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ORIGINAL ARTICLE

Long-Term Results Following Repair for Degenerative Mitral Regurgitation – Analysis of Factors Influencing Durability

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Background The majority of patients with degenerative mitral regurgitation (DMR) are amenable to reconstructive procedures. There is debate regarding factors that influence long-term durability with respect to repair technique, valve remodelling and progressive myxomatous change.

Methods A total of 685 patients with DMR underwent mitral valve repair by a single surgeon between 1991 and 2011 with follow-up completed at 31 December 2016. Repair rate for patients undergoing surgery for DMR was over 90%. Mean age was 64 years (18–89) with 66.2% male, 47% NYHA class III–IV, and 20% had permanent atrial fibrillation (PAF). Major associated procedures were performed in 28% of patients (189); including coronary artery bypass graft (CABG) (127), aortic valve replacement (15), aortic root surgery (3) and tricuspid valve annuloplasty (61).

Results Operative mortality (≤30 days) occurred in four patients (0.58%). At 20 years, survival was 58%, freedom from reoperation was 90% and freedom from reoperation and non-operated recurrent MR >2+ (relapse) was 78%. Factors influencing survival were advancing age, left ventricular (LV) dysfunction (ejection fraction <60% or end systolic dimension >40 mm), New York Heart Association (NYHA) III–IV and PAF. Predictors of relapse were the degree of residual intraoperative mitral regurgitation ($p < 0.001$), anterior leaflet prolapse ($p < 0.001$) and the addition of a sliding annuloplasty in isolated posterior leaflet repair ($p = 0.023$). The majority of reoperations were for technical issues related to the original repair. A competent valve at 6 months to 3 years postoperatively predicted an excellent long-term result.

Conclusion The great majority of degenerative mitral valves are repairable regardless of age with excellent long-term results achievable following surgery. Survival is reduced by significant symptoms, LV dysfunction and preoperative PAF. Repair is best performed before these features develop. Durability is largely dependent on the technical performance of the repair and degree of residual MR on the post-pump transoesophageal echocardiogram. We recommend surgery should be performed by surgeons specialising and skilled in mitral valve repair.

Keywords Degenerative mitral regurgitation • Mitral valve repair • Annuloplasty • Survival • Durability • Reoperation

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Introduction

Degenerative mitral valve disease is the predominant cause of mitral regurgitation (MR) requiring surgical intervention. Degenerative pathology is largely due to myxomatous disease with leaflet prolapse and is highly amenable to reconstructive procedures so that mitral valve repair is the procedure of choice for the great majority of patients with significant degenerative mitral regurgitation (DMR). The benefits and advantages over a replacement procedure are well documented [1–5].

In considering the long-term expectations from a mitral valve repair in terms of reoperation and recurrent MR, it is unclear as to the interplay between disease progression, the surgical technique of the repair and the subsequent post repair remodelling process.

Several published series have determined that early reoperation is due to technical failures and later reoperation most likely due to progressive valve disease with recurrent prolapse and leaflet thickening [6–9]. What is uncertain is whether these long-term valve related failures in some way result from technical aspects of the repair and evolving postsurgical changes in the leaflets and annulus, rather than progressive myxomatous disease. It is important to recognise and anticipate that the repaired valve and annuloplasty device will undergo changes relative to the techniques used to repair the valve and an awareness and understanding of these is necessary to improve the long-term durability.

The long-term success of a mitral valve repair is often measured by freedom from reoperation over time, however, to fully assess initial repair durability it is necessary to consider significant recurrent MR that has not been reoperated on but can impact on the patient's wellbeing and survival [10,11]. This has been illustrated in other long-term follow-up studies where the endpoint of recurrent MR >2 + shows a more realistic appraisal of the success of the repair [6,7,12,13].

This study examines the long-term outcomes following mitral valve repair for DMR and, in particular, examines the reasons for early and late recurrence in this group of patients.

Methods

Patients

The present study details a single surgeon's experience with patients who underwent surgery for DMR between 1991 and 2011. From the outset, the intent was to attempt a valve repair on every patient undergoing surgery for DMR. This was not always considered possible in the early phase of the experience leading to choice of replacement over repair in some patients with complex bileaflet disease. It also resulted in some on-table and early failures. Nevertheless, overall, a repair was able to be achieved in over 90% of patients coming to surgery for DMR (82.2% from 1991 to 1999 and 96.4% from 2000 to 2011).

This study includes 677 patients who underwent mitral valve repair. In this cohort, eight patients underwent a second repair and were re-entered as a new patient making a total of 685 procedures. Data was collected retrospectively from 1991 to 2000 and prospectively from 2000 and 2011. Follow-up continued to 31 December 2016. Approval for this study was obtained from the Uniting Care Health Ethics Committee.

Patient Demographics and Comorbidities

Demographic data and comorbidities are detailed in Table 1. In this cohort, 35 patients had undergone previous cardiac surgery and 291 patients underwent associated procedures in addition to the mitral valve repair.

Perioperative Details

Perioperative details including procedural techniques are provided in Table 2. Indications for surgery were for symptoms and/or severity of MR. Dyspnoea was assessed using the New York Heart Association (NYHA) criteria. Preoperative transthoracic echocardiography (TTE) was used to assess left ventricular (LV) function. For this study, LV dysfunction was defined as an ejection fraction (EF) <60% and/or an end systolic dimension (ESD) of >40 mm.

The operations were performed through a median sternotomy or a partial sternotomy (small number). Myocardial protection was with moderate hypothermia and antegrade and retrograde cardioplegia.

Intraoperative prepump transoesophageal echocardiography (TOE) was used routinely and performed by a cardiologist specialising in TOE and included measurements of the annulus diameter, leaflet size and assessment of the risks of systolic anterior movement post repair as well as tricuspid valve (TV) function and annulus size. The mitral annulus size was characterised as normal <35 mm, moderate dilatation 35–45 mm and severe dilatation >45 mm.

