

Single-centre Experience with Mitral Valve Repair in Asymptomatic Patients with Severe Mitral Valve Regurgitation

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Interact Cardiovasc Thorac Surg 2013;16(6):731-37

ABSTRACT

Aim

Guidelines recommend surgical mitral valve repair in selected patients with asymptomatic severe mitral valve regurgitation (MR), but the role of repair remains a matter of debate. Survival analyses of operated asymptomatic patients have been reported, but long-term haemodynamics and quality of life are not well defined. The aim of this study was to report the long-term follow-up focusing on these aspects.

Methods

Our database identified patients who underwent primary isolated mitral valve repair for severe MR and were asymptomatic by New York Heart Association Class I and in sinus rhythm. To obtain sufficient length of follow-up, only patients operated on before 2006 returned for an echocardiogram and quality-of-life assessment (SF-36).

Results

Between May 1991 and December 2005, 46 asymptomatic patients with severe MR and a normal left ventricular function (ejection fraction >60%) were operated on. Mean age was 50.2 ± 13.2 years and 89% of patients were male. There were no operative deaths. Mean follow-up was 8.4 ± 3.9 years with 386 patient-years, survival was 93.3% at 12 years and comparable with the general age-matched Dutch population. Follow-up echocardiography showed that 92% had no to mild MR, and 3 patients had moderate MR. Left ventricular function was good/impaired/moderate in 66/29/5% of patients. Quality-of-life SF-36 assessment showed that mean physical and mental health components were 83 ± 17 and 79 ± 17 , which was comparable with that of the general age- and gender- matched Dutch population.

Conclusion

Our experience shows that mitral valve repair for severe MR in asymptomatic patients is safe, and has satisfactory long-term survival with a low recurrence rate of MR, good left ventricular function, and excellent quality of life that is comparable with the general Dutch population.

INTRODUCTION

Mitral valve regurgitation (MR) is the most common regurgitant heart valve lesion and is most commonly caused by degenerative valve disease¹. Cardiologists and surgeons often hesitate to recommend surgery in patients with no or minimal symptoms. In this regard, the usefulness of mitral valve surgery in asymptomatic patients with MR remains controversial, even though guidelines do recommend it for selected indications¹.

Previous studies have reported long-term survival analyses, which led to a worldwide consensus and acceptance of surgical repair of the native valve for preventing left ventricular dysfunction and myocardial damage². Through preservation of the normal valvular tissue and subvalvular apparatus, valve repair optimizes postoperative ventricular function and is preferred over valve replacement. Compared with valve replacement, mitral valve repair has a lower surgical mortality risk and provides better survival³. The decision to proceed with surgical repair, especially in asymptomatic patients, is easier if a repair seems feasible. However, with nothing to gain in symptomatic improvement, surgery exposes the patient to perioperative morbidity and mortality, the risk of failed repair with subsequent hazards of prosthetic valve complications³.

It has been suggested that surgery should not be delayed until severe symptoms develop, because irreversible left ventricular dysfunction could develop while waiting for the onset of symptoms⁴. However, the concept of mitral valve repair was developed in a limited number of patients from a few selected experienced centres and supporting evidence from other institutes is poor^{2,5}. The rationale for preventive, reconstructive mitral valve repair in asymptomatic patients therefore deserves a critical examination. No analyses have yet explored long-term valvular haemodynamics, quality of life, or a comparison with the general population, while these aspects could potentially create a strong recommendation for surgery in asymptomatic patients. This study aims to describe these outcomes after mitral valve repair for asymptomatic MR (i.e. New York Heart Association [NYHA] Class I for dyspnoea) in a large tertiary centre.

METHODS

Study design and patient population

The medical records of 46 consecutive patients with asymptomatic severe MR who underwent primary isolated mitral valve repair at the Department of Cardiothoracic Surgery of the Erasmus MC Rotterdam were reviewed. A heart murmur was found during a work-related medical examination, coincidental identification by the general practitioner, or coincidental identification during a work-up for other general surgery. Severe MR was measured and quantified according to the existing valvular guidelines. A truly asymptomatic status of

patients was defined by a NYHA Class I and sinus rhythm. To allow for a sufficient length of follow-up, only those patients operated on between May 1991 and December 2005 were included. The total number of mitral valve repairs during these years was 1099 (Figure 1). The study protocol was approved by the institutional review board of the Erasmus MC Rotterdam (MEC 07-416). Individual patient consent for the study was waived.

