Surgical Repair of Posterior Mitral Valve Prolapse: Implications for Guidelines and Percutaneous Repair

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Background. **Guidelines recommend early surgery for mitral regurgitation (MR) provided repair can be accomplished safely and consistently. However, many patients with degenerative disease are not referred for surgery or undergo replacement rather than repair. Data documenting early and long-term results of surgical repair of posterior prolapse, the most common lesion, are essential to broaden application of repair techniques and provide direction for percutaneous valve repair. This study provides data on long-term survival and valve function after repair of posterior leaflet prolapse.**

Methods. **Of 3,383 patients undergoing surgery for isolated posterior leaflet prolapse, repair was performed in 97%; 3,074 underwent standard quadrangular resection with annuloplasty. Follow-up for survival averaged 6.5 ± 4.5 years and for reoperation, 4.0 ± 3.9 years. Analysis of 4,913 echocardiograms for recurrent MR was performed in a subgroup of 2,575 patients.**

Results. **There were two hospital deaths (0.07%), and 15-year survival was 76%, superior to the age- and sex-matched US population. At 10 years, freedom from mitral reoperation was 97%, and 77% had no or 1+ MR; 11% had 3+ or 4+ MR. Repair durability was jeopardized by failure to use a prosthetic annuloplasty, left atrial enlargement, and left ventricular remodeling and dysfunction.**

Conclusions. **Mitral valve repair for posterior prolapse is a low-risk, durable surgical procedure. The repair must address both leaflet and annulus. Recurrent MR that is moderately severe or severe is uncommon in the decade after operation. These data support recommendations for early surgery and demonstrate that complete repair addresses multiple components of the valve, providing direction for percutaneous approaches.**

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American College of Cardiology/American Heart Association (ACC/AHA) Practice Guidelines for Management of Patients with Valvular Heart Disease recommend early surgery for patients with degenerative mitral valve disease if there is a high chance of successful repair and mortality is low [1–4]. The guidelines' recommendation for early surgery in asymptomatic patients with severe mitral regurgitation (MR) has not been universally accepted [3, 5]. In addition, the advent of percutaneous procedures for mitral valve repair has brought into question whether both the leaflets and the annulus must be addressed to achieve successful repair. Examination of published series focusing on surgical repair provides some insight into these areas of controversy. However, most reports of mitral valve repair include heterogeneous populations with varying sites of prolapse (posterior, anterior, bileaflet) undergoing a variety of procedures (eg, quadrangular resection, chordal transfer, artificial chordae, edge-to-edge repair, annuloplasty of

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various types). These analyses have helped to guide management algorithms for experienced mitral valve surgeons dealing with complex bileaflet disease to achieve successful repairs [6]. Yet two thirds of surgical patients have posterior leaflet prolapse, usually involving the middle scallop [5, 7, 8], for which standard repair, including a leaflet procedure (resection, with or without sliding repair) and annular procedure (prosthetic annuloplasty), can be performed without advanced techniques. Data from the Society of Thoracic Surgeons (STS) Database suggest that that only a small proportion of patients with degenerative mitral valve disease are treated at high-volume centers by "expert" mitral repair surgeons [9]. Although techniques for posterior leaflet repair have been widely applied for decades, many patients with potentially repairable valves still undergo replacement, and there are surprisingly few data addressing results of surgical repair for this most routine clinical presentation. The objective of this longitudinal study of a large cohort of such patients was to assess long-term survival and durability of standard surgical repair to provide guidance for wider application of these techniques.

Patients and Methods

Study Population

From January 1985 to January 2008, 4,258 patients with isolated degenerative mitral valve disease underwent primary isolated mitral valve repair at Cleveland Clinic. Mitral regurgitation was the primary indication in all. Patients having previous or concomitant operations for coronary artery disease, aortic valve disease, hypertrophic cardiomyopathy, or ascending aortic aneurysm were excluded. Results in an early subgroup of these patients were reported previously [5]. Of the 4,258 patients, 3,383 (79%) had isolated posterior leaflet prolapse, 97% of whom had valve repair. Valve repair by quadrangular resection, with (n = 1,457 patients) or without (n = 1,617) sliding repair, and annuloplasty was performed in 3,074, and these patients are the focus of this study (Fig 1).

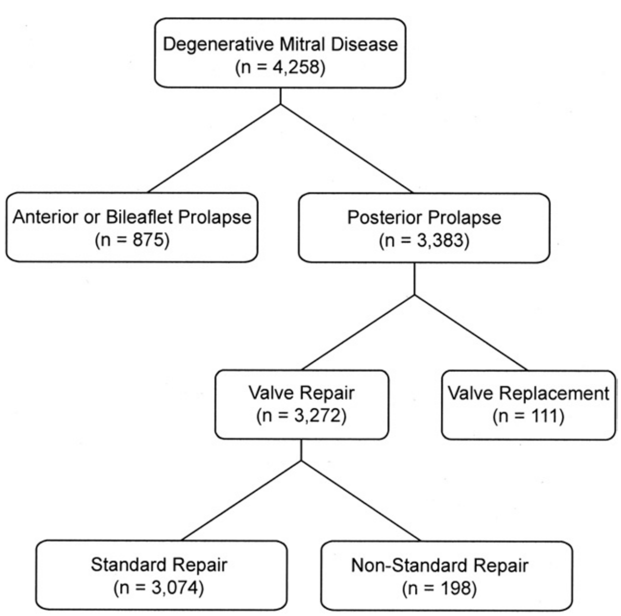

Fig 1. Study population. Of 3,383 patients with isolated posterior leaflet prolapse, mitral valve repair was performed in 96.7%, and 3,074 underwent a standard repair that included quadrangular resection and annuloplasty. These patients represent the study group.