Repair techniques evolved continually over the 20-year period of this experience. For the posterior leaflet (PL) repair techniques were predominately quadrangular resection (slightly wider at the base to avoid tension at free edge) with local annular plication (QR) or a sliding annuloplasty (QR + slide). In the latter period of this experience the annular plication was abandoned and localised prolapse was corrected with the use of 4-0 GoreTex chords (Gore-Tex; W. L. Gore & Associates Inc., Newark, DE, USA) with minimal or no resection (PL-AC). For the PL the neochord length was determined to ensure the PL was sitting in the inflow of the left ventricle and length would vary depending on the height of the PL. Anterior leaflet (AL) prolapse was largely corrected with 4-0 GoreTex chords and an associated small triangular resection if there was excess billowing tissue. A single GoreTex suture was used for each pair of artificial chords and passed through the base of the papillary muscle as a pledgeted supported mattress stitch. Initially in this experience, chords were fixed on the AL by passing through the AL and a

Table 1 **Patient demographics, comorbidities and preoperative echocardiographic data.**

Preoperative Characteristics	N	%	Median	Range
Patients[a]	685			
Age at surgery				
Male	453	66.1	64	19-89
Female	232	33.9	65	18-89
NYHA Functional Class[b]				
I	114	16.9		
II	272	40.4		
III	198	29.4		
IV	89	13.2		
Angina Pectoris	75	10.9		
History of Myocardial Infarction	22	3.2		
Previous Cardiac Surgery	35	5.1		
Infective Endocarditis				
Active	7	1.0		
Healed	18	2.6		
Undefined	2	0.3		
Hypertension	165	24.1		
Atrial Fibrillation				
Permanent	136	19.8		
Paroxysmal	79	11.5		
Mechanism of MR				
Posterior Leaflet Prolapse		433		63.2
Anterior Leaflet Prolapse		70		10.2
Bi-Leaflet Prolapse		169		24.7
Ruptured Chordae		377		55.0
Other		13		1.9
Preoperative Echocardiographic Data	**n**	**%**	**Median**	**99% Range**
LVEF %	614	89.6	65	40-84
LVEDD (mm)	566	82.6	58	40-80
LVESD (mm)	377	55.0	36	22-54
LV Status[b]				
Normal	325	59.2		
Dysfunction	224	40.8		
LV Volume ml	327	47.7	126	66-220
LA Diameter mm	524	76.5	47	28-70
LA Area cm^2	513	74.9	31	17-59
RVSP mm Hg	436	63.6	41	24-96
Mitral Regurgitation[b]				
Grade <3-4	23	3.5		
Grade 3-4	642	96.5		
Mitral Valve Annulus mm[b]				
Normal 35	47	7.0		
Moderate Dilation 35-45	420	62.6		
Severe Dilation >45	204	30.4		

Abbreviations: NYHA, New York Heart Association; MR, mitral regurgitation; EDD, end diastolic dimension; EF, ejection fraction; ESD, end systolic dimension; LA, left atrial; LV, left ventricular; RVSP, right ventricular systolic pressure.

[a]8 patients entered a second time at reoperation for a repeat mitral valve repair.

[b]Proportion of classified values only.

Table 2 Perioperative details including procedural techniques.

Operation Details	N	%
Technique of Repair	673	
Quadrangular Resection	518	
Triangular Resection	12	
Slide Post Leaflet	178	
Chordal Transfer	16	
Chordal Shortening	8	
Artificial Chordae - Anterior Leaflet	152	
Artificial Chordae - Posterior Leaflet	81	
Artificial Chordae – Anterior + Posterior	23	
Anterior Leaflet Resection	32	
Commissural Fusion	55	
Posterior Leaflet Reduction	52	
Leaflet Enlargement or Patch	8	
Papillary Muscle Repositioning	5	
Alfieri	1	
Decalcification & Reconstruction	43	
Closure Perforation	8	
Other	3	
Annuloplasty Ring		
Colvin Galloway	1	0.1
Cosgrove	221	32.3
Pericardial	114	16.6
Physio	323	47.2
No Annuloplasty Ring or Band	26	3.8
Post Pump TOE MR Grade[a]		
0-Tr	598	87.3
1+	61	8.9
>1+	20	2.9
Associated Procedures		
CABG	127	
Aortic Valve Replacement	15	
Aortic Root Replacement	3	
Tricuspid Valve Annuloplasty	61	
Atrial Fibrillation Ablation	91	
Left Atrial Reduction	13	
Other	68	
Postoperative Complications		
Complications		
Operative Death (< = 30 days)	4	0.6
Haemorrhage Requiring Reintervention	17	2.5
PPM	27	3.9
ICD	1	0.1
PE	1	0.1
CVA Persisting >72 hrs	2	0.3
TIA	22	3.2
Pericardial Drainage	5	0.7
Debridement (DSI)	10	1.5
Other	73	10.7

Abbreviations: CABG, coronary artery bypass graft; CVA, cerebrovascular accident; DSI, deep sternal wound infection; ICD, implantable cardioverter defibrillator ; PE, pulmonary embolus; PPM, permanent pacemaker; TIA: transient ischaemic attack; TOE, transoesophageal echocardiography; MR, mitral regurgitation.
[a]Proportion of classified values only.

small pericardial pledget and then tied down on the pledget with the knot on the left atrial (LA) side. The ends of the GoreTex knot were then fixed onto the surface of the AL with a 5-0 braided suture so providing a flat surface for coaptation. This was later changed, once the two arms of the GoreTex suture passed through the AL and length determined, a knot was tied with three throws on the atrial side of the leaflet and the sutures then passed back through the adjacent AL and the formal fixation knot completed on the LV side of the AL thus leaving a smooth surface for coaptation. For the AL the length was judged to match the adjacent normal opposite leaflet by putting the free edge of both leaflets under tension with stay sutures on either side of the GoreTex chord [14].

An annuloplasty band or ring was implanted in the great majority of patients. Twenty-six (26) patients, mainly early in this experience, did not receive an annuloplasty device when the leaflet disease was localised and the annulus was not dilated. Early in the experience annuloplasty was performed using a glutaraldehyde treated strip of autologous pericardium. Subsequently this was changed to a Cosgrove annuloplasty band (Edwards Lifesciences, Irvine, CA, USA) or Carpentier-Edwards Physio Ring (Edwards Lifesciences). The annuloplasty device was sized against the surface area of the anterior leaflet using the Carpentier-Edwards sizing devices.

Up until 2005, a tricuspid annuloplasty was performed in patients with moderately severe to severe tricuspid regurgitation (TR). Subsequent to 2005, a tricuspid annuloplasty was also performed in patients where the annulus was greater than 40 mm regardless of the degree of TR.

Associated procedures performed included coronary artery bypass grafting (CABG), aortic valve replacement (AVR), aortic root replacement, atrial fibrillation ablation, tricuspid valve surgery and LA reduction.