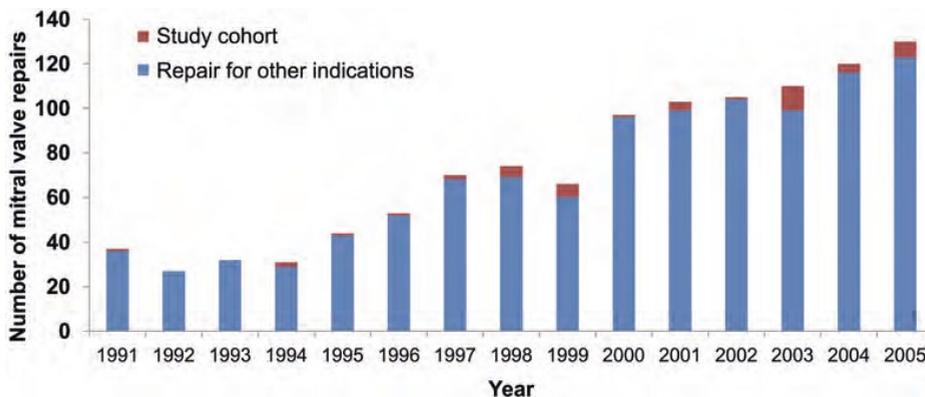


Figure 1. Number of mitral valve repairs during the study period.

Patients were followed with regular visits to the outpatient clinic. The civil registry was consulted and, subsequently, patients were invited through a telephone call to come for an outpatient visit with echocardiogram, electrocardiogram, and quality-of-life assessment. Five patients declined participation. Data were collected from hospital records, operative reports, and correspondence with the patients and treating physicians.

Perioperative details and follow-up were reported in accordance with the 2008 guidelines for reporting morbidity and mortality after cardiac-valve interventions⁶. Operative events were defined as those occurring within 30 days after surgery or any event later during the same postoperative hospital stay.

Surgical techniques

Intraoperative transoesophageal echocardiography was carried out routinely before and after repair. The majority of patients (>90%) were operated on by the same surgeon. The techniques of mitral valve repair used in this series were basically those described by Carpentier, but certain modifications were introduced over the years, for instance, the use of expanded polytetrafluoroethylene sutures to reinforce or replace chordae tendinae. All patients received warfarin during the first 3 months post-surgery, if in sinus rhythm.

Clinical follow-up

All patients had a comprehensive examination, including M-mode and 2-dimensional echocardiography, as well as conventional and Doppler examinations in our centre. All tests were conducted by experienced echocardiographers. Since the vena contracta width and the regurgitant orifice area have not been validated after mitral valve repair, the severity of residual MR was graded by expert consensus based on a score that considered (i) jet penetration, (ii) continuous-wave Doppler jet intensity and character, (iii) pulmonary artery pressure, (iv) pulmonary venous flow pattern, and (v) left atrial size ⁷. Left ventricular function was scored as good, impaired, moderate or poor.

Quality of life

The quality-of-life assessment was performed using the SF-36 questionnaires. According to the guidelines, this questionnaire was sent to the patient and completed at home before each study visit ⁸. The questionnaire consists of 36 scale-rated health-related questions, grouped into eight multi-item domains that are not disease-specific and that measure functioning in different aspects of daily life: ‘physical functioning (PF)’; physical health related to age- and role-specific activities: ‘role-physical (RP)’; ‘bodily pain (BP)’; ‘general health (GH)’; ‘vitality (VT)’; ‘social functioning (SF)’; personal feelings of performance in age- and role-specific activities: ‘role-emotional (RE)’ and ‘mental health (MH)’. The eight domains form two physical and mental health composite scores. The PF, RP, BP and GH domains contribute to the scoring of the ‘physical component summary (PCS)’ measure, whereas the VT, MH, RE and SF domains contribute to the ‘mental component summary (MCS)’. To compare these outcomes to the general age-matched Dutch population, we used Dutch norms that were previously published by Aaronson et al. ⁹.