Table 1. Patient Characteristics (n = 3,074)

Characteristic	n[a]	No. (%) or Mean ± SD
Age (y)	3,074	57 ± 13
NYHA functional class	3,073	
I		956 (31)
II		1,717 (56)
III		350 (11)
IV		50 (1.6)
Mitral regurgitation grade	3,074	
3+		223 (7.3)
4+		2,851 (93)
Ejection fraction, echocardiogram	2,489	0.58 ± 0.066
Atrial fibrillation or flutter	3,074	371 (12)
Cardiac dimensions		
LA diameter (cm)	2,615	4.9 ± 0.84
LA volume (mL)	2,615	65 ± 37
LV inner diameter, diastole (cm)	2,740	5.7 ± 0.77
LV inner diameter, systole (cm)	2,725	3.4 ± 0.70
LV end-diastolic volume (mL)	2,740	165 ± 50
LV end-systolic volume (mL)	2,725	51 ± 25

[a] Number of patients with data available.

LA = left atrial; LV = left ventricular; NYHA = New York Heart Association; SD = standard deviation.

Preoperative MR grade was assessed semiquantitatively by echocardiography using standard techniques; all patients had moderately severe (3+, 7.5%) or severe (4+, 92%) MR. Data were extracted from Cleveland Clinic's Cardiovascular Information Registry, a repository of clinical and surgical data manually abstracted concurrently with patient care. Echocardiographic data were extracted from Cleveland Clinic's Echocardiography Database. Use of these data for research was approved by the Institutional Review Board (IRB), with patient consent waived. Of the 3,074 patients, 31% were in New York Heart Association (NYHA) functional class I (asymptomatic), 56% in class II, 11% in class III, and 1.6% in class IV at operation (Table 1). Mean patient age was 57 ± 13 years, although age has declined somewhat with time (Fig 2). Mean preoperative left ventricular ejection fraction was 0.58 ± 0.066, end-systolic dimension was 3.4 ± 0.72 cm, and end-systolic volume was 51 ± 25 mL.

Surgical Technique

Surgical approach was upper hemisternotomy in 1,834 patients (60%) [10], sternotomy in 1,149 (37%), robotic in 67 (2.2%), right thoracotomy in 23 (0.75%), and unstated

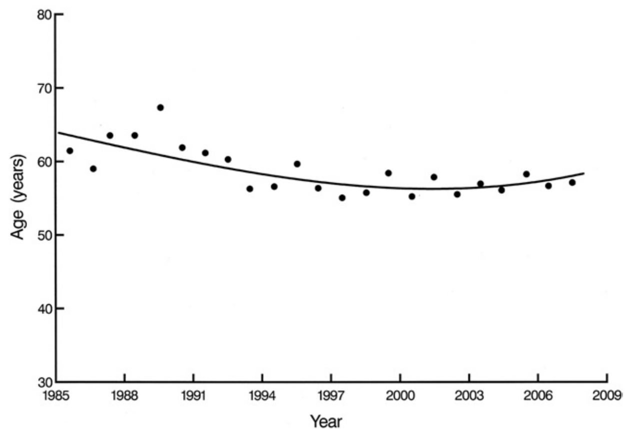

Fig 2. Mean age of patients undergoing repair of posterior leaflet prolapse as a function of time. Closed circles represent yearly age estimates. Solid line is trend line.

in 1. In all cases, the unsupported, prolapsing portion of the posterior leaflet was resected. For tall leaflets (>1.5 cm), a sliding repair was performed. Annuloplasty techniques included a prosthetic annuloplasty (Cosgrove-Edwards band in 2,769 [90%], Carpentier-Edwards classic ring in 94 [3.1%]) or posterior annular suture plication reinforced with bovine pericardium (207 patients, 6.7%).

Clinical Follow-Up

SURVIVAL AND REOPERATION. Patients undergoing heart valve surgery are followed systematically at 2, 5, 10, 15, and 20 years after operation. At each anniversary-type follow-up, patients are mailed an IRB-approved questionnaire; nonresponders are contacted by telephone using an IRB-approved script. Patient consent is required for use of follow-up information. Follow-up for mitral valve reoperation depended entirely on this active follow-up. Active follow-up averaged 4.0 ± 3.9 years, with 11% of living patients followed at least 10 years and 3% at least 12 years; 11,969 patient-years of data were available for analyses of reoperation. Information on vital status was supplemented by data from the Social Security Death Index (cross-sectional passive follow-up) [11, 12], yielding 19,918 patient-years of data for survival analysis, with 20% of living patients followed at least 10 years and 3% at least 16 years. Graphs of reoperation were truncated at 12 years and those of survival at 16 years.

RETURN OF MITRAL REGURGITATION. A subgroup of 2,575 patients was followed for return of MR by postoperative echocardiography at Cleveland Clinic, yielding 4,913 echocardiograms for analysis of MR grade; 858 patients (33%) had more than one echocardiogram. Because only 3% of echocardiograms were obtained past 10 years, depictions of their analysis are truncated then.

Data Analysis

SURVIVAL. Nonparametric survival estimates were obtained by the Kaplan-Meier method. A parametric method was used to resolve the number of phases of instantaneous risk (hazard function) and to estimate shaping variables (see http://www.clevelandclinic.org/heartcenter/hazard) [13]; multivariable analyses (with variables listed in Appendix A) were performed simultaneously for each hazard phase. Variable selection used bagging [14, 15]. In brief, 200 bootstrap resampled data sets were analyzed with a probability value of less than 0.05 as the retention criterion. Results were aggregated, including clustering of transformations of scale and closely correlated variables. Variables or clusters represented in at least 50% of analyses were used for final model fitting.

