Results of Modern Mitral Valve Repair in Patients with Marfan Syndrome

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Abstract

Objectives Mitral valve (MV) regurgitation is a common manifestation in patients with Marfan syndrome (MFS) and is age dependent. Valve pathology shares some features with myxomatous MV disease. Surgical treatment is still being debated and not well characterized in patients with MFS.

Patients and Methods We retrospectively evaluated the results of mitral valve repair (MVR) of symptomatic patients with MFS who underwent surgery between January 2004 and April 2011. MFS was diagnosed following the Ghent criteria. MVR was performed in 12 patients. Three patients underwent minimally invasive MVR despite severe thorax deformities. Mean follow-up was 60.1 months (95% CI: 48–72) and was complete.

Results Thirty-day mortality was 0%. One patient died because of arrhythmia 66 months after MVR. Transthoracic echocardiography at last visit showed mild mitral regurgitation in one patient (8.3%) and no mitral regurgitation in the remaining patients (91.7%).

Conclusion MVR was associated with excellent survival and a low rate of complications. Transthoracic echocardiography showed good results of the repaired valves even years later. Minimally invasive repairs are feasible even in deformed thoraces, lowering the risk for future aortic surgery. Because of excellent mid-term to long-term results, MVR may also be justified in asymptomatic Marfan patients.

Keywords
- Marfan syndrome
- mitral valve
- mitral valve repair
- minimally invasive
- neochordae
- artificial chordae

Introduction

Marfan syndrome (MFS) is a disorder of the connective tissue with a prevalence of 1 in 5,000 individuals. It is inherited in an autosomal dominant fashion with complete penetrance but with considerable phenotypic variability and different patterns of organ involvement including the cardiovascular, ocular, skeletal, and pulmonary system, skin and dura. The high mortality of untreated cases with an average life expectancy of 32 years,[1] however, is almost exclusively a result of cardiovascular complications such as acute aortic dissection or rupture and mitral valve (MV) dysfunction. With optimized multidisciplinary expert care and prophylactic aortic root replacement, Marfan patients have a close to normal life expectancy.[2]

Mitral valve prolapse (MVP) is present in 49% of patients with MFS and is the leading cause of mortality in infants with MFS.[3,4] MV pathology in MFS shares features with idiopathic MV disease, such as chordal elongation, chordal rupture, and excess leaflet tissue.[4] However, there are some differences. A study of Bhudia et al documented that patients with MFS presented at a younger age than those with

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idiopathic disease, and they were less likely to be men. Isolated posterior leaflet prolapse was less common in MFS and bileaflet prolapse typical. Both leaflets were longer and thinner in MFS patients compared with those with idiopathic MV disease.[5] The same clinical determinants that predict outcomes in idiopathic MVP also predict outcomes in MVP associated with MFS.[3] Fleischer et al in their immunhistochemical studies found fibrillin abnormalities of aortic valve, aortic wall, and MV tissues in all patients with MFS.[6] The findings of these abnormalities were most severe in patients older than 20 years.[6] Myxoid infiltration and collagen alterations are roughly similar to those found in both entities, but MFS patients have more severe elastic fiber alterations than idiopathic MV disease patients. These findings lead to suspicions and concerns, specifically, if the connective tissue defect may lead to impaired repair durability.

The aim of this study was to evaluate the clinical outcome of mitral valve repair (MVR) in MFS patients and to report about a series of three patients who underwent successful minimally invasive MVR through small lateral minithoracotomies despite severe chest deformities.

Patients and Methods

Between January 2004 and April 2011, 14 MFS patients underwent MV surgery. Of the 14 patients, 2 of them had MV replacement because of endocarditis. In these cases, the leaflets were destructed by the infection and could not be preserved. The remaining 12 patients with MFS underwent MVR. We retrospectively analyzed outcomes in these patients. We relied on previously described routines to diagnose the MFS using established criteria of the Ghent nosology.[3,7] For our study, we only considered individuals who fulfilled criteria of classical MFS and those who were older than 18 years.