Statistical analysis

Continuous data are presented as mean \pm 1 standard deviation; categorical data are presented as proportions. Cumulative survival and freedom from reoperation were analyzed using the Kaplan–Meier method. Age- and gender-matched survival in the general population were calculated using the Dutch population life tables (<http://statline.cbs.nl/>). Quality of life comparison of the study population with the general age-matched Dutch population was performed using the paired *t*-test (observed paired with age-matched norm). All tests were two-sided; a *P*-value of <0.05 was considered statistically significant. Statistical analyses were performed using SPSS 17 for windows (SPSS, Chicago, IL, USA) and GraphPad PRISM version 5 (GraphPad Prism Software, Inc., San Diego, CA, USA).

RESULTS

Baseline and procedural characteristics

The baseline characteristics are presented in Table 1. Mean age was 50.2 ± 13.2 and 89% of patients were male. All patients had a normal left ventricular function as defined by a preoperative ejection fraction of $>60\%$ measured on echocardiography. Posterior leaflet prolapse was diagnosed in 76% and in 52% of patients, the annulus was severely dilated. In 45 (98%) patients, a mitral ring was implanted, which was a Carpentier-Edwards Physioring in 40 patients. Quadrangular resection was performed in 78% of patients and posterior leaflet sliding in 65%. Other techniques are listed in Table 2.

Table 1. Baseline characteristics

Characteristic	N = 46
Age (mean \pm standard deviation [SD])	50.2 ± 13.2
Range	(25.2-78.2)
Male gender	41 (89%)
Aetiology	
Degenerative	2 (4%)
Myxomatous	39 (85%)
History of endocarditis	5 (11%)
Valvular characteristics	
Anterior mitral valve leaflet prolapse	8 (17%)
Posterior mitral valve leaflet prolapse	35 (76%)
Cusp perforation	5 (11%)
Annulus dilatation	45/46
None	1 (2%)
Moderate	20 (43%)
Severe	24 (52%)
Annulus calcification	2 (4%)

Operative (early) outcomes

In our centre, mitral valve repair is the routine procedure for asymptomatic patients. In all patients ($n = 46$), the procedure was performed as preoperatively planned with echocardiography. There were no cases in whom repair was doubtful; there were no conversions to mitral valve replacement. Intraoperative echocardiography after repair revealed a direct significant reduction in the degree of MR in all patients to $\leq 1+$. The mean length of stay was 9.7 ± 5.7 days, during which 2 patients had a transient ischaemic attack (TIA). Four (8.7%) patients required a re-exploration for bleeding/tamponade. There were no cases of 30-day mortality.

Table 2. Procedural characteristics

Operative technique	N = 46
Ring implantation	45 (98%)
Cosgrove-Edwards ring	5 (11%)
Carpentier-Edwards Physio ring	40 (89%)
Size	
28	1 (2%)
30	6 (13%)
32	12 (26%)
34	12 (26%)
36	8 (17%)
38	4 (9%)
40	1 (2%)
Quadrangular resection	36 (78%)
Papillary muscle shortening	4 (9%)
Chordal shortening	3 (7%)
Artificial chords	4 (9%)
Chordal transfer	5 (11%)
Posterior mitral valve leaflet sliding	30 (65%)
Annulus decalcification	2 (4%)
Flipover	5 (11%)
Patch	5 (11%)

Long-term outcomes

The mean follow-up was 8.4 ± 3.9 years and comprised 385.5 patient-years. During follow-up, 3 patients died (0.78%/patient-year); the cause of death was cardiac (at 1.9 years), and non-cardiac as a result of stroke (at 3.4 years) and pulmonary embolism after kidney transplantation (at 2.8 years). Cumulative survival at 12 years was 93.3% and comparable with the age- and gender-matched survival in the general Dutch population (Figure 2). One patient required a reoperation at 1.7 years for severe MR during which the patient received a prosthetic valve (0.26%/patient-year). Valve-related complications during follow-up included three cerebrovascular accidents (0.78%/patient-year) and one transient ischaemic attack (0.26%/patient-year).