REPAIR DURABILITY. Repair durability was assessed by mitral valve reoperation in the entire cohort and return of MR in the echocardiographic follow-up subgroup. Freedom from reoperation was analyzed as for all-cause mortality.

Prevalence of each MR grade across follow-up time was estimated by longitudinal ordinal logistic regression for repeated measurements (PROC GENMOD; SAS, Inc, Cary, NC). Because frequency of occurrence of severe

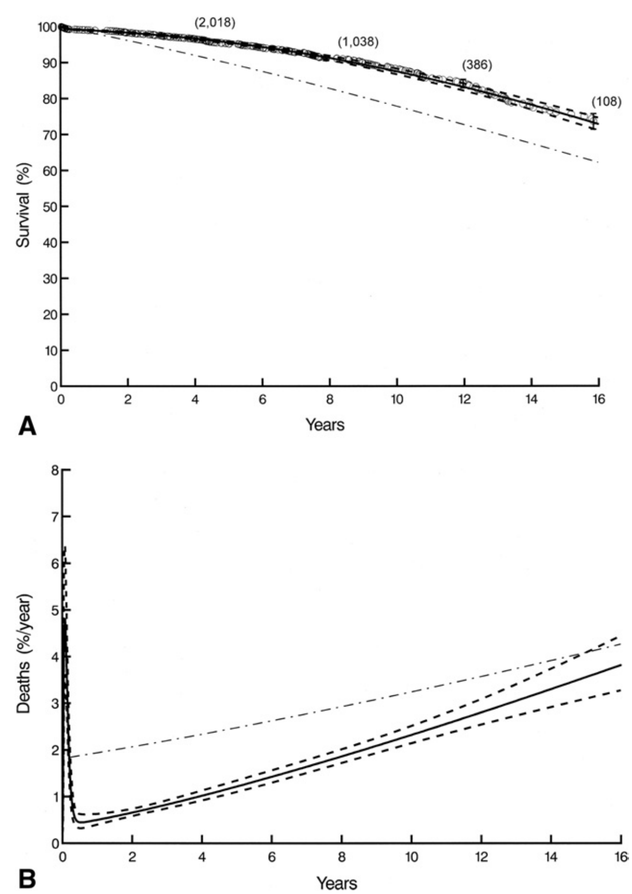

Fig 3. Death after mitral valve repair for posterior leaflet prolapse compared with expected survival of an age- and sex-matched US population cohort (dot-dash-dot line). Each circle represents a death, vertical bars are asymmetric 68% confidence limits (CL, equivalent to ± 1 standard error), solid line is parametric estimate enclosed within dashed 68% CLs, and numbers in parentheses are patients remaining at risk. (A) Survival. (B) Hazard function (instantaneous risk) for death. Solid line is hazard estimate enclosed within 68% CLs.

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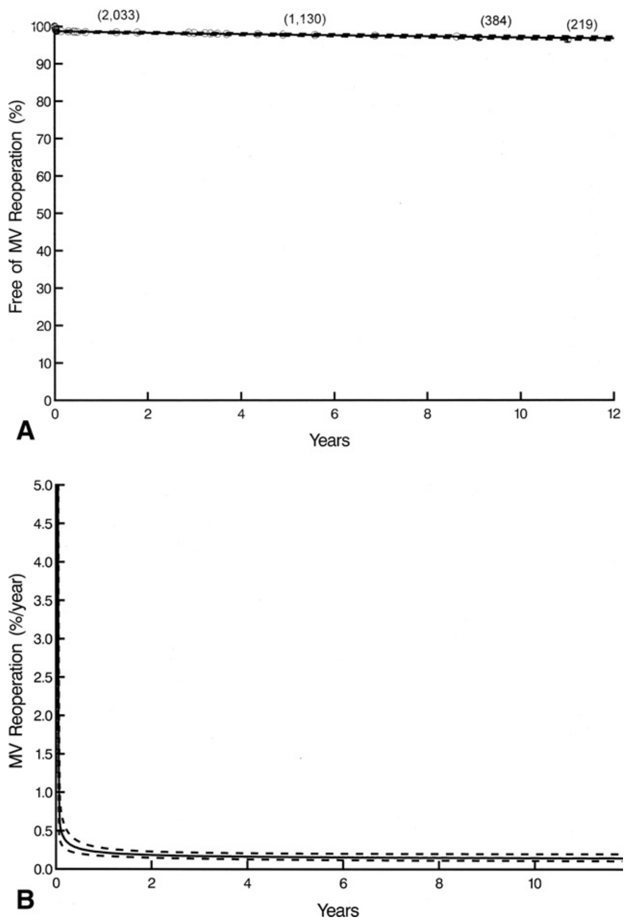

Fig 4. Mitral valve (MV) reoperation after repair of posterior leaflet prolapse. (A) Freedom from reoperation. Format is as in Figure 3A. (B) Hazard function (instantaneous risk) for reoperation. Format is as in Figure 3B.

MR (4+) was low, grades 3+ and 4+ were combined for analysis. Results are accompanied by crude independent estimates of prevalence of each grade within sequential time frames for informed comparison. Because MR returned rapidly within the first 2 weeks and far more slowly thereafter, separate analyses for risk factors were made for echocardiograms obtained within 2 weeks of operation and those obtained thereafter. To compensate for the limited capability of PROC GENMOD to explore multivariable relations, we screened variables using ordinary ordinal logistic regression (PROC LOGISTIC; SAS) with a liberal criterion ($p < 0.1$) assuming independence of observations. This analysis yielded candidates for the repeated-measurements multivariable model. These and their transformations, if any, were entered at once into the model, then eliminated individually until all variables remaining had a probability value of 0.05 or less.