On completion of the repair a ''water test'' was done by removing retractors and distending the LV with saline. While not always reliable, it generally gave a good indication of competence, length of leaflet coaptation, position of the line of closure and the correction of prolapse. The ultimate assessment of repair was the post-pump TOE and this was performed in all but six patients where there were issues with the availability of, or function of the echo machine.

A TTE was routinely performed prior to discharge. Warfarin was prescribed for a minimum of 6 weeks or longer depending on rhythm and any evidence indicative of thrombo-embolisation.

Follow-Up and Outcomes

Patient follow-up was by the surgeon at 4 weeks postoperatively and thereafter planned for 1- to 2-yearly with a TTE and review by the surgeon and or referring cardiologist.

Where follow-up was deficient, patients and local doctors were contacted by mail or phone. Nevertheless, complete follow-up was compromised in part by the large distances involved, patient relocations and the reluctance of some patients to have further echocardiography performed.

Patient details were matched to records held by the Queensland Registry of Births, Deaths and Marriages (BDM) and the date of death, where noted, was used for analysis. Patients were assumed to be alive as of 31 December 2016 if there was no statistical match in BDM records.

In cases where a patient underwent reoperation with mitral valve repair or replacement, survival time was calculated using the date of reoperation as the date of censoring and the outcome at that time recorded as survived.

On the follow-up echocardiograms the degree of MR on colour flow Doppler was classified as none to a trace (0-Tr), 1+, 2+, 3+, 4+. Moderate to severe and severe MR was considered >2+ and consistent with other published follow-up data [7,12].

Relapse was defined as reoperation on the mitral valve for any cause and patients who developed recurrent MR >2+ on any follow-up TTE but did not undergo reoperation during the time frame of the study.

Statistics

Data are analysed based on procedure. Continuous data presented in the tables are summarised as median and range (unless otherwise noted), categorical variables are presented as frequency and percentage of number of complete records for each field (in these cases the total known record count is shown). Incomplete data was assumed to be missing at random. Comparisons in the tabular data, where made, employed either the Mann-Whitney U test or the Chi-squared test as appropriate. A p-value of 0.05 was used to assess statistical significance. Analysis was carried out using SPSS Version 18.0 (PASW Statistics for Windows, Version 18.0. Chicago, USA SPSS Inc.).

Actuarial analysis for survival employed the Kaplan-Meier method with comparison of outcomes carried out using the Log-Rank test. Predicted survival curves were generated using information extracted from the Australian Institute of Health and Welfare General Record of Incidence of Mortality calculates mortality risk based on year of surgery, age and gender matched general population groups.

For evaluation of freedom from reoperation on the mitral valve as an isolated endpoint and valve relapse (defined as either reoperation for repair or replacement of the mitral valve or recurrence of MR >2 +), only data available through patient follow-up has been employed. The period free of the event is taken as either the date on which the patient underwent the follow-up echocardiograph or the date of reoperation, whichever occurred earliest. In both cases, freedom from the event of interest was analysed using the Kaplan-Meier method with comparison of outcomes carried out using the Log-Rank test.

Exploration of factors impacting on patient survival and valve durability employed Cox regression analysis. Factors included in the evaluation of the multivariate model were identified as significant using initial uni-variate analyses.

Results

Postoperative Mortality and Morbidity

There were four operative deaths (deaths within 30 days): respiratory failure of a patient on a ventilator preoperatively with pulmonary oedema and severe MR; heart failure with

poor LV function postoperatively; sudden death at home 3 weeks post surgery in a patient with severe preoperative LV dysfunction; and a patient who suffered anticoagulant related haemorrhage 1 day after discharge. One patient died in hospital at 33 days after an early mitral valve replacement for a failed repair with haemolysis. There were two late in hospital deaths; one patient died in rehabilitation at 115 days with cardiac and respiratory failure and arrhythmia and another patient who was readmitted with a pericardial effusion and sepsis and died of respiratory failure at 116 days. A summary of the postoperative complications is provided in Table 2.

Long-Term Follow-Up

Survival

Table 3 shows the results of univariate and multivariate analysis to identify factors associated with survival. Reduced survival was related to advancing age, preoperative NYHA class III–IV, LV dysfunction and PAF. Associated CABG and previous MI were significant in the univariate but not multivariate analysis. Figure 1(a) and (b) depict the Kaplan Meier curves for overall survival and survival by preoperative LV status (with predicted survival for age and gender matched populations). While survival of patients without LV dysfunction was similar to an age and gender matched general population, those in the LV dysfunction cohort appeared to experience reduced survival when compared to that predicted by the age and gender matched population.

Reoperation

Thirty-seven (37) patients (5.4%) required reoperation over the period of follow-up; 13 <30 days, nine between 30 days and 1 year, 15 beyond 1 year. More than half of the patients reoperated under 1 year were early in this experience. Recurrent MR>2+ was present in 32 of the reoperated group. Figure 2 depicts the Kaplan Meier curve for freedom from reoperation as an isolated endpoint. Freedom from reoperation at 20 years was 90%.

Table 4 provides a summary of factors considered as the reason for reoperation. The majority of failures appear due to technical aspects of the operative repair and resultant changes in the valve and annulus that developed with time and were partly dependent on the techniques used.

Relapse

In addition to the patients who underwent reoperation on the mitral valve for any cause there were 17 patients who developed recurrent MR > 2+ and did not undergo reoperation during the timeframe of this study. Figure 3 depicts freedom from relapse while Table 5 reports the results of univariate and multivariate analysis to identify factors associated with this endpoint. The strong association with relapse was the degree of residual MR on post-pump transoesophageal echocardiography (TOE) ($p < 0.001$). This analysis suggests that residual MR of more than 0-Tr was associated with higher incidence of reoperation and recurrent MR>2+ (Figure 4). In 12% of repairs the post-pump TOE had greater than 0-Tr MR and 47% of relapse patients occurred in this group. Actuarial analysis shows that 90% of those who had 0-Tr on the post-pump TOE remained free of reoperation or MR >2+ at 15 years. Repairs involving anterior leaflet ($p = 0.008$) and bileaflet prolapse ($p = 0.029$) were also at increased risk for relapse.

A comparison between the three major techniques used for repairing isolated PL prolapse: QR, QR + slide and PL-AC with or without a triangular resection showed no significant difference between QR and PL-AC but the addition of a sliding annuloplasty to a QR was associated with a higher rate of relapse ($p = 0.023$).