Three minimally invasive MVR were performed through a right midlateral ($n = 2$) or anterolateral minithoracotomy. Mean follow-up was 60.1 months (95% CI: 48–72). Patients were seen in our outpatient clinic every 6 to 12 months, which included a physical examination and transthoracic echocardiography (►**Table 1**). End points of the study were death, endocarditis, stroke, and reoperation for failure of valve repair. The follow-up was complete. We evaluated MV function and regurgitation of the repaired valve in transesophageal echocardiography pre- and intraoperatively. Transthoracic echocardiography was performed before discharge from hospital and in our outpatient clinic every 6 to 12 months. Quantification of MV regurgitation was performed by our cardiologists following the guidelines of the American Society of Echocardiography and as detailed in our previous studies.[3,8]

MVR was used whenever possible. We assessed preoperatively if minimal access surgery was possible and preferred this for the first operation. Standard hypothermic cardiopulmonary bypass with bicaval cannulation was performed. For myocardial protection, Bretschneider cardioplegia was used. After opening the left atrium, the MV was analyzed systematically segment by segment using two nerve hooks. Areas of excessive or restricted leaflet motion, coaptation level, amount of prolapsing tissue, and the degree of ring dilatation were detected. MVR was performed using the technique initially described by Carpentier et al.[9–11] A triangular or quadrangular resection was used for posterior leaflet prolapse combined with a bilateral sliding plasty in cases of excessive tissue. The decision to perform a quadrangular resection and a sliding plasty relies on the leaflet morphology. In case of excessive tissue with a huge annulus, the excessive tissue was resected. A sliding plasty was either performed to correct different heights of leaflet edges or to plicate and reduce the annulus size. Over time MVR techniques changed toward less leaflet resection in favor of leaflet preservation using artificial chordae for correction of prolapse as described by Perrier et al.[12] Ring dilatation was repaired by annuloplasty using either Carpentier Edwards Physio II or Myxo ETlogix Ring (Carpentier-Edwards, Irvine, California, United States). Elongated or ruptured chordae were replaced by 3–0 Gore- tex sutures (Gore, Flagstaff, Arizona, United States) (►**Table 2**). Testing of the repaired MV was again done by nerve hooks, inserting of saline, and by intraoperative transesophageal echocardiography after weaning from cardiopulmonary bypass. Postoperatively, patients were treated with coumadin for 3 months with an international normalized ratio between 2 and 3. When sinus rhythm was present, no anticoagulants were needed after 3 months.

Preoperative computed tomography (CT) scan or magnetic resonance imaging (MRI) was performed for strategic planning of access and feasibility of minimally invasive MVR and exclusion of concomitant aortic disease (►**Fig. 1**). In all three

Table 1 Preoperative characteristics of patients with Marfan syndrome who underwent mitral valve repair

	Mitral valve repair ($n = 12$)
Mean age (y)	41.7 (range, 18–65)
Male	6 (50%)
Previous aortic surgery	4 (33.3%)
Mean ejection fraction (%)	46.5 (26–60)
NYHA class $\geq$ 3, pre	12 (100%)
Mitral regurgitation grade $\geq$ 3	12 (100%)
Isolated AML prolapse	2 (16.6%)
Isolated PML prolapse	3 (25%)
PML cleft	2 (16.6%)
Bileaftlet prolapse	5 (41.6%)
Endocarditis	0
Mean logistic EuroSCORE (%)	5.2 (4.5–5.9)
Minimally invasive MVR	3

Abbreviations: AML, anterior mitral leaflet; MVR, mitral valve repair; NYHA, New York Heart Association; PML, posterior mitral leaflet.
Note: Means and 95% confidence intervals are shown.

Table 2 Intraoperative characteristics of patients with Marfan syndrome who underwent mitral valve repair

	Mitral valve repair ($n = 12$)
Extracorporeal circulation time (min)	179 (170–188)
Aortic cross-clamp time (min)	130 (125–135)
Concomitant procedures	6 (50%)
Valve sparing root replacement	3 (25%)
Biological composite valve grafting	1 (16.6%)
Quadrangular/triangular resection	8 (66.6%)
Slidingplasty PML	3 (25%)
Annuloplasty	12 (100%)
Physioring	7 (58.3%)
Myxoring	5 (41.6%)
Chordal replacement	4 (33.3%)
Direct cleft suture	2 (16.6%)
Edge-to-edge suture	2 (16.6%)

Abbreviations: PML, posterior mitral leaflet.
Note: Means and 95% confidence intervals are shown.