PRESENTATION. Categorical data are summarized by frequencies and percentages and continuous variables by mean and standard deviation (SD). Uncertainty is expressed as ± 1 SD, ± 1 standard error, or equivalent asymmetric confidence limits (CL 68%). The hazard function is presented as rate per 100 patients (percent per year) in accordance with current US Food and Drug Administration guidelines.

Survival is compared with that of an age- and sex-matched US population (www.cdc.gov/nchs/products/pubs/pubd/vsus/vsus.htm). For this, conditional survival from age at operation was generated for each patient using a parameterized representation of sex-specific US life tables. These individual curves were averaged to yield overall matched population survival estimates.

Results

Survival

There were 2 hospital deaths (0.07%; CL, 0.03%, 0.2%). Overall unadjusted survival estimates at 1, 5, 10, and 15 years were 99%, 96%, 87%, and 76%, respectively. These figures compare favorably with expected survival of the age- and sex-matched US population, and this was true across all age groups (Fig 3A). Instantaneous risk of death (hazard function) resolved into three phases: a rapidly declining early hazard phase dominating to almost 6 months, a constant hazard phase dominating from 6 months to about 2 years, and a late rising hazard phase dominating thereafter (Fig 3B). Incremental risk factors included a history of heart failure, which increased risk early after operation. Old age and left ventricular dysfunction were risk factors in the constant and late hazard phases (Table 2, Appendix B).

Table 2. Incremental Risk Factors for Death After Posterior Mitral Leaflet Repair

Risk Factor	Coefficient ± SE	*p* Value	Reliability (%)[a]
Early hazard phase[b]			
History of heart failure	2.9 ± 0.94	0.0016	63
Constant hazard phase[c]			
Older age[d]	1.0 ± 0.20	<0.0001	51
Greater preoperative LA volume	0.0009 ± 0.0019	<0.0001	62
Body size			
Lighter weight[e]	3.5 ± 0.80	<0.0001	82
Heavier weight[f]	2.01 ± 0.39	<0.0001	82
Lower preoperative LVEF	−0.041 ± 0.016	0.009	71
Late hazard phase[g]			
Older age[h]	−11 ± 1.5	<0.0001	98
LV dysfunction	0.96 ± 0.22	<0.0001	85

[a] Percent of occurrences in 200 bootstrap models. [b] Intercept = −6.5 ± 0.73, $\delta = 0$; $Ln(t_{1/2}) = -2.3 \pm 0.169$, $\upsilon = 0$; $Ln(m) = -1.4 \pm 0.50$, where Ln is natural logarithm. [c] Intercept = −16.1 ± 2.6. [d] Exp(age/50), exponential transformation. [e] (80/weight), inverse transformation. [f] $(Weight/80)^2$, squared transformation. [g] Intercept = −0.92 ± 1.21, $\tau = 1$, $\alpha = 1$, $\gamma = 1$; $Ln(\eta) = 0.81 \pm 0.127$. [h] (50/age), inverse transformation.

LA = left atrial; LVEF = left ventricular ejection fraction; SE = standard error.

Table 3. Incremental Risk Factors for Mitral Valve Reoperation

Risk Factor	Coefficient ± SE	*p* Value	Reliability (%)[a]
Early hazard phase[b]			
Younger age[c]	1.7 ± 0.66	0.009	76
Elevated BUN	0.020 ± 0.0096	0.03	55
Lower hematocrit[d]	−1.8 ± 0.60	0.003	67
Greater preoperative posterior wall thickness	2.9 ± 1.02	0.004	51

[a] Percent of occurrences in 200 bootstrap models. [b] Intercept = −3.3 ± 2.4, $\delta = 0$; $\text{Ln}(t_{1/2}) = -3.8 \pm 0.071$, $\upsilon = 0$; $\text{Ln}(m) = -2.9 \pm 0.51$, where Ln is natural logarithm. [c] (50/age), inverse transformation. [d] Ln (hematocrit), logarithmic transformation.

BUN = blood urea nitrogen; SE = standard error.

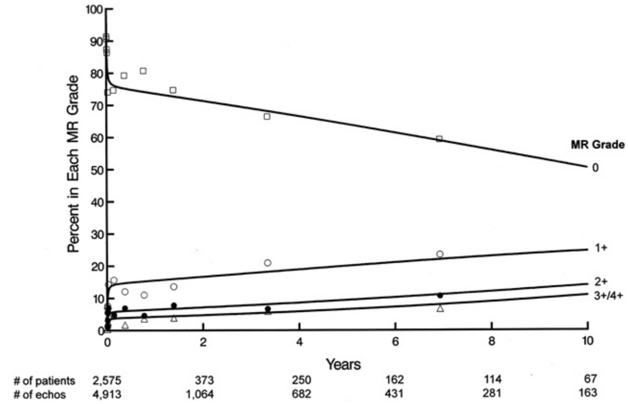

Fig 6. Temporal trend in return of postoperative mitral regurgitation (MR). Squares = no MR, open circles = 1+ MR, closed circles = 2+ MR, triangles = 3+/4+ MR.

Mitral Valve Reoperation

Fifty-three patients underwent mitral valve reoperation. Overall unadjusted freedom from reoperation at 1, 5, 10, and 12 years was 98%, 98%, 97%, and 96% (Fig 4A). Instantaneous risk of reoperation resolved to three phases: an early hazard phase dominating for 2 weeks, which accounted for half the events, a constant phase to 3 years, and a slowly decreasing phase thereafter (Fig 4B). Risk of reoperation diminished to 0.3% per year by 2 years and 0.2% per year by 7 years. Risk factors for early reoperation included younger age at operation (Table 3, Fig 5).

