Comparison of recovery after mitral valve repair and replacement

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Objective: We sought to examine the comparative improvement in health status after primary mitral valve repair versus replacement in patients with mitral valve regurgitation in a longitudinal setting.

Methods: We prospectively followed 267 patients with mitral valve regurgitation who underwent primary mitral valve repair (n = 163) and replacement (n = 104) between January 2002 and January 2005. Health status was evaluated at baseline and 1, 3, and 12 months after surgery with the validated short-form 36 and analyzed using generalized estimating equations with adjustment for propensity scores.

Results: Compared with patients undergoing mitral valve replacement, patients requiring valve repair were younger and more likely to be male. The probability of postsurgical readmission because of cardiac events was low and similar between the two treatment groups. New York Heart Association functional class was significantly improved after both procedures, with better improvement achieved by mitral valve repair ($P < .01$). For both treatment groups, scores for most of the short-form 36 domains were depressed at 1 month; however, after 3- and 12-month lags, dramatic improvements were achieved in most of the domains. Adjusted changes in the physical component score were similar between the two arms at each follow-up. For the mental component score, patients who underwent repair showed significant improvements compared with patients who underwent replacement at both 3 months (difference: 4.84 points, $P = .005$) and 12 months (difference: 5.92 points, $P < .001$).

Conclusions: Our study suggests that after mitral valve surgery, there is significant improvement in New York Heart Association functional class and health status, especially in patients undergoing mitral valve repair.

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Mitral regurgitation (MR) (acute or chronic) affects approximately 5 in 10,000 people.¹ Although the numbers are not as overwhelming as are those related to coronary artery bypass graft surgery, this is still a substantial societal burden. Traditionally, operative procedures in mitral valve (MV) surgery consisted mainly of valve replacement with tissue bioprosthetic or mechanical valves. More recently, valve repair has become a generally accepted alternative to replacement for surgical treatment of MR.^{2,3} Patients undergoing MV repair may potentially have reduced incidence of thromboembolism and endocarditis, as well as reduced anticoagulation requirements, compared with those undergoing MV replacement. Furthermore, MV repair may lead to greater functional durability than can be achieved with bioprosthetic or mechanical valves, ultimately leading to improved long-term results. Preservation of the intrinsic mitral apparatus allows for improvement of postoperative ventricular function, which may reduce the long-term

Abbreviations and Acronyms

MCS	= mental component score
MR	= mitral regurgitation
MV	= mitral valve
NYHA	= New York Heart Association
PCS	= physical component score
SF-36	= short-form health survey [36 items]

recurrence of symptoms and postoperative MR for patients undergoing MV repair as opposed to replacement.^{4,5}

Outcomes assessment in MV surgery has traditionally focused on perioperative mortality and morbidity, or long-term survival.^{6,7} However, patients who are to undergo MV surgery are typically interested in their postsurgical health status, including symptoms, functionality, and quality of life. Furthermore, functional status and quality of life have increasingly been considered as important patient-related outcome measures of the efficacy of surgical treatment, which can be used to help patients for decision making regarding choice of therapy. However, to date there are limited data on health status (symptom burden, functional status, and quality of life) post-MV surgery, an important outcome of therapeutic interventions for patients with cardiac valve disease.^{8,9}

The Outcomes Assessment of Mitral Valve Replacement and Repair study is a multicenter, prospective, observational registry assessing and comparing a spectrum of outcomes after replacement and repair in patients with MR, with a focus on health status. The purpose of the present evaluation is to prospectively examine the comparative effects of MV repair and replacement on recovery from surgery, with a focus on postoperative quality of life and health status.

Materials and Methods**Patient Population**

From January 2002 to January 2005, a total of 274 patients with MR (repair: 167; replacement: 107) admitted for their first MV surgery were enrolled at Emory University, Mid-America Heart Institute, Yale University, and Toronto General Hospital. Among these 274 patients, 7 (4 with repair; 3 with replacement) died during follow-up and were excluded from the health status analysis. A total of 171 patients completed all assessments at baseline and 1, 3, and 12 months of follow-up.

Potential patients for the study were identified through daily screening of operations at the participating institutes. All patients were screened for contraindications to transesophageal echocardiography before surgery. Patients were excluded if they had previous MV surgery, required concomitant aortic valve surgery, or were unable to consent because of a language barrier or being too sick, or died before consenting to participate in the study. The institutional review board at each site approved the study, and all patients provided written informed consent.