Long-term echocardiographic examination during follow-up was available in 38 patients at a mean of 9.2 ± 3.5 years. Of these, 92% ($n = 35$) had no to mild MR grade at follow-up and 3 patients had moderate MR (Figure 3A). Left ventricular function was good or mildly impaired in 95% of the patients (Figure 3B). There were only 2 patients with moderate LV function and none with poor function.

At the time of the last follow-up, 74% ($n = 29$) of patients were asymptomatic (NYHA Class I), 21% ($n = 8$) were in NYHA Class II, 5% ($n = 2$) in NYHA Class III, and none in NYHA Class IV. Data on cardiac rhythm were available from 41 patients, of whom there

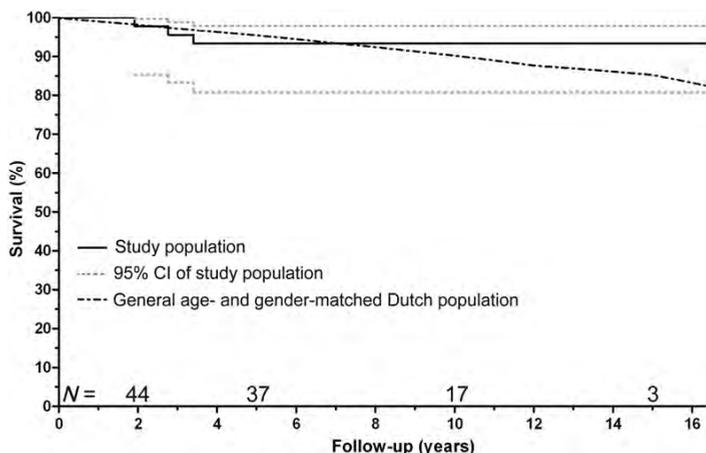


Figure 2. Long-term survival of patients with asymptomatic severe mitral valve regurgitation compared with the general age- and gender-matched Dutch population.

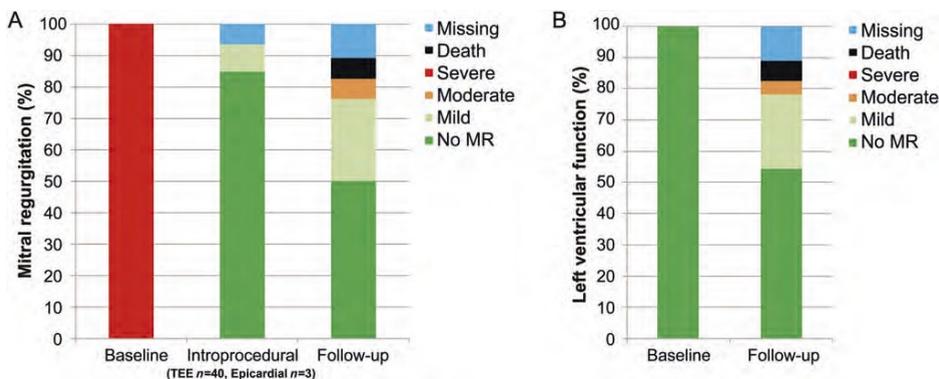


Figure 3. Long-term echocardiographic outcomes of patients with asymptomatic severe mitral valve regurgitation who underwent repair. There was an early reduction in the severity of mitral regurgitation in all patients that was maintained during the follow-up (A), and good left ventricular function (B).

were 4 (10%) with episodes of atrial fibrillation during follow-up. The remaining patients were in sinus rhythm.

The SF-36 questionnaire was completed by 36 patients and showed that quality of life was good and comparable with that of the general age-matched Dutch population (Figure 4 and Table 3). Remarkably, the individual physical domains and the composite PCS showed an even better quality of life than that of the general population.