Recurrent Mitral Regurgitation

All patients left the operating room with MR grade 1+ or less. In the first 2 weeks after surgery, the percentage with MR grade 0 decreased steeply to 80%, whereas percentages with MR grades 1+, 2+, and 3+/4+ increased to 13%, 6%, and 5%, respectively (Fig 6). After 2 weeks, the percentage of patients with MR grade 0 decreased at a slow but constant rate, with corresponding increases in percentages with MR grades 1+ to 3+/4+. At 10 years, 77% of patients had 0 or 1+ MR, 13% 2+ MR, and 10% 3+/4+ MR. The initial rapid change in MR grade was associated with earlier date of operation, pericardial annuloplasty, left atrial enlargement, and left ventricular structural and functional alteration (Table 4). Slow, long-term return of MR was associated with earlier date of operation, pericardial annuloplasty, and larger left ventricular end-diastolic volume. Although 89% of patients receiving a prosthetic annuloplasty had 0 or 1+ MR at 10 years, only 77% of those receiving a pericardial annuloplasty did. Surgeon experience did not influence repair durability ($p > 0.2$).

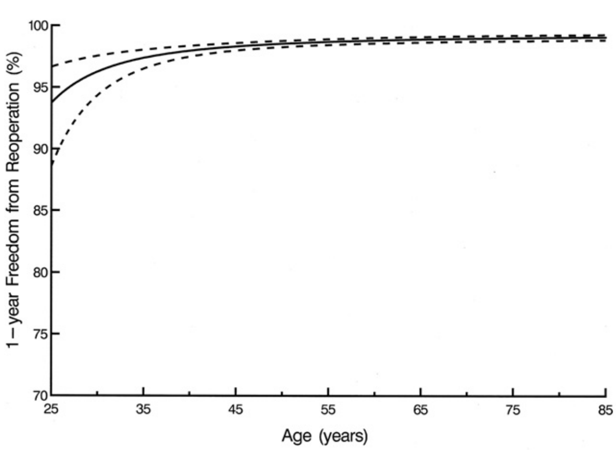

Fig 5. Predicted 1-year freedom from reoperation according to age at mitral valve repair. Graph is a nomogram of multivariable equation represented by Table 3, with blood urea nitrogen set to 17 mg/dL, hematocrit to 40%, and posterior wall thickness to 1.1 cm. Solid line is parametric estimate, and dashed lines are 68% confidence limits equivalent to ± 1 standard error. Note expanded scale.

Comment

Surgical mitral valve repair for posterior leaflet prolapse is associated with low operative risk, excellent long-term survival, and long-lasting durability. Best results are obtained when repair is performed before onset of symptoms or change in cardiac structure or function. Standard repair techniques that address both the leaflets and the annulus are necessary to achieve these results in patients with severe MR.

Degenerative Mitral Valve Disease

Degenerative mitral valve disease is the most common indication for surgical mitral valve repair [5, 7, 8, 16–18]. This condition is not rare: using strict echocardiographic criteria, Framingham Heart Study investigators determined that prevalence of mitral valve prolapse is 2.4% in the general population [19]. Up to 5% of these patients ultimately exhibit MR of sufficient severity to require intervention [20]. Among patients presenting for surgery, segmental posterior leaflet prolapse is the most common finding [5, 7, 8].

Pathologic changes associated with degenerative mitral valve disease include annular dilatation, leaflet thickening, myxoid degeneration, chordal elongation and rupture, and annular and leaflet calcification [5, 7, 8, 16].

ADULT CARDIAC

Table 4. Risk Factors for Return of Mitral Regurgitation

Risk Factor	Estimate ± SE	*p* Value
Early phase (0–2 weeks)[a]		
No prosthetic annuloplasty	1.3 ± 0.34	<0.0001
Greater LA volume[b]	0.099 ± 0.023	<0.0001
Older age[c]	0.37 ± 0.11	0.0005
Severe LV dysfunction[d]	0.71 ± 0.29	0.01
Greater intraventricular septal thickness[e]	0.33 ± 0.12	0.006
Earlier date of operation[f]	−1.4 ± 0.14	<0.0001
Lower bilirubin	−0.34 ± 0.17	0.05
Late phase (>2 weeks)[g]		
No prosthetic annuloplasty	0.77 ± 0.39	0.05
Dilated annulus	0.54 ± 0.24	0.02
Preoperative atrial fibrillation	0.55 ± 0.24	0.02
Greater LV end-diastolic volume[h]	0.17 ± 0.089	0.05
Earlier date of operation	0.98 ± 0.14	<0.0001
LV ejection fraction	−0.029 ± 0.013	0.02

[a] Intercepts for cumulative logit model: 3+/4+, −1.8 ± 0.64; 2+ or 3+, −0.76 ± 0.63; 1+, or 2+, or 3+/4+, 0.41 ± 0.63. [b] (LA volume/60)^2, squared transformation. [c] (age/50)^2, squared transformation. [d] LV dysfunction: none/mild versus moderately severe/severe; binary variable. [e] (Intraventricular septal thickness)^2, squared transformation. [f] Ln(interval from 1/1/1985 to date of operation), logarithmic transformation. [g] Intercepts for cumulative logit model: 3+/4+, −1.4 ± 0.27; 2+ or 3+/4+, −0.37 ± 0.25; 1+, or 2+, or 3+/4+, −0.88 ± 0.26. [h] (LV end-diastolic volume/150)^2, squared transformation.

LA = left atrial; LV = left ventricular; SE = standard error.

Although mitral repair preserves and uses abnormal leaflet tissue, we and others have demonstrated that repair is durable for decades [17].