patients, in whom we performed minimal access surgery chest deformities were present. One patient had a pectus excavatum and kyphoscoliosis, another patient had severe pectus excavatum, and the third patient had a pectus carinatum and kyphoscoliosis. Minimal access MVR was performed through a midlateral or anterolateral minithoracotomy depending on preoperative CT or MRI examinations for planning of incision site. Cannulation of the right-sided femoral vessels for extracorporeal circulation and transthoracic cross-clamping of the aorta was performed. For venous cannulation we used a two-stage cannula. For visualization of the MV, we used a 5-mm thoracoscope. We performed a standardized telephonic interview to identify individuals with reoperations, endocarditis, and stroke outside our center. Follow-up including echocardiography was complete in all patients.

Results

In all patients, the MV could be successfully repaired. Repairs were feasible without intraoperative episodes of systolic anterior leaflet motion (SAM) that would need to be corrected immediately. After a follow-up of 60.1 months (95% CI: 48–72), dyspnea improved from New York Heart Association class 3.2 (95% CI: 2.9–3.5) to 1.4 (95% CI: 1.2–1.6). We observed no endocarditis or stroke after MVR in our cohort of Marfan

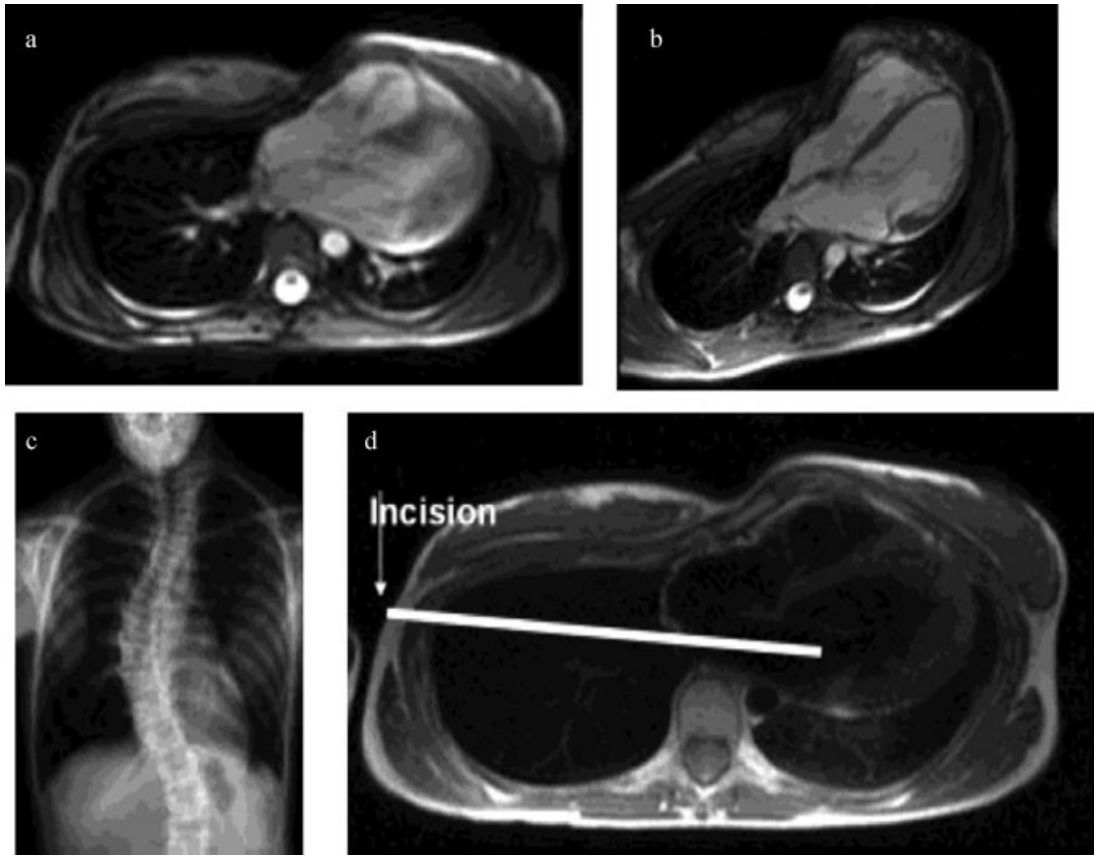

Fig. 1 Minimally invasive mitral valve repair of a Marfan patient with severe kyphoscoliosis and pectus excavatum. (a) and (b): Magnetic resonance imaging (MRI) scans showing severe pectus excavatum; (c) X-ray showing a severe kyphoscoliosis; (d) MRI-based planning of the incision before anterolateral or midlateral minithoracotomy. In this 26-year-old female patient, sternotomy is aggravated and with an increased risk due to a severe kyphoscoliosis and pectus excavatum. MRI is done for planning the optimal access to the left atrium and exposure of the mitral valve. Minimal access repair is done with video-thoracoscopic assistance. The white bar indicates the planned incision and view on the mitral valve.

patients. No patient required reoperation of the repaired MV. Transthoracic echocardiography at last visit showed good results in 11 patients with no evidence of mitral regurgitation and only 1 patient with mild mitral regurgitation (►**Table 1**).

No patient died within the first 30 days postoperatively. One patient with a preoperative impaired left ventricular function had recurrent episodes of ventricular tachycardia on intensive care unit after MVR that required cardiopulmonal resuscitation and therefore underwent an implantable cardioverter-defibrillator implantation. Fourteen months after MVR, the patient needed valve sparing aortic root replacement because of progression of the aortic root diameter. Transthoracic echocardiography was performed 62 months after MVR, which showed good results of the mitral and the aortic valve, but a reduced left ventricular function with an ejection fraction of 20%. Persistent atrial fibrillation led to several hospital stays. Sixty-six months after MVR, the patient died because of arrhythmia (►**Table 3**).

Discussion