The degree of residual MR as assessed on a follow-up TTE done at 6 months to 3 years (mean 1.1 years) postoperatively is predictive of the likelihood of future relapse. Demonstration of a competent valve or trace of MR at this time period is predictive of an excellent long-term result (Figure 5).

Systolic Anterior Movement

Systolic anterior movement (SAM) occurred in 23 patients (3%) post-pump. Ten (10) patients failed to respond to conservative measures and underwent a second pump run. Seven (7) were corrected by further reducing the height of the posterior leaflet, one by changing the ring and two with the insertion of posterior leaflet chords.

Endocarditis

Four (4) patients developed endocarditis requiring reoperation. In two, the infection was limited to the ring which was replaced by a strip of bovine pericardium and in two, with extensive infection on the aortic valve as well, valve replacements were performed.

Tricuspid Regurgitation

Sixty-one (61) patients underwent an associated tricuspid annuloplasty; 19 prior to 31 December 2005 and 42 after 2005. On long-term follow-up (>10y yrs post operation), the degree of TR was recorded in 139 patients who had not had an associated tricuspid annuloplasty at the time of repair. Of these only five patients (3.6%) had moderately severe to severe TR (3–4+).

Discussion

Repair Rate

This study represents a single surgeon's experience that evolved over a 20-year period. There was a substantial learning curve and the rate of repair increased with experience, however, overall 91.5% of DMR valves coming to surgery were repaired and 8.5% replaced. From 2000 to 2011, 491 patients underwent mitral valve surgery for DMR and repair was achieved in 96.5%. The reasons for replacement in the 3.5% of patients were three for on table failure, 13 with extensive annular and or leaflet calcification (two with

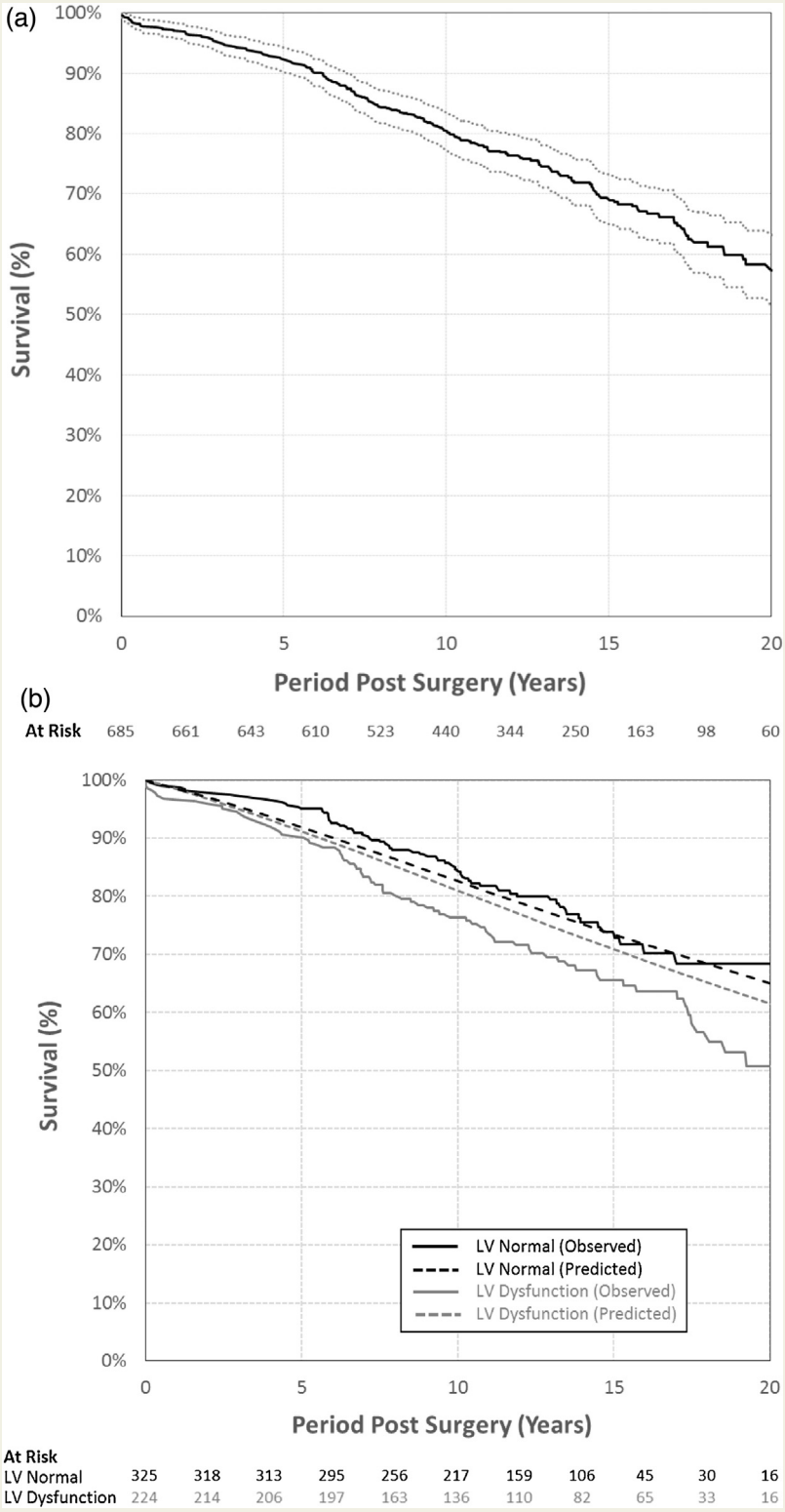

Figure 1 (a) Actuarial survival with 95% confidence interval is shown. (b) Comparison of the actuarial survival for patients with normal left ventricular (LV) function and abnormal LV function (Log-Rank: p = 0.011). Age and gender matched normal population for each group is shown. The survival of patients with normal LV function is similar to age and gender matched normal population.

Table 3 Cox Regression analysis of Survival.

