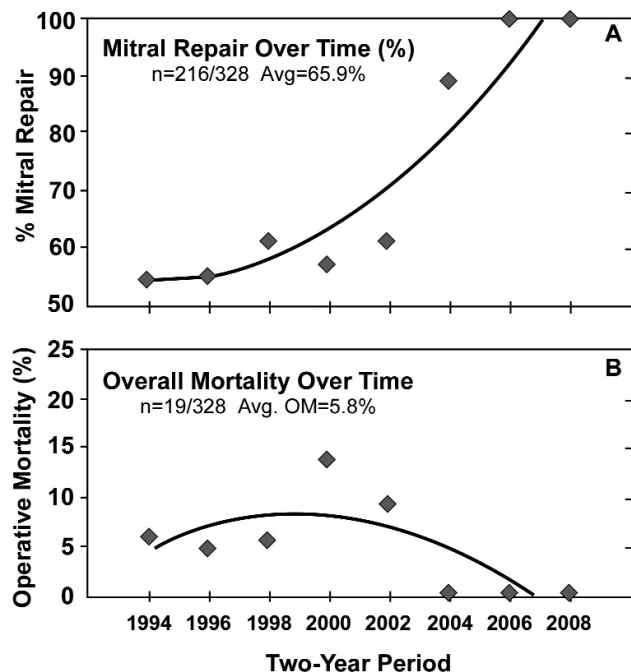


Figure 3: Trends in overall mitral valve repair rate and mortality.

associated with aprotinin use.

Since changing to ACR for managing prolapse in 1995, only four repair failures have occurred that required reoperation (2.1%; 4/188 over a 13-year period). One failure was due to the late rupture of 4-0 Gore-Tex chords, one to a late disruption of ACR leaflet insertion, a third patient had endocarditis, and a fourth with rheumatic repair before pericardial patching, who continued to retract the posterior leaflet after ring annuloplasty alone. The first and third patients were re-repaired successfully, while the second and fourth patients received mechanical valves. Since changing to 2-0 Gore-Tex sutures for ACR in 2002, and also emphasizing several other technical points (20,22), no further structural failures have occurred. Over this same period, only two prolapse patients and one ischemic patient developed moderate recurrent MR that was treated medically (1.5%). Of 25 patients receiving concomitant Cox-maze IV procedures since 2003, 24 (96%) had converted to sinus mechanism by six months post-operatively. Although, in several of these patients atrial fibrillation recurred later, the procedure seemed quite effective initially, and was consistent with more formal analyses (27).

## Discussion

In evaluating mitral surgery, advantages exist in assessing series with large sample sizes and indeed, several large studies have suggested that mitral valve

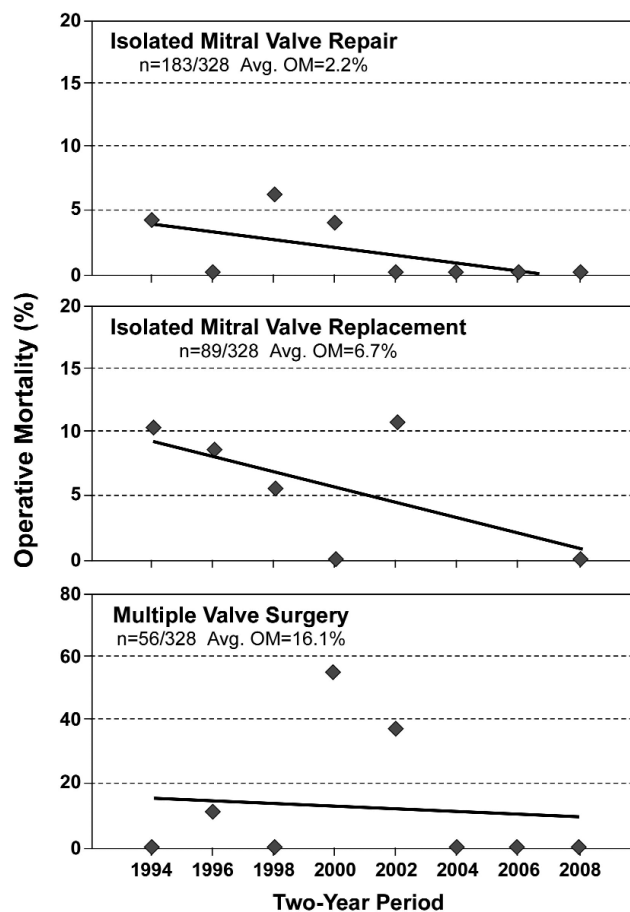


Figure 4: Trends in individual operative mortality (OM).