Data Collection

Before surgery, clinical assessment and health-related quality of life were evaluated with a set of questionnaires including recent cardiac events/procedures, medications, and health status. Follow-up was done through direct communication (telephone or letter) at 1, 3, and 12 months after surgery to obtain recovery information including postsurgery cardiac events, death, and stroke. Health status was also assessed at each postoperative time interval using the same instruments as at baseline. Additional information, including baseline demographic and clinical data, was obtained from the Society of Thoracic Surgeons Database or an equivalent clinical database at each site.

Health Status Measurement

Health status assessments were evaluated with the Medical Outcomes Trust Short-Form 36-item Health Survey (SF-36).¹⁰ SF-36 is a general-purpose questionnaire that has been used in multiple studies and offers the broadest review of quality of life. This comprehensive short-form assesses 8 dimensions of health: physical function, role limitation attributable to physical problems, bodily pain, general health perceptions, vitality (energy and fatigue), social function due to physical or emotional problems, role limitation due to emotional problems, and mental health. The responses to each of these questions were summed and transformed to 8 individual scores, ranging from 0 to 100 for each domain, with higher scores indicating better functioning. These individual scores can be combined into a summary physical component score (PCS) and mental component score (MCS). Validity, reliability, and typical response rates of all SF-36 domains as quantitative measures of clinical symptoms and quality of life were independently established.¹¹

Statistical Analysis

Demographic and clinical characteristics at baseline and outcomes measures at each follow-up were compared between patients undergoing MV repair and patients undergoing replacement. Continuous variables (age and the average time between baseline and follow-up evaluations) were compared with the Wilcoxon rank-sum test. Categorical variables were compared using the chi-square or Fisher exact test.

Time to event outcomes, such as death and rehospitalization due to cardiac events (eg, cardiac arrhythmia, heart failure, additional MV surgery), were assessed by Cox proportional hazards regression analysis after adjusting for key preoperative variables, namely, baseline SF-36 scores, surgical type, demographic factors (age as a continuous variable, gender), and clinical characteristics, including history of hypertension, diabetes, myocardial infarction, Canadian Cardiovascular Society angina class, and New York Heart Association (NYHA) functional class. Proportionality assumption was assessed.

Propensity Score

MV repair and replacement are not in equipoise, and most patients will undergo MV repair if possible. To reduce treatment selection bias and determine the influence of type of MV surgery on outcomes, a propensity score was developed using logistic regression accounting for baseline characteristics, recruiting sites, and health status covariates for each observation.¹² The actual propensity

TABLE 1. Comparison of baseline demographic and clinical characteristics

Characteristics	Patients with complete data (n = 171)			The whole population (n = 267)		
	Mitral repair (n = 108)	Mitral replacement (n = 63)	P value	Mitral repair (n = 163)	Mitral replacement (n = 104)	P value
Age (y, mean $\pm$ SD)	59.4 $\pm$ 12.4	63.0 $\pm$ 11.4	.059	58.1 $\pm$ 12.2	61.6 $\pm$ 12.9	.014
Male (n, %)	66 (61.7)	26 (41.3)	.010	110 (67.5)	44 (42.1)	<.0001
Hypertension (n, %)	43 (44.3)	33 (54.1)	.23	74 (45.4)	50 (48.1)	.67
Diabetes (n, %)	8 (8.3)	7 (11.5)	.50	17 (10.4)	12 (11.5)	.78
Previous MI (n, %)	6 (6.2)	7 (11.5)	.24	12 (7.4)	15 (14.4)	.06
CHF III/IV (n, %)	34 (36.2)	25 (41.0)	.55	58 (35.6)	45 (43.3)	.21
Angina III/IV (n, %)	10 (9.4)	8 (12.7)	.49	15 (9.2)	17 (16.4)	.08
Preoperative LVD	44.8 $\pm$ 11.1 (86)	42.4 $\pm$ 12.4 (38)	.29	46.2 $\pm$ 10.9 (112)	43.7 $\pm$ 11.9 (53)	.19
Preoperative EF > 55% (n, %)	52/93 (55.9)	21/46 (45.7)	.23	66/122 (54.1)	31/70 (44.3)	.20
Postoperative EF > 55% (n, %)	51/91 (56.0)	21/46 (45.7)	.08	67/121 (55.4)	31/70 (44.3)	.11
Ischemic MR	9/85 (10.6)	3/40 (7.5)	.59	11/111 (9.9)	5/63 (7.9)	.90

CHF, Congestive heart failure; MI, myocardial infarction; LVD, left ventricular dimension; EF, ejection fraction; MR, mitral regurgitation; SD, standard deviation.

score (between 0 and 1) is the estimated probability that an individual receives the treatment of interest. The propensity score was adjusted for in a series of analyses allowing a comparison of MV repair and replacement more comparable to a nonrandomized study.