		Univariate			Multivariate		
		HR	95% HR	Sig.	HR	95% HR	Sig.
Age	<55			<0.001** align="center"			<0.001** align="center"
	55-64	3.88	(1.85-8.11)	<0.001	3.44	(1.64-7.21)	0.001
	65-74	8.19	(4.11-16.32)	<0.001	6.90	(3.43-13.90)	<0.001
	> = 75	25.24	(12.62-50.49)	<0.001	19.45	(9.53-39.71)	<0.001
Gender (Male)		0.85	(0.64-1.13)	0.267			
NYHA (III/IV)*		2.22	(1.67-2.95)	<0.001	1.37	(1.02-1.84)	0.035
Hypertension		1.23	(0.91-1.67)	0.183			
Atrial Fibrillation (Permanent)		2.08	(1.55-2.79)	<0.001	1.40	(1.04-1.90)	0.028
Pre-Op LV Function (Dys)		1.40	(1.06-1.84)	0.017	1.51	(1.15-2.00)	0.003
Associated Procedure CABG		2.15	(1.59-2.9)	<0.001	1.25	(0.91-1.71)	0.17
Prior History of MI		2.51	(1.43-4.41)	0.001	1.51	(0.84-2.72)	0.168
Previous Cardiac Surgery		1.50	(0.79-2.84)	0.216			

Abbreviations: CABG, coronary artery bypass grafting; MI, myocardial infarction; LV, left ventricular; NYHA, New York Heart Association; HR, hazard ratio.
*HR compared to combined NYHA I/II.
**Between category analysis.

associated endocarditis on the calcific bar) and one with endocarditis. Therefore, in experienced hands, the major reason for replacing a degenerative valve is heavy annular and or leaflet calcification particularly where the repair is complex and when additional procedures are required.

Survival

In the multivariate analysis, long-term survival was negatively influenced by preoperative NYHA class, advanced age, PAF and LV dysfunction and again emphasises the importance of early repair surgery in patients with severe

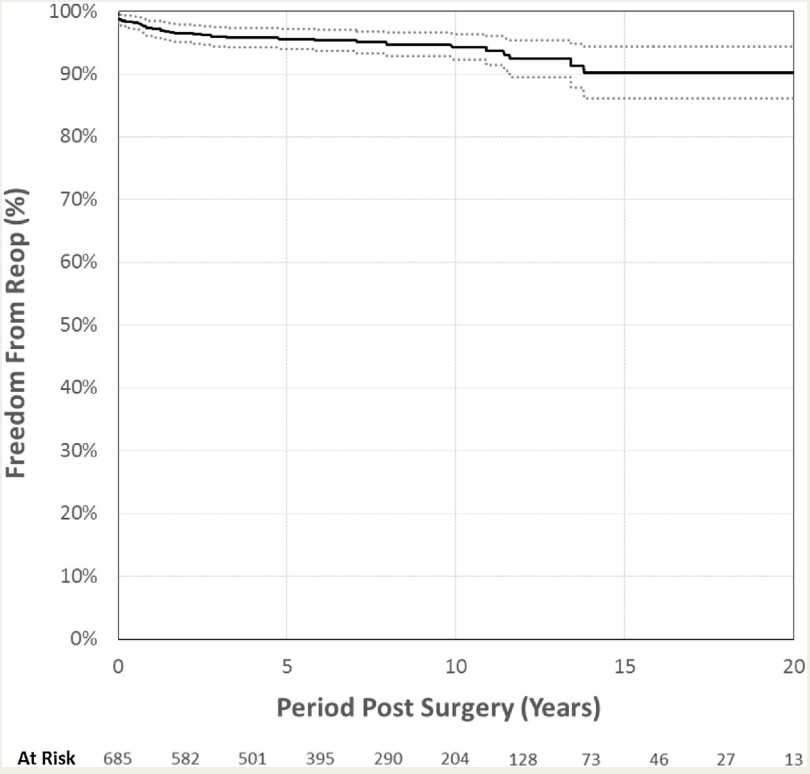

Figure 2 Actuarial freedom from reoperation on the mitral valve as an isolated endpoint with 95% confidence interval.

Table 4 Primary Factors Leading to Reoperation.

Factor	Number
Leaflet shrinkage, scarring post resection+/-annular dilatation	9
Residual or recurrent prolapse at or adjacent to the repair site	7
Dehiscence – breakdown of the repair	6
Bacterial Endocarditis: • limited to the ring with no mitral regurgitation (2)	4
• on an aortic prosthesis with extension to the mitral valve (2)	
Erosion of the anterior leaflet adjacent to the posterior leaflet repair	3
Haemolysis	2
Ring dehiscence	1
Edge to edge repair without ring	1
Unknown	4

mitral regurgitation before LV deterioration, symptomatic deterioration and atrial fibrillation occurs [6,15–17]. The American and European guidelines [18,19] support this approach providing there is a very high (>90–95%) likelihood the valve is repaired and with an operative mortality of less than 1%. As shown by Boling [20] and Chikwe [21] the individual surgeon repair rate in the USA is widely variable but dependant on experience and mitral surgery volume. In centres specialising in valve repair, repair rates near 100% are achieved [22] leading to the necessity for centres of excellence for mitral repair [23]. Australian surgeons are not exposed to the very high volumes seen in some overseas units. This makes it even more important that centres of excellence are established where valve repair can be concentrated to give the best outcomes for patients with DMR. Even in elderly patients, valve repair is still the procedure of choice [4,24]. In this experience 107 patients between 75 to 89 years were repaired with one perioperative death. Operative mortality and survival was not influenced by associated CABG as previously reported [15].

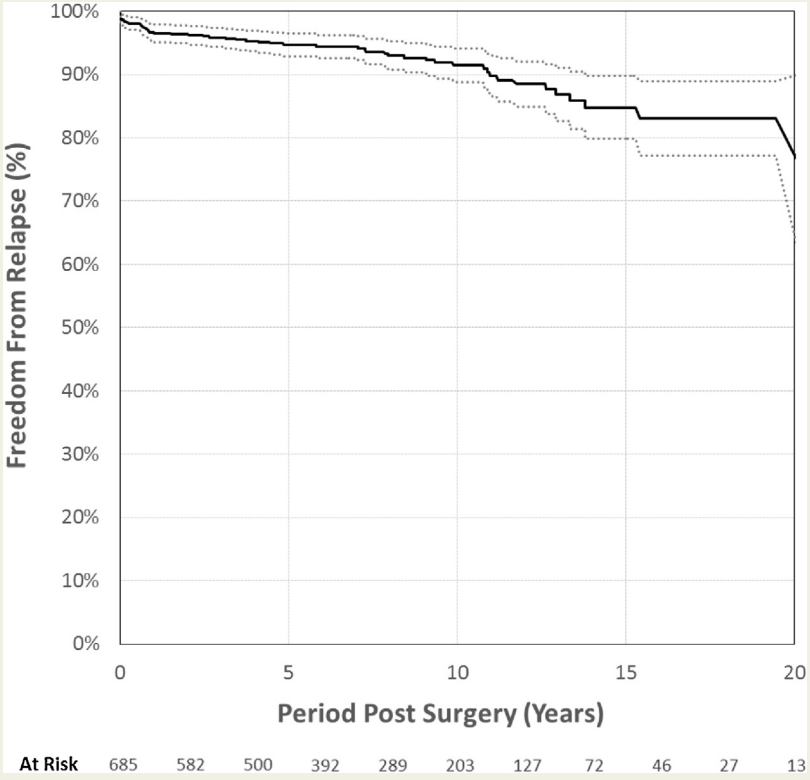

Figure 3 Actuarial freedom from relapse (Reoperation +/− MR >2 +) with 95% confidence interval.
Abbreviation: MR, mitral regurgitation

Table 5 Cox Regression Analysis of Relapse.