repair is associated with a lower operative mortality (3,7). Similar analyses of late outcomes have indicated that mitral repair is associated with a better long-term survival for ischemic MR (4), degenerative valve disease (5), and across the spectrum of all mitral pathologies (6). In the authors' collective view, the concept of improved outcomes after effective mitral valve repair is now a resolved question. However, while large series improve the statistical power for evaluating treatment benefits, they have the disadvantage of viewing each patient from a distance. Thus, a place also exists for individual surgeons to periodically evaluate smaller experiences, with the advantage of having detailed knowledge of each patient and understanding any subtle nuances that might be obscured in a large series. In the current data set, problems such as inconsistency of technical approach, missing data, omitted patients or misclassifications did not exist, because every case was managed and documented personally by one operating surgeon. In his 1972 Connor lecture (31), Dr. John Kirklin stated that each surgeon should "...address this evaluation with the same seriousness

and skill he uses in treating individual patients", and that was the goal of the present study.

One trend in recent cardiac surgical outcomes has been that of falling operative mortality (7). However, this also is a problem because sufficient events may not be available in future studies to support multivariable modeling. This was the case in the present series, and in fact mortality fell to zero, a number that is difficult to evaluate statistically. Consequently, a trends analysis was carried out to assess practice changes over time and, based on the trends data in Figures 1 and 2, it is unlikely that observed improvements were due to changing patient profiles. As seen in larger series (3), the population was becoming older with more LV dysfunction and multiple valve procedures, while other baseline prognostic variables were relatively constant. This finding would suggest a real outcome improvement.

Interestingly, univariable mortality across risk factors was relatively constant, which suggested a common etiologic factor. In fact, half of the deaths were due to refractory pulmonary infection/multiorgan failure, which is more common in higher-risk patients but may have a constant occurrence across risk factor categories. The effective management of postoperative immune dysfunction markedly reduced this cause of death, and is likely a major change accounting for falling mortalities (29). However, low cardiac output syndrome due to inadequate myocardial protection was still occurring in some patients, and the Daily heart jacket eliminated that cause of death among the present patients. Routine amiodarone anti-arrhythmic prophylaxis eliminated mortality from arrhythmia (28), better cardiopulmonary bypass techniques potentially improved stroke rates (32), and an increased use of multiple mammary artery grafts for CABG may have been important (26). Finally, the general perioperative care clearly has improved, and all of these changes in the aggregate seem to have been effective.

With regards to the etiology of valve disease, mortality during the early periods was highest in endocarditis patients and lowest in myxomatous prolapse, which was consistent with previous studies (3). It is interesting that the rheumatic etiology fell over time while degenerative etiologies seemed to increase, which also was consistent with recent series (7). The higher mortality for rheumatic patients may reflect a preference for valve replacement in the early years, but with conversion to repair the rheumatic outcomes now are excellent. The 96% early success of the Cox-maze IV ablation also may have contributed, and in patients with severe rheumatic disease and long-standing atrial fibrillation it is gratifying ultimately to achieve a functional repair, to attain sinus rhythm, and to require only aspirin as anticoagulation (21). Thus, reductions in operative mortality have occurred for all etiologies;

moreover, as the disease incidence was relatively constant over time, sufficient patients now have been managed in each category so as to increase the certainty of these observations.