Posterior Leaflet Repair in Degenerative Disease

SURGICAL APPROACH. In North American clinical practice, approximately 40% of mitral valves are repaired and 60% replaced [21]. However, in experienced centers, repairs exceed 90% [5, 7, 8, 16–18]. Quadrangular resection, developed by Carpentier and colleagues [22], is commonly used to treat posterior leaflet prolapse or flail. In this study, quadrangular resection was the standard approach to isolated posterior leaflet prolapse, with sliding repair used for tall posterior leaflets [23, 24]. Annuloplasty, either pericardial or prosthetic, was used in all patients in this analysis. The approach to posterior leaflet repair is standardized and reproducible [17]. More recently, the authors have begun to use triangular resection and other modifications to these techniques, particularly in the setting of minimally invasive and robotically assisted mitral valve repair. Durability with this approach has been excellent at other centers [25, 26]. The incision used to approach the mitral valve was not a risk factor for death, reoperation, or return of MR, suggesting that posterior leaflet repair can be achieved with a number of approaches.

SURVIVAL AFTER MITRAL VALVE REPAIR. Operative risk for isolated mitral valve repair in patients with degenerative disease is less than 1% [2, 5, 7, 8]. Reported 10-, 15-, and 20-year survivals after surgery are 92%, 76%, and 48%, respectively, superior to survival in the general population [8, 16, 17, 27]. Our 15-year survival of 76% is comparable. The observation that survival in patients undergoing posterior prolapse repair is superior to that of the general population may relate in part to the socioeconomic profile of patients undergoing cardiac surgery and their access to health care, but it contrasts with worse-than-expected survival of similarly aged patients undergoing aortic valve replacement [28].

Among those undergoing repair, advanced heart failure symptoms and left ventricular remodeling and dysfunction have been associated with diminished early and late survival [5, 7, 8]. In addition, left atrial enlargement, which frequently precedes left ventricular changes, is associated with lower postrepair survival.

REPAIR DURABILITY. Repair durability was assessed by both freedom from reoperation and return of MR on echocardiogram. As in previous studies, freedom from reoperation was high, exceeding 90% at 10 years [5, 7, 8, 16, 17, 27]. Reoperations tended to occur in two time frames, with half performed within 2 weeks of repair and the remainder distributed during a late phase of risk that diminished to 2 per 1,000 patients by 7 years. Previous studies demonstrate that early reoperations tend to be procedure related and are caused by technical issues and, perhaps, attempts to repair intrinsically unsalvageable valves; late reoperations are most commonly the result of progressive degenerative changes [29]. These findings of two phases of risk emphasize the need for intense early and continued periodic late echocardiographic surveillance of patients undergoing repair of posterior leaflet prolapse.

Changes in left ventricular structure and function were associated with reduced durability, suggesting a potential advantage to early repair. That younger age at operation was a risk factor for reoperation suggests that some of these patients may have a more aggressive form of degenerative valve disease, with more rapid progression with time. Advanced age did not diminish repair durability and therefore should not be considered a contraindication to valve repair (versus replacement) in patients with posterior leaflet prolapse. The experience reported herein includes operations performed by 19 surgeons; individual surgeon experience did not influence repair durability, highlighting reproducibility of the surgical techniques described.

Some patients exhibiting recurrent MR in follow-up did not undergo reoperation. At 10 years, 11% of patients had moderately severe or severe MR (3+ or 4+). Other investigators have documented similar figures for return of MR with time [8, 27]. However, in a study of 242 patients undergoing repair of degenerative mitral valve disease, Flameng and colleagues reported only 71% freedom from severe MR at 7 years, with a linearized rate of recurrence ranging from 2.5% to 6.9% per year, depending on surgical technique used [30]. In a later study by the same group, recurrence remained at 2% to 3% per year with current repair techniques [31]. In contrast to Flameng and colleagues [30, 31], who studied patients with varying diseases treated by multiple surgical approaches, we focused on the most common presentation and standard surgical techniques; in our population, return of MR was far less frequent. These results emphasize the importance of both a leaflet repair and a prosthetic annular procedure to optimize outcomes.

Clinical Implications

PRACTICE GUIDELINES. The ACC/AHA practice guidelines for managing patients with valvular heart disease favor repair over replacement in patients with severe nonischemic MR, and provide a class IIa recommendation for mitral valve repair in asymptomatic patients without changes in left ventricular size or function when the likelihood of successful repair without residual MR exceeds 90% [1]. However, there is controversy concerning the recommendation for surgery in such patients. Indeed, our findings favor early repair, demonstrating extremely low operative risk and excellent durability. As in previous reports, we found that survival, reoperation, and return of MR are unfavorably affected by more severe symptoms, ventricular hypertrophy or dysfunction, and left atrial enlargement [2, 5, 7, 8].

However, our data raise a point of caution. Younger patients with severe MR represent an increasing proportion of the surgical population and have an increased risk of early reoperation. It is possible that patients presenting at a young age with severe MR have more extensive valvar and cardiac changes, representing a more challenging point on the spectrum of degenerative mitral valve disease. Although such patients should be considered for repair, they require intense early echocardiographic follow-up.

PERCUTANEOUS REPAIR. A variety of novel techniques for percutaneous repair of regurgitant mitral valves are in clinical trials. These include both annular and leaflet procedures. Early clinical results demonstrate the feasibility of percutaneous edge-to-edge repair for managing leaflet prolapse and of percutaneous annuloplasty through the coronary sinus [32, 33]. Although refinements in technique and patient selection will improve outcomes of percutaneous mitral valve repair, surgical results suggest that best outcomes in patients with degenerative mitral valve disease depend on combined leaflet repair and prosthetic annuloplasty. Ultimately, successful percutaneous repair may depend on application of more than a single repair technique or device.