		Univariate			Multivariate		
		HR	95% HR	Sig.	HR	95% HR	Sig.
Age	<55			0.315**			
	55-64	1.16	(0.52-2.62)	0.714			
	65-74	1.48	(0.69-3.19)	0.315			
	> = 75	2.19	(0.90-5.32)	0.083			
Gender (Male)		0.65	(0.37-1.13)	0.129			
NYHA (III/IV)*		1.26	(0.73-2.15)	0.41			
Hypertension		1.59	(0.90-2.82)	0.108			
AF (Permanent)		1.19	(0.63-2.27)	0.596			
Annulus Size	Normal			0.134**			
	Moderate	0.59	(0.23-1.54)	0.284			
	Severe	1.04	(0.39-2.8)	0.933			
Ring Type	None/Colvin			0.195**			
	Cosgrove	0.83	(0.27-2.59)	0.748			
	Physio	1.14	(0.36-3.65)	0.827			
	Pericardial	0.44	(0.13-1.48)	0.186			
Leaflet	PLP			<0.001**			<0.001**
	ALP	2.63	(1.17-5.91)	0.02	2.85	(1.26-6.49)	0.012
	BLP	3.06	(1.70-5.52)	<0.001	3.39	(1.87-6.17)	<0.001
Ruptured Chords		0.68	(0.39-1.17)	0.161			
Post Pump TOE	0-Tr			<0.001**			<0.001**
	1+	4.06	(2.17-7.62)	<0.001	3.73	(1.98-7.01)	<0.001
	>1+	6.86	(3.06-15.40)	<0.001	8.31	(3.66-18.89)	<0.001
Pre-Op LV Function (Dys)		1.33	(0.78-2.29)	0.298			

Abbreviations: NYHA, New York Heart Association; PLP, posterior leaflet prolapse; ALP, anterior leaflet prolapse; BLP, bileaflet prolapse; TOE, transoesophageal echocardiography; AF, atrial fibrillation; HR, hazard ratio.

*HR compared to combined NYHA I/II.

**Between category analysis.

Relapse

Factors reported to increase the incidence of reoperation following MV repair include an absence of an annuloplasty device [6,25,26], AL prolapse [6], extent of myxomatous disease [6,10], and degree of residual MR immediately post repair [15,16].

In this series freedom from reoperation was 90% at 20 years while freedom from reoperation and/or recurrent MR >2+ (defined as relapse) was 78% at 20 years.

Multivariate Cox regression analysis has shown that the most significant factor for predicting relapse is the degree of residual MR on post-pump TOE. The evaluation of residual MR on the post-pump TOE is the critical decision point that will determine the long-term fate of the valve. The desired degree of residual MR is 0-Tr and anything more increases the risk of recurrence and or reoperation. In this series 0-Tr was not achieved in all cases but the rate improved with experience. Prior to 1995 the rate was 70.5% versus 89.9% post 1995 ($p < 0.001$). The approach to patients with more than 0-Tr MR on the post-pump TOE evolved over time. Early in this experience MR 1+ and in some cases more than MR 1+ was accepted. Subsequently, a degree of MR greater than 1+ would require a second pump run and revision. If the residual MR was 1+ it was generally accepted but only after close evaluation of the TOE to assess any obvious correctable factors which would create a risk for recurrence, namely residual prolapse or restriction, incorrect size and or implantation of the ring or band, the presence of systolic anterior movement. This emphasises the importance of skilled echocardiograhic evaluation. A long length of coaptation is desirable and is dependent upon the length and position of the posterior leaflet. A second or third pump run with a successful revision of the repair was performed in 13 patients.

Anterior leaflet prolapse (ALP) and Bileaflet prolapse (BLP) were also predictors of relapse in this series. Use of GoreTex chords was the predominant technique for repairing ALP and these were implanted in 62 of 70 patients with ALP and with the addition of a triangular resection in 10. In BLP, GoreTex chords were used to the anterior leaflet in 113 of 169 patients and triangular AL resection in 21. We reviewed all patients who had GoreTex chords placed to the AL and compared these to those who had an AL resection as an addition or in isolation and found that the relapse rate appeared less in those who had a resection but this did not reach significance ($p = 0.095$). In ALP with localised