Missing Data

Data may have been missing because the interview was not administered or forms were not filled out completely at each time point (reflected by varying degrees of missing data across the domains) or because patients died before the follow-up visit. To supplement complete case analysis and assess any potential impact of missing information on the analysis, we performed multiple imputation by a Monte Carlo Markov chain approach¹³ to impute missing SF-36 scores for surviving patients in the 8 domains at the 4 time points. Covariates used in multiple imputation included treatment assignment, demographic factors, clinical characteristics, and all SF-36 scores at the 4 time points.

The generalized estimating equations approach¹⁴ was used to compare SF-36 scores at each of the 4 time points between the 2 treatment arms, with or without adjustment for the propensity score. Changes in SF-36 scores from baseline at 1, 3, and 12 months were also compared using the same method. The propensity score was added to the multivariate models as a covariate term, in addition to treatment assignment and visit sequence (1, 3, and 12 months). Interaction terms among treatment assignment, visit, and quartile of the propensity score were examined.

All tests of statistical significance were 2-tailed. Statistical analyses were performed with the Statistical Analysis System, version 9.1 (SAS Institute Inc, Cary, NC), and S-plus, version 7 (Mathsoft Inc, Seattle, Wash).

Role of the Funding Source

The sponsor of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. The writing committee had final responsibility for the decision to submit for publication.

Results

Baseline Characteristics

The demographic and clinical characteristics for patients with complete evaluation at each follow-up time point and the whole study population are shown in Table 1. For both patient populations, patients in the MV replacement group were older than those in the MV repair group. Women were more likely than men to have MV replacement. In addition, more women had class III/IV congestive heart failure at the time of surgery (52.2% vs 28.6%, $P < .0001$). For the overall population, there was a tendency for patients in the MV replacement group to have higher rates of history of myocardial infarction ($P = .06$) and class III/IV angina ($P = .08$). The proportion of patients with history of hypertension, diabetes, and class III/IV congestive heart failure was not significantly different between the 2 treatment groups (all $P > .2$) for both patient populations. Baseline characteristics for the 171 patients who had completed evaluation during the study period were similar to those for the 96 patients who did not complete follow-up, except that patients who did not finish the study tended to be younger (57 years vs 61 years, $P < .03$).

Clinical Outcomes

There were no significant differences between the 2 treatment groups in the length of time between the intervention and the interview dates at each of the 3 follow-up time points (1 month: 40.0 days for repair vs 40.8 days for replacement, $P = .80$; 3 months: 114.2 vs 122.7, $P = .25$; 12 months: 378.9 vs 381.2, $P = .74$).

There was significant improvement in the NYHA functional class from baseline at each of the follow-up time points for both treatment groups. The percentages of patients in class III/IV were significantly lower for the MV

Figure 1. NYHA functional class III/IV at baseline and follow-up. NYHA, New York Heart Association; MV, mitral valve.

repair group than for the replacement group at 3 and 12 months (Figure 1).

During follow-up, readmissions for cardiac events were low and there was no significant difference between the 2 treatment groups (6.6% for repair and 11.9% for replacement, $P = .28$). The most common reason for readmission was cardiac arrhythmia (2.2% for repair and 4.8% for replacement, $P = .42$). The proportions of readmission due to each of the cardiac events were similar between the 2 groups. Mortality was low, with 7 patients (repair: 4; replacement: 3, $P = .88$) dying during follow-up.

Changes in SF-36 Scores

Results from the complete data set (171 patients). At baseline, the average, unadjusted scores for physical function (57.4 vs 41.0, $P = .0006$), role physical (43.1 vs 19.1, $P = .0003$), bodily pain (74.0 vs 61.2, $P = .003$), and PCS (39.9 vs 33.3, $P = .003$) were significantly higher for the MV repair group than for the replacement group, indicating that patients requiring MV repair had better physical function than did patients undergoing replacement. No significant differences were found in other domains at baseline.