Study Limitations

By design, this study focused only on patients with documented isolated posterior mitral leaflet prolapse, the most common finding in patients presenting for surgical treatment of degenerative disease. Therefore, these results may not be applicable to those with anterior leaflet or bileaflet prolapse. Echocardiographic follow-up at Cleveland Clinic was available in 2,575 of 3,074 patients (84%) and was not obtained by a fixed schedule. In addition, echocardiographic follow-up was not available beyond 10 years in most patients. It is possible that patients with recurrent MR were more symptomatic, prompting them to seek medical attention and obtain echocardiograms, and thus our findings underestimate durability. Alternatively, it is possible that patients with recurrent MR were more likely to die, eliminating the ability to obtain repeat echocardiograms. Nevertheless, with 4,913 echocardiograms extending to a decade beyond surgery, this analysis was able to demonstrate a pattern of rapid early and slow late return of MR that will guide future studies and inform frequency of echocardiographic follow-up. The relationship between return of MR and survival could not be evaluated, because both are outcomes of mitral valve repair, and statistical methodology to examine such a relationship is just beginning to emerge. Echocardiograms obtained during this study included semiquantitative assessments of MR using established techniques that represented standard care at the time; quantitative echocardiography was not performed routinely during the time frame of this study [2].

Conclusions

This study, the largest focusing on patients with the most common indication for mitral valve repair, augments current AHA/ACC practice guidelines by suggesting that severe MR from isolated posterior prolapse is by itself an indication for a low-risk durable mitral valve repair with high likelihood of success. In addition, these data provide direction for new approaches to mitral valve repair. Specifically, the finding that both leaflet repair and prosthetic annuloplasty are necessary to optimize results has important implications for development and application of percutaneous approaches to mitral valve repair in patients with posterior leaflet prolapse.

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Appendix A: Variables Used in Multivariable Analyses

Demography

Age (y), sex, height (cm), weight (kg), body surface area (m^2), body mass index ($kg \cdot m^{-2}$).

Preoperative status

New York Heart Association functional class (I–IV), Canadian Angina class (0–4), emergency operation, heart failure.

Mitral valve pathology

Valve fibrosis or thickening, valve calcification, elongated chordae, chordal rupture, elongated papillary muscle, dilatation of mitral annulus, dilated left ventricle, regurgitation grade (0 to 4+ scale), left atrial (LA) diameter and volume.

Left ventricular (LV) structure and function

LV mass index ($g \cdot m^{-2}$), LV inner diameter in diastole (cm), LV end-diastolic volume (LVEDV, mL), LV inner diameter in systole (cm), LV end-systolic volume (mL), posterior wall thickness (cm), interventricular septal thickness (cm), LV relative wall thickness, LV dysfunction grade (0 = none, 1 = mild, 2 = moderate, 3 = severe), previous myocardial infarction, LV ejection fraction, LV fractional shortening.

Other cardiac comorbidity

Atrial fibrillation, coronary artery stenosis (left main trunk, left anterior descending coronary artery, circumflex coronary artery, right coronary artery ≥50%, any), number of coronary systems with ≥50% stenosis, family history of coronary artery disease, ventricular arrhythmia, complete heart block, history of endocarditis, history of heart failure.

Noncardiac comorbidity

History of hypertension, treated diabetes (insulin- versus non–insulin-treated), stroke, smoking, peripheral arterial disease, chronic obstructive pulmonary disease, renal failure, blood urea nitrogen (mg/dL), creatinine (mg/dL), bilirubin (mg/dL), cholesterol (total, high-density lipoprotein, low-density lipoprotein; mg/dL), triglycerides (mg/dL), hematocrit (%).

Details of procedure

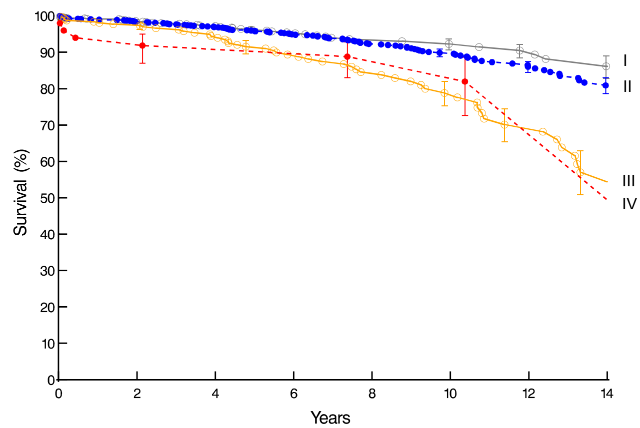
Surgical approach (minimally invasive versus maximally invasive), mitral valve repair details (leaflet resection, sliding leaflet repair, chordal resection, cleft repair, leaflet suture, leaflet debridement, type of annuloplasty, tricuspid valve repair.

Experience

Date of operation (years from January 1, 1985, to operation), surgeon.

Appendix B

Long-term survival according to New York Heart Association functional class. Error bars represent 68% confidence limits (Appendix B Fig 1).



Appendix B Fig 1.

DISCUSSION

DR MICHAEL A. ACKER (Philadelphia, PA): I want to congratulate Dr Johnston and his other Cleveland Clinic authors for this impressive prospective observational study that clearly demonstrates the long-term benefit of posterior leaflet mitral valve repair with respect to survival, freedom of reoperation, and freedom from recurrent mitral insufficiency. These results support the strong consideration of mitral valve repair for isolated posterior leaflet pathology even in the asymptomatic patient with a normal heart but with severe MR (mitral regurgitation). In addition, these results set a high benchmark for which we must compare and expect relative equivalence for the emerging percutaneous mitral valve repair technology. As importantly, this study sets another benchmark for cardiac surgeons and our programs pertaining to the infrastructure necessary to conduct meaningful clinical research. It is not enough to be proceduralists interested in our own 30-day mortality, but rather, as pioneered by the Cleveland Clinic, we must set up a complex and expensive infrastructure of data repositories, biostatistical cores, and people to follow our patients prospectively and long term to determine the true efficacy and success of the procedures we do. I have five questions to ask Dr Johnston.