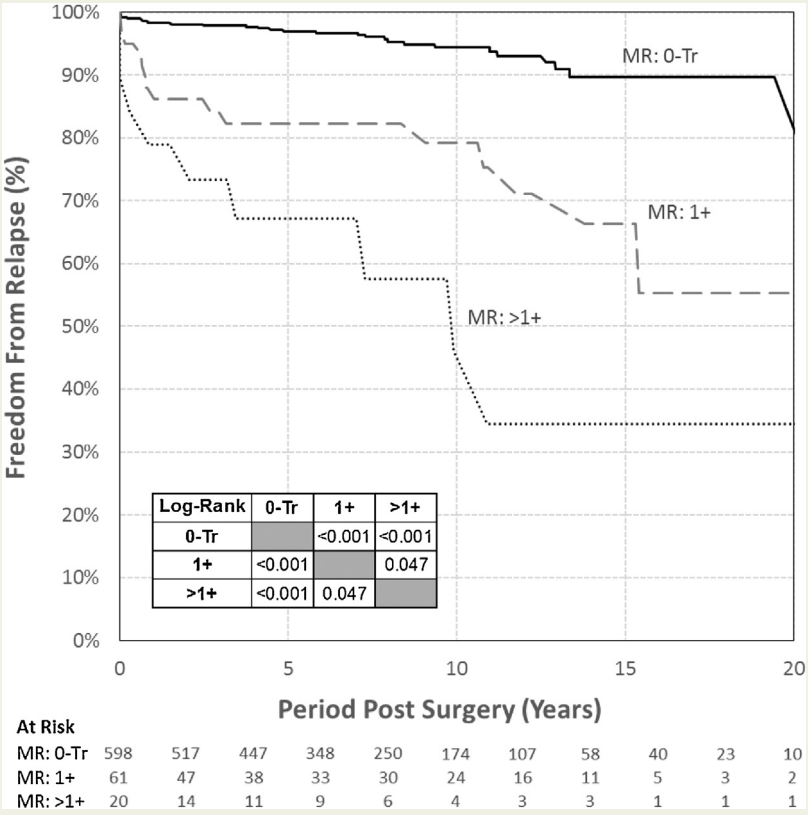

Figure 4 Actuarial freedom from relapse (Reoperation +/− MR >2 +) with respect to the degree of MR on the post pump TOE.
Abbreviation: MR, mitral regurgitation; TOE, transoesophageal echocardiography

billowing with excessive tissue we consider AL resection is the preferred technique providing the overall area of the AL is not compromised.

In determining the cause for recurrent MR and reoperation following repair it is generally accepted that early failure is procedure related and late failure is due to progressive disease [7–9,12,27] indicating that, at least for some patients, recurrence is inevitable. We examined the reasons for, and findings in, patients who underwent reoperation on the valve. There were 37 requiring reoperation and, in addition, there were five patients who had surgery elsewhere that required reoperation giving a total of 42 reoperations for evaluation. There were four with endocarditis and four others where documentation was insufficient. In the remaining cohort the findings at reoperation demonstrate that the majority can, in fact, be traced back to technical aspects of the original repair. Although there was a high incidence of early reoperations, in those experiencing a ''late'' reoperation the recurrence of some MR was seen early and progressed over time and then often at reoperation the recurrence appeared related to how the valve was left on completion of the initial repair. We came to appreciate some of the progressive changes that evolved in the valve were related to the repair technique. Observed were PL shrinkage particularly after a slide procedure, stiffness and calcification along resection lines, shortening of the posterior leaflet and encroachment of the ring or band into the orifice with some pannus exacerbating PL shortening. These changes lead to progressive loss of coaptation and increasing MR. With the development of recurrent MR annular dilation was also observed in some patients with a band.

For failed ALP there were a number of patients with recurrent prolapse at the repair site following an initial successful repair—at reoperation the reason was not obvious. Possible explanations are that the neochordal length was initially incorrect, or there had been slippage of the neochordal attachments or LV remodelling with changes in LV dimensions.

For PLP, published reports of long-term follow-up generally show excellent long-term results with a variety of techniques including the traditional Carpentier QR and annular plication [16,25,28] to triangular resection [15] and or chordal replacement with GoreTex [29].

In this experience, the techniques for repairing the PL evolved over time due in part to recognition of the findings at reoperation. The predominant technique was (QR) and local annular plication. In the latter part of this experience this was replaced by repairing localised PL prolapse with GoreTex chords with or without a small resection thus leaving the annulus intact, preserving tissue and increasing the coaptation surface [29]. Falk [30] compared these two methods of repairing PL prolapse and on early follow-up there

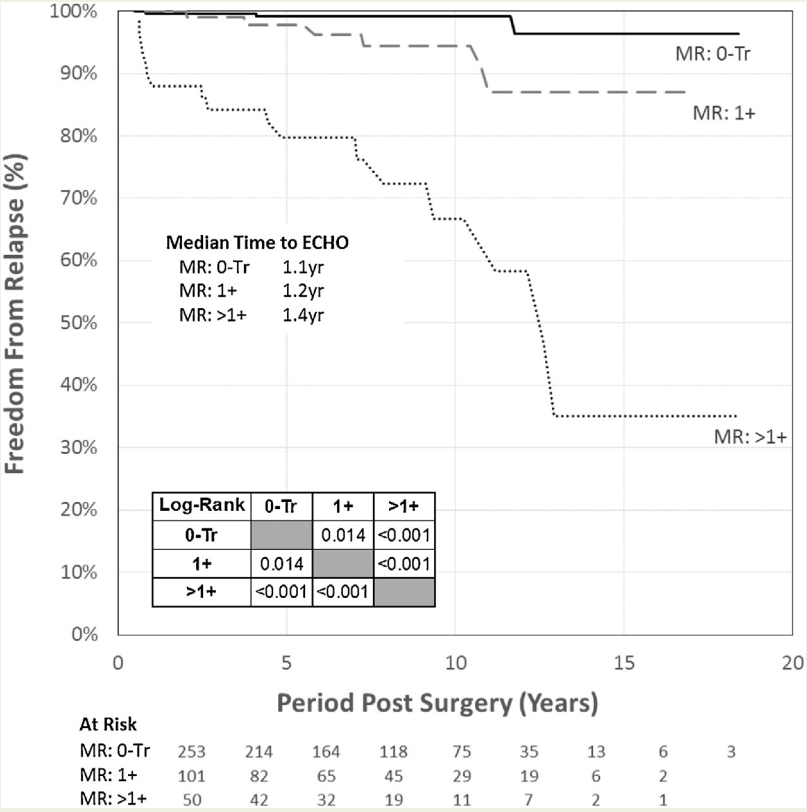

Figure 5 Actuarial freedom from relapse (Reoperation +/− MR >2 +) with respect to the degree of MR on the 1-year follow-up TTE.
Abbreviation: MR, mitral regurgitation; TTE, transthoracic echocardiograph

was no significant difference but coaptation surface was greater with chords suggesting this may influence the long-term result particularly considering the evolving changes we have observed.

Comparison of the three major techniques to correct PLP namely QR, PL-AC+/− triangular resection and QR + slide revealed there was no difference between PL-AC and QR but the follow-up period for PL-AC was considerably shorter. While QR + slide proved to be a predictor for relapse ($p = 0.023$) the indication was for more extensive PL pathology. The inferior results of QR + slide was not so much the fault of the technique but its execution. In recognition of this, a more conservative approach to resecting tissue was taken and a slide was only used for extensive posterior leaflet prolapse with excessive tissue. The disconnection of the posterior leaflet was limited to the area of excessive abnormal tissue and an adequate leaflet height of 1.5 cm was retained to allow for any subsequent remodelling and shrinkage. Following this, if any part of the PL was prominent or standing up on the saline test then it was repositioned further into the inflow with GoreTex neochords.