At an early stage of the present series, and based on the experiences of the 1980s, patients with simple myxomatous prolapse, pure annular dilatation and ischemic MR uniformly underwent mitral valve repair using Carpentier's approach. Those with complex bileaflet prolapse, Barlow's valves with generalized prolapse, rheumatic disease, endocarditis or HOCM (with severe MR) largely received prostheses. This selective approach was based on the techniques of the time, but allowed only a 50-60% repair rate (Fig. 3A). The repair of prolapse was largely by leaflet resection/reconstruction, and pericardial patches were rarely used. With a continued 5-10% operative mortality for valve replacement (Table I, Fig. 4), an attempt was made to increase the repair rates. By 1995, ACR without leaflet resection became routine in the present program and also in that of others (11,20), and allowed the repair of all myxomatous prolapse, including Barlow's valves. Based on positive reports, pericardial leaflet augmentation was incorporated and, when combined with ACR, allowed a more effective repair of rheumatic, endocarditis, HOCM and congenital valves (22). When using combinations of ring annuloplasty for annular dilatation, pericardial leaflet augmentation for leaflet disease, and ACR for chordal problems, it seemed that virtually all mitral pathologies could be repaired. The early success was excellent, and late failure rare. Finally, it is likely that near-uniform conversion to mitral repair has been important in reducing the overall operative mortality.

Based on these experiences, an opportunity exists to extend the benefits of repair to the majority of patients with mitral valve disease. In rheumatic valves, scarred/retracted leaflets can be augmented with pericardial patches (15,18). Submitral pathology, such as chordal fusion, thickening, calcification or retraction, can be resected, and the anterior leaflet reattached to the papillary muscles with ACR (21). Relieving any submitral tethering or obstruction may be important to achieve good long-term results in rheumatic disease (33,34). Similar methods can be used to repair leaflet or chordal defects in endocarditis (15), and pericardial leaflet augmentation can be useful in congenital valves (24). In HOCM pathologies, ACR allows the resection of obstructing anterior papillary/chordal complexes and the transposition of chordal support to the posterior papillary muscle, simultaneously relieving the mitral component of outflow tract obstruction and MR (23). As a result of this conversion to repair, many problematic aspects of valve surgery practice, such as reoperation for thrombosed, degenerated or infected

prostheses, seem to be decreasing (Figs. 1 and 4), possibly because of fewer valve-related complications after repair. In contrast to early concepts, one advantage of repair may be the greater durability of the body's own tissues compared to any prosthetic material, accounting for low valve-related complications and better risk-adjusted survival (4-6).

The use of Gore-Tex ACR to repair myxomatous prolapse may be even more durable than resectional techniques (14,20), since overall chordal support is augmented and is not based on residual myxomatous chords (35). Avoiding leaflet resection maintains the leaflet surface area, and not only promotes early valve competence but also allows a greater long-term margin of safety. Late results with autologous pericardial leaflet augmentation also have been good (18), and the combination may be especially durable. Finally, Carpentier's original concept of a full rigid ring annuloplasty may provide an improved long-term margin of safety, by permanently decreasing the anterior-posterior dimension and increasing the surface area of leaflet coaptation (36).

Another recent innovation in mitral surgery has been the conversion to minimally invasive approaches (37). Currently, at the author's center isolated posterior leaflet prolapse is repaired routinely with robotic methods (19), using identical ACR techniques as in open patients. As described previously (38), ACR without leaflet resection is ideal to combine with robotic technology, and in the authors' experience early and intermediate-term outcomes have been equivalent to open procedures. The conversion to robotic approaches may be responsible, in part, for the falling numbers of open repairs in recent years (Table I), although while similar results can be achieved these reductions in patient morbidity are worthwhile. Currently, the present authors continue to advocate open repair for more complex pathologies (19); however, if the late outcomes for robotic repair remain stable, then robotic approaches will most likely be applied to more bileaflet or complex rheumatic disorders.

*In conclusion*, the available data suggest that the early and late outcomes of mitral surgery are better after valve repair than after prosthetic replacement. As techniques continue to evolve, and the use of ACR and pericardial leaflet augmentation increase, then repair rates will approach 100%. At the same time, the operative mortalities for all mitral surgery are falling very close to 0%, due to a combination of improvements in perioperative care and increasing repair rates. The transition to a more uniform repair may improve both early and late outcomes, such that the benefits of repair can potentially be extended across the spectrum of mitral disorders. An era may be approaching of

unprecedented results in the surgical treatment of mitral valve disease.

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