After adjustment for the propensity scores, no differences were found at baseline between treatment groups in individual domain and summary scores. At 1 month, patients in both groups worsened in most subscales while improving in general health perception and mental health, with more improvement obtained in the MV repair group ($P < .05$). From 3 months on, the effect of treatment on health status was persistent over time, with patients undergoing MV repair achieving better improvements in all domains. The magnitudes of the differences in most domains were substantial and increased over time, corresponding to better improvements in performance in physical and social

activities, general satisfaction, and emotional state for MV repair as opposed to replacement (Figure 2).

Estimated relative improvements from baseline and at 1, 3, and 12 months in PCS and MCS for both treatment groups based on the adjusted analysis are shown in Figure 3. Scores for PCS were depressed at 1 month for both groups, but they showed marked improvements at 3 and 12 months after surgery for both groups ($P < .0001$). The relative improvements between the 2 groups were not statistically significant. At 1 month, MCS remained about the same for the repair group, whereas it worsened for the replacement group; however, the change did not reach significance ($P = .13$). The repair group showed significant improvements compared with the replacement group and had significantly better changes from baseline in adjusted mean scores at both the 3-month (difference: 4.84 points, $P = .005$) and 12-month (difference: 5.92 points, $P < .001$) time periods.

Results on incomplete data (267 patients). Average, unadjusted, unimputed scores at baseline and 1, 3, and 12 months from 267 patients were in general similar to those from the 171 patients with complete data (data not shown). Imputed, adjusted (controlling for the propensity score) SF-36 scores at each time point are, again, similar to those from the patients with complete data (data not shown). However, compared with the 171 patients who had complete data for each of the 4 time points, the average relative gains in MCS for MV repair versus replacement was smaller both at 3 months (difference: 3.20 points, $P = .03$) and at 12 months (difference: 3.34 points, $P = .01$).

Sensitivity Analysis

Additional analyses were performed to examine the influence of missing data on the results. The primary analysis, the results of which are described above, was based on the data sets for surviving patients with or without multiple imputation. Two additional analyses were performed for PCS and MCS to examine the consequences of exclusion of patients who died versus setting all SF-36 scores equal to 0 for those patients who died, with or without multiple imputation. In these supplemental analyses, we assessed the relative effects of MV repair versus replacement, using the same covariates listed earlier. Summaries are provided in Table 2. Estimates of the relative effects of MV repair versus replacement are presented with corresponding P values. For PCS, the results were similar between data sets with or without imputation, both when excluding deaths and when setting scores to 0 for patients who died. For MCS, results based on imputed data with scores for deceased patients set to 0 yielded the lowest or the most conservative estimates of the effect of MV repair versus replacement. Nevertheless, the relative benefits of MV repair remain highly significant for MCS regardless of the approach used to treat 7 patients who died during follow-up.

Figure 2. Adjusted SF-36 scores at baseline and 1, 3, and 12 months by treatment group in patients with complete data. *SF-36*, Short-form health survey [36 items]; *MH*, mental health; *RE*, role-emotional; *BP*, bodily pain; *SF*, social function; *GH*, general health; *PF*, physical function; *VT*, vitality; *RP*, role-physical.

Discussion

The current study demonstrates that patients undergoing MV repair or replacement experienced significant recovery 1 year after intervention. Symptoms and NYHA functional class were greatly improved by surgery. The probability of postsurgery readmission because of cardiac events was low and similar between the 2 treatment groups.

The primary aim of surgical intervention for MR is to improve the overall functional capacity and health status of patients. As a result, evidence of a meaningful benefit from the patients' perspective in the postintervention period is increasingly recognized as an important consideration in the assessment of treatment strategies. The present analysis found that patients in both treatment groups acquired dramatic improvement in their personal health and emotional state at 3 and 12 months after surgery. They were able to perform daily physical and/or social activities without physical limitations or emotional problems, particularly among those who underwent MV repair.

Currently, few data are available to describe health status recovery for patients undergoing MV surgery. Le Tourneau

and colleagues¹⁵ studied 24 patients undergoing MV repair and 16 patients requiring replacement. Despite an improvement in NYHA functional class, exercise performance did not improve. In another study, Myken and colleagues¹⁶ noted no difference in coping capacity, social support, and emotional support between patients receiving mechanical or bioprosthetic valve replacement. Quality of life was assessed at a single time. Goldsmith and colleagues¹⁷ evaluated quality of life in 61 consecutive patients (40 underwent repair, 21 underwent replacement) enrolled at a single center. Quality of life as measured by SF-36 was assessed before and at 3 months after surgery. Better improvements were achieved by patients who underwent MV repair. Overall, the studies to date are mostly small, with insufficient numbers of measurements to accurately predict quality of life outcomes of MV surgery.