A critical issue with any posterior leaflet technique is ensuring the valve is not left with a deficiency of tissue. Undue stresses on leaflets adjacent to repair sites can lead to late prolapse with chordal rupture particularly where the PL is not positioned well down in the inflow of the LV.

What is not understood is the biological behaviour of myxomatous disease over time post repair and its influence on outcome. David [6] found that with more extensive the disease in the valve recurrence was more likely and Flemmeng [10] had poorer outcomes with Barlow's valve. Flemmeng [12] attributed progressive disease for an ongoing yearly attrition rate resulting in freedom from MR >2+ in only 60% of patients at 7 years postoperatively. Shimokawa [7] found leaflet thickening and AL prolapse were the main causes of recurrence and concluded this was due to progressive disease. Some leaflet thickening was noted in our series but occurred too early to implicate progressive disease. It is possible this may be an inflammatory response. Eliminating regurgitation and creating a good length of coaptation will reduce stress on any remaining diseased leaflets and chords.

To further investigate the influence of progressive disease we looked at the degree of MR on the follow-up TTE done in the time frame of 6 months to 3 years after the repair (see Figure 4). This suggests that, if the valve is competent at this early stage, then the incidence of subsequent reoperation or recurrent MR >2+ is extremely low. This supports our contention that the major factor influencing the long-term result is the technical aspects of the repair and the way the valve is

left at the end of the operation. These findings are supported by a recently published study with longitudinal echocardiographic follow-up post mitral valve repair where Chan [31] found that patients who required a subsequent reoperation were most likely to have recurrent MR of 2+ or higher within the first year after the operation.

Annuloplasty

Annular dilation is a common finding in DMR. Twenty-six (26) patients, mostly early in the experience with normal or minimally enlarged annulus, did not have an annuloplasty device. They did not have a higher incidence of relapse.

Three (3) main annuloplasty devices were a doubled over strip of glutaraldehyde fixed pericardium, a Cosgrove band and a Physio Ring. The pericardial bands were sized over a standard Carpentier Edwards sizing device and implanted with standard interrupted annuloplasty sutures placed as for a Cosgrove band. The difficulty was maintaining the sizing due to the concertina like effect when tying down of the mattress annuloplasty sutures. The great majority of pericardial bands were used early on with posterior leaflet repair or in association with endocarditis.

There was no significant difference between the annuloplasty devices in terms of reoperation and recurrent MR >2+.

Mitral stenosis was a rarity with these annuloplasty devices.

Systolic Anterior Movement (SAM)

No patient should be allowed to return to the intensive care unit (ICU) with SAM and MR. Early in this experience, SAM unresponsive to conservative measures was corrected by a further reduction of the height of the posterior leaflet using a Carpentier slide technique. However, recurrent MR subsequently occurred in half these patients and three required reoperation due to subsequent shrinkage of the residual PL and loss of coaptation.

Systolic anterior movement became much less of a problem by looking for risk factors for SAM on the pre-pump TOE and adjusting the repair to ensure the PL was well down in the inflow and coaptation line away from the LV outflow tract. In two patients who subsequently did have SAM post-pump, this was dealt with effectively by inserting PL Gor-eTex chords on the second pump run. In our experience, a further PL resection and height reduction on a second pump for SAM is a risk for later recurrent MR.

Annular Calcification

Major calcification in the annulus and or in the valve was the predominant cause for resorting to a replacement. However, 43 patients with annular calcific bars did undergo a successful repair after enbloc removal of the calcific bar and atrioventricular reconstruction.

Tricuspid Regurgitation

Sixty-one (61) patients had an associated annuloplasty. Earlier in this experience it was only performed when there was associated significant TR. However, as evidence emerged [32] recommending annuloplasty when there was tricuspid annular dilatation regardless of the degree of tricuspid regurgitation so as to prevent progressive TR after mitral repair, more annuloplasties were done in patients with a tricuspid annulus >40 mm.

We reviewed findings of the TTEs performed on patients more than 10 years after a valve repair where the degree of TR was reported. Only five of 140 patients had moderately severe to severe TR (3–4 +). Only one of these 140 patients had a TV annuloplasty at the time of mitral repair. This is consistent with the recent publications from David showing that, in degenerative disease, the subsequent development of TR following mitral repair is uncommon and that the tricuspid diameter alone is not predictive of developing subsequent TR [33,34]. With a mitral repair operation the indications for the addition of tricuspid annuloplasty in the absence of moderate to severe TR requires reappraisal.

Clinical Implications

Surgical techniques and their execution are critical to achieving long-term durability. This not only requires a competent valve on completion but recognition of subsequent remodelling that has the potential to compromise the result. Repair rates for DMR should be >95%. In Australia, this requires high volume repair specialists particularly for anterior and bileaflet subsets with the expectation that today, recurrence rates will be improved on the historical experience presented here. The indications for an associated tricuspid annuloplasty in the absence of moderate to severe TR require reappraisal.

Limitations

This study involved retrospective collection of data for the first half of the study and prospective thereafter. Survival data in part relied on BDM and, as such, patients relocating interstate or overseas may have been misclassified. Follow-up data regarding cause of death was unreliable and potentially some deaths may be due to undocumented deterioration of the mitral repair. Follow-up echocardiography data was not obtained in a core laboratory but relied on individual cardiologists in many instances and there was incomplete long-term echocardiographic follow-up which reduces the accuracy of estimating survival free of significant MR.

Conclusions

This study demonstrates that it is feasible to repair degenerative mitral valves in the vast majority of patients. The repair is safe irrespective of patient age and can be performed with a low risk of cerebrovascular events. The long-term outcome is excellent. The outcome of surgery is enhanced if performed before patients become severely symptomatic or demonstrate evidence of LV dysfunction on echocardiography. The single most important predictor of subsequent reoperation and recurrent significant MR is the degree of incompetence of the repaired valve assessed with a post-pump TOE.

A TTE performed at around 1-year postoperatively showing minimal MR is predictive of an excellent long-term result.

The outcomes documented in this study indicate that reoperation and recurrent MR are largely due to technical aspects of the initial repair rather than progressive degenerative disease of the mitral valve. The study emphasises the importance of long-term follow-up to determine the outcome of valve repair surgery and highlights the importance of careful follow-up to help modify technical aspects of the repair to improve long-term results.

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