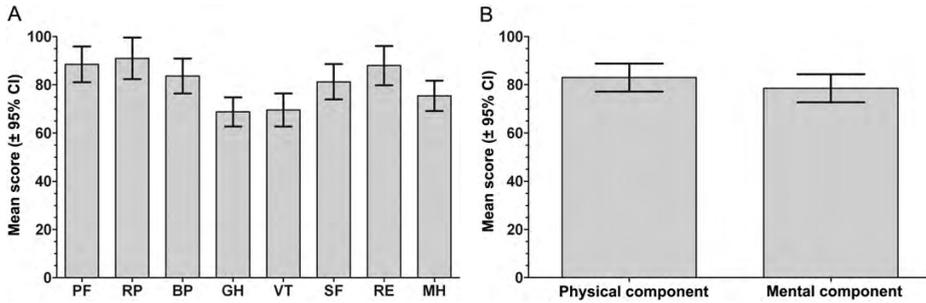


Figure 4. Long-term quality of life of patients with asymptomatic severe mitral valve regurgitation compared with the general age-matched Dutch population.

Table 3. Quality-of-life comparison with the general age-matched Dutch population

	Study population N = 36 (mean ± SD)	General Dutch population (mean ± SD)	P-value
PF	88.5 ± 21.9	76.2 ± 10.6	0.001
RP	91.0 ± 25.4	69.7 ± 7.8	<0.001
BP	83.7 ± 21.5	71.2 ± 2.8	0.002
GH	68.8 ± 17.8	66.4 ± 5.4	.044
VT	69.6 ± 20.3	67.1 ± 2.7	0.49
SF	81.3 ± 21.7	81.8 ± 3.3	0.88
RE	88.0 ± 24.1	80.3 ± 3.0	0.057
MH	75.4 ± 18.6	75.6 ± 1.5	0.95
PCS	83.0 ± 17.3	70.9 ± 6.5	<0.001
MCS	78.6 ± 17.2	76.2 ± 2.6	0.42

PF: physical functioning; RP: role-physical; BP: bodily pain; GH: general health; VT: vitality; SF: social functioning; RE: role-emotional; MH: mental health; PCS: physical component score; MCS: mental component score; SD: standard deviation

DISCUSSION

In asymptomatic patients with a normal left ventricular function undergoing surgical repair of severe MR, long-term outcomes were excellent. Survival at 12 years was 93.3% and comparable with the general age- and gender-matched Dutch population. Furthermore, 92% of surviving patients had none to mild MR grade and 95% had a good or mildly impaired left ventricular function at 9-year follow-up. Lastly, quality of life as measured by SF-36 questionnaires was not impaired and is comparable with the general age-matched Dutch population.

Current valvular guidelines indicate that mitral valve surgery, preferably mitral valve repair, might be beneficial in asymptomatic patients with severe MR and LV dysfunction, atrial fibrillation, and/or pulmonary hypertension¹. However, the role and timing of surgery

remain controversial. Observational studies comparing these two treatment options have shown promising results for surgical patients. A propensity-matched analysis reported significantly better event-free survival at 7 years for those patients who underwent surgery (99 vs 85%, $P = 0.001$)¹⁰. This was confirmed by Montant et al.⁴ who reported a 86% survival rate at 10 years compared with only 50% for patients who were treated conservatively.

The American guidelines specifically recommend referring patients to centres of excellence who have much experience with mitral valve repair. The rationale is that, in this relatively young patient population (the mean age in our series was 50 years), mitral valve repair is much preferred over mitral valve replacement¹¹. Surgery is indicated if the chance of repair is $> 90\%$, however, inexperienced surgeons/centres might not always succeed in valve repair, resulting in the need for mechanical valve replacement¹². It has been confirmed that annual hospital volume of mitral operations is a significant predictor of improved in-hospital rates of major adverse cardiac or cerebrovascular events, and a higher valve-repair rate^{12,13}. Therefore, experience may partly explain the large variation in the rate of valve repair among cardiac centres¹⁴.