One, recently there have emerged several new and different types of annuloplasty rings: complete versus partial, flexible versus rigid, saddle versus flat, unique shapes for functional versus degenerative. Does it make a difference?

Two, your standard repair was a quadrangular resection and annular plication. Do you think that a simpler triangular resection without plication can be done with equal long-term success?

Three, very often degenerative mitral valve disease primarily manifested by severe posterior leaflet prolapse or flail also has some degree of anterior leaflet prolapse. Can you comment on specific criteria in the operating room when you decide whether to leave that anterior leaflet alone or when do you have to address it?

Four, what was the most common reason for posterior leaflets to repair in your two groups and how often were you able to re-repair those valves?

And finally, please comment on the likelihood that the emerging percutaneous repair technologies of edge to edge and various coronary sinus devices will reach the high bar of freedom of recurrence long term that you have set, and how close do the percutaneous technologies have to be for them to have a meaningful clinical impact?

I want to again thank the Society for the privilege of discussing this paper.

DR JOHNSTON: Dr Acker, thank you very much. To your first question as to the type of ring, there were essentially three different types of annuloplasty employed in this analysis: a rigid Carpentier classic ring, a flexible annuloplasty band, and a pericardial annuloplasty. The numbers of the first two were relatively large, but the only risk factor that emerged was failure to employ some type of prosthetic annuloplasty. Based on previous studies, we don't believe that there would be a significant difference as long as the annuloplasty is effective, but this study did not provide data to allow us to comment on some of these newer shaped rings.

As far as your question on triangular resection, there are a number of surgeons who are employing these techniques, and we believe that the early results of triangular resection are equivalent. However, I think answering the question about long-term durability will require a similar analysis, and the numbers to date are too small to provide meaningful data.

As far as the question of anterior versus posterior prolapse, our approach was to look at the primary pathology for these patients. A number of patients had some degree of anterior prolapse, but if the initial preoperative evaluation and the surgeon's evaluation in the operating room focused on the posterior leaflet and the repair was a posterior leaflet procedure, those patients were included in the cohort for analysis.

Our study did not look specifically at the issue of re-repair, although this is ongoing in another analysis.

As far as the transcatheter techniques which are emerging, our belief is that a successful transcatheter repair, based on these data, will have to address both the leaflets and the annulus. Whether the technologies employed to perform annuloplasty by transcatheter techniques are equivalent to the annular fixation achieved with a ring or band with open surgery is a question that will require close scrutiny over time.

Thank you very much for your comments.

DR THIERRY MESANA (Ottawa, Ontario, Canada): I have a question about the rate of conversion. Did you exclude the patient who you converted to a replacement in the OR (operating room) at the time of repair? And second, you have very few patients with more than 2 years' echo[cardiographic] follow-up. Did you follow all these patients clinically to say they had no mitral regurgitation?

DR JOHNSTON: Thank you. As to the echo[cardiographic] follow-up, I can answer that first, the number of patients that was available for echo follow-up at 5 years was still 200 patients. Certainly the echocardiographic follow-up is not as complete as we would wish, but it reflects the availability of echo[cardiogram]s in our practice setting, and the number of available echo[cardiogram]s is more than that analyzed in any previous study. So we believe that it provides meaningful data but certainly not what we would wish to have, a 100% echo[cardiographic] follow-up.

We specifically excluded those patients who were converted from repair to replacement at the time of initial operation in order to evaluate most specifically those patients undergoing standardized repair. In addition, we excluded those patients who had nonstandard repair procedures, Gore-Tex chords or chordal transfer, or other techniques, even if isolated to the posterior leaflet.

DR GIOVANNI SPEZIALI (Pittsburgh, PA): You kind of answered already my question with your last comment, because my question was about different types of repair that do not involve leaflet resection, specifically implantation of artificial chordae, the so-called American correction, on which some of the new emerging technologies that use off-pump mitral repair are based. And my question to you was, would your conclusion apply to these other technologies that do not involve any kind of leaflet resection? Thanks.

DR JOHNSTON: Thank you. We certainly are interested in the impact of evolving technologies on the success rate for repair. Our intent in this study was to minimize the variability within the patient cohort and thus to provide the most accurate data to serve as a benchmark for evaluation of these new techniques. While we are excited about the possibility that these may provide less invasive ways of repairing the mitral valve, if we are to change our techniques, we need to do better than this data.

DR SULAIMAN B. HASAN (Charleston, WV): I thoroughly enjoyed that study. I am assuming that the vast majority of these patients were done through a median sternotomy. Do you have any data on the patients done through mini thoracotomy, whether the success rate was the same?

DR JOHNSTON: We included all approaches to the mitral valve in this analysis as long as the repair technique met the criteria. About 60% of operations were performed through an upper hemisternotomy, a smaller portion through a full sternotomy, and about 3% to 5% each through a right thoracotomy and robotic approaches. But as long as the repair technique was standardized, those were all included.

DR W. RANDOLPH CHITWOOD (Greenville, NC): I have a brief question, Dr Johnston. Dr Rankin presented recently a paper at the Southern Thoracic Surgical Association that said basically current mitral repair surgery should have an asymptote that is close to zero mortality. You achieved this closely. Do you think most mitral valve repair surgeons can expect to have no mortality? You obviously have a selected younger group of patients. Can we expect these results from all of our members when many do less than 15 mitral operations per year?

DR JOHNSTON: We think that this reflects the population of patients with this particular pathology. The number of patients with more complex valve pathology, including combination of anterior leaflet prolapse and restriction, may not be accurately reflected in this study. But posterior leaflet prolapse is the most common indication for repair, and it is possible that that population of patients is self-selected in the way you described.