MV repair may be more technically challenging to perform than replacement, and the results may also be dependent on surgeon volume. However, our results suggest that patients undergoing MV repair have improved ventricular function and better postoperative quality of life compared

Figure 3. Adjusted changes in PCS and MCS from baseline at 1, 3, and 12 months by treatment group in patients with complete data. *PCS*, Physical component score; *MCS*, mental component score; *MV*, mitral valve.

with patients undergoing replacement. The optimal timing of MV surgery may therefore be earlier in the course of the disease when repair is possible, before irreversible left ventricular injury occurs.¹⁸ Indeed, this position was recently advocated by the American Heart Association/American College of Cardiology consensus statement on the treatment of vascular disease.¹⁹ Previous studies demonstrated lower perioperative and long-term morbidity and mortality rates for patients undergoing MV repair versus replacement surgery.²⁰ Our study reveals that patients' perspective of health status is also improved with MV repair, providing further support for the choice of MV repair over replacement. Reports from economic analysis also support the results of the current study. For example, Barlow and colleagues²¹ noted a significantly lower mean cost with MV repair (\$11,606 vs \$14,469).

The present study has several possible limitations. First, this was not a randomized trial; therefore, surgical procedures were at the discretion of the individual surgeon, and patient characteristics in the 2 treatment arms were intrinsically different. Propensity score adjustment was used to reduce treatment selection bias, allowing for a fairer comparison of the 2 techniques. Yet, without treatment randomization, any unmeasured sources of confounding cannot be excluded. Unfortunately, it would be difficult and potentially unethical to recruit patients for a randomized trial when repair is possible.

A second potential limitation is the issue of missing data. Because willingness to participate was necessary to be enrolled and followed up, our results could be affected by response given the high rate of missing data. Explorations of any potential biases from missing patients were made, and no differences involving the rates of missing data and base-

TABLE 2. Additional benefits of mitral valve repair versus mitral valve replacement from different models

	Estimated additional benefits of MV repair versus replacement (<i>P</i> value)		
	1 mo	3 mo	12 mo
Physical component score			
Deaths excluded			
No imputation	−1.0 (.54)	−0.6 (.74)	1.4 (.38)
Imputation	−0.9 (.54)	−0.4 (.80)	0.8 (.60)
Deaths as 0			
No imputation	−1.9 (.25)	−0.9 (.65)	1.1 (.58)
Imputation	−1.3 (.44)	−0.5 (.74)	0.9 (.51)
Mental component score			
Deaths excluded			
No imputation	3.6 (.04)	4.3 (.01)	4.0 (.01)
Imputation	2.3 (.12)	3.2 (.03)	3.3 (.01)
Deaths as 0			
No imputation	2.2 (.24)	3.9 (.04)	3.5 (.07)
Imputation	1.6 (.28)	2.8 (.05)	2.7 (.05)

MV, mitral valve.

line characteristics were detected, except that patients who did not finish follow-up were younger. Multiple imputation and sensitivity analyses were performed, and our main conclusions about health status changes were materially unaffected.

A third consideration is that treatment assignment was not blinded, and the patients' knowledge of the procedure might have influenced responses to the SF-36 questionnaire. However, the incorporation of patients' perspectives of their health is critical and congruent with the suggestion by the Institute of Medicine to make the health care system more patient-centered.²²

Finally, our study population may not include the sickest patients because of the illness status and timing of surgery, which may make the generalizability imperfect. However, on the basis of the patient characteristics and the proportion of patients distributed between the treatment groups, we are confident that our conclusion can be applied to the current practice.

Conclusions

This is the first multicenter longitudinal study following a cohort of patients undergoing MV repair and replacement over time with repeated measures of health-related quality of life. Our study demonstrated that there were significant improvements in NYHA functional class and health status 1 year after MV surgery, with greater improvements among patients undergoing MV repair. Continued efforts should be directed toward understanding the mechanisms of improved health status in patients undergoing MV repair. The results of our study suggest that MV repair should be strongly considered for MR whenever possible, and that the optimal

timing of surgery may be different in patients with repairable pathology.

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