These recommendations imply that surgery should be performed in high-volume, experienced centres. In our series, of 46 patients, 3 deaths occurred in 385 patient-years, and survival was 93% at 12-years of follow-up. These rates correspond well to those of the general Dutch population.

In conventionally treated asymptomatic patients, indications for surgery arise in about 25–30% within 5 years^{10,15}. With regard to the risk-benefit ratio, the benefit of surgery is still unclear and whether it is justified depends on the surgical risks and chance of successful repair. Therefore, asymptomatic patients may mostly benefit from repair if they have low comorbidity and/or if there is a low risk associated with surgery¹. In our series, we are able to safely perform valve repair in 100% of the cases where there were no conversions to valve replacement and no procedural mortality or stroke. These outcomes are similar to other series of asymptomatic patients^{2,10,16,17} and reflect strict patient-selection policy¹⁸.

Most asymptomatic MR studies have predominantly reported survival and reoperation analyses. Medium-term echocardiographic follow-up has also been reported¹⁷, but long-term follow-up echocardiographic results are limited. David et al. found that freedom from MR $\geq 2+$ was 96% at 10 years¹⁶. However, only 11 of the initial 199 patients (5.5%) actually had a 10-year echocardiographic follow-up. In addition, Gillinov et al. showed that 71% at 10-year follow-up had grade $\leq 1+$ MR irrespective of preoperative NYHA Class, but the mean follow-up was only 6.9 years, and the authors did not specify how many patients were at risk². In our current series, mean echocardiographic follow-up was at 9.2 years and 34.5% (16/46) completed > 10 -year echocardiography. A remarkable 92% of patients had less-than moderate MR, suggesting that longevity of valve repair is not an issue in asymptomatic patients. Furthermore, 95% of patients had normal or mildly impaired LV function.

Moreover, quality-of-life analyses are an important aspect of follow-up in these asymptomatic patients, since repair is performed to prevent the onset of symptoms due to congestive heart failure¹⁹. Most patients are in NYHA Class I at medium- or long-term follow-up^{16,17}, such analysis, however, might not be a valid measure of quality of life²⁰. We found that quality of life—as measured with SF-36 questionnaires—was comparable with the general age-matched population. This provides additional arguments to perform surgery, since it seems to prevent progression of the disease. Further data on quality of life in conservatively treated patients are necessary to put these results into perspective, although the higher rate of mortality and heart failure in conservatively treated patients may already be evidence that quality of life is impaired.

One of the major concerns remains the incidence of cerebrovascular events, as highlighted in previous studies^{4,16}. In our series, the risk of (non)fatal stroke was similar at 0.78% per patient-year. Compared with the overall Dutch population, in which the incidence of developing stroke is 0.23% per patient-year in 55–64 year olds²¹, patients after mitral valve repair may be at higher risk. This is likely related to the higher incidence of atrial fibrillation and consequently, the risk of stroke^{22–24}.

In our series, atrial fibrillation during follow-up occurred in nearly 10% of the patients, but none of them had a stroke or TIA. However, the limited number of patients may have prevented us from finding a correlation. It is highly recommended to perform regular echocardiography and electrophysiological follow-up assessments in which early diagnosis of atrial fibrillation and administration of appropriate therapy may prevent stroke.

Limitations

This was a small single-centre analysis, with its inherent limitations. Due to its retrospective nature, there were no data available on preoperative quality of life. Unfortunately, quality-of-life norms of the Dutch population only allow age-matching, but not age- and gender-matching⁹. The occurrence of atrial fibrillation during follow-up may have been underestimated since some patients may not have been detected at the time of electrocardiography.

Ideally, a control group of patients with asymptomatic MR who did not undergo surgery would have been included. Unfortunately, our database did not include these patients, and retrospective identification of such a group could not be performed.

CONCLUSION

Our experience shows that mitral valve repair for severe MR in asymptomatic patients is safe, and has satisfactory long-term survival with a low recurrence rate of MR, good LV functioning, and excellent quality of life that is comparable with the general Dutch

population. However, this was a retrospective single-centre study with a small number of patients and, therefore, we encourage further exploration and acceptance of this indication for mitral valve repair.

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