The frequency of MVP has been reported in a wide range of 12 to 88%.[2,4,8,13–15] But, echocardiographic methods and diagnostic criteria were different in these studies, and therefore, it is difficult to compare prevalence of MVP. Patients with MFS having severe MVR presented at a younger age than those with idiopathic disease, and they were less likely to be men. Isolated posterior leaflet prolapse was less common in MFS and bileaflet prolapse more typical. Both leaflets were longer and thinner in MFS patients compared with those with idiopathic MV disease.[4,5,14,16] The same clinical determinants that predict outcomes in idiopathic MVP also predict outcomes in MVP associated with MFS.[3] A recent study with 204 MFS patients documented the age-dependent manner of MVP and MVR. They found that severe MVR developed exclusively in individuals with preexisting MVP who already present with some degree of MVR on initial echocardiography.[8] Despite striking differences, similar characteristics in idiopathic MVP rather than typical features of MFS predict outcomes of MVR. These findings support the common practice of applying established criteria for the timing of MV surgery to patients with MFS.[17]

To date, few studies about MV surgery in Marfan patients are available. Techniques for MV repair are based on experience with idiopathic MVP. The classical technique described by Carpentier involves the resection of prolapsing tissue is the most commonly performed and has excellent long-term results.[9,18] It is mostly combined with implantation of an annuloplasty ring to correct for annular dilatation. A newer technique of "respect rather than resect" tissue has been described recently and is based on the use of artificial chordae to reconstruct support of the free edge of prolapsing segments and transform the leaflet into a smooth vertical buttress to ensure a good surface of coaptation without resection.[12,19–22]

Long-term survival following MVR in patients with idiopathic MVP is similar to age-matched controls provided the operation is done in a timely fashion before the onset of symptoms.[23]

The localization of leaflet prolapse is also of prognostic relevance because many reported series suggest much lower repair rates for anterior or bileaflet prolapse compared with posterior leaflet prolapse.[24] Although freedom from reoperation after 15 years after MVR is around 95% for idiopathic MVP, some studies have documented the potential for recurrence of significant MV regurgitation of 1 to 2% of patients per year.[18,25]

In our cohort, we had no early mortality that was also previously reported by Gillinov et al and Bhudia et al. In these studies, long-term survival after MVR was 83.3% after 10 years in the cohort of Gillinov et al that is comparable with the reported 80% of Bhudia et al and with 78.9% of Fuzzelier et al.[5,26,27] No patient of our study needed late MV replacement. Other series also reported good long-term performance of the reconstructed valves with a low risk of late MV replacement with freedom from MV reoperation of 87.1 to 96% at 10 years.[5,26] In our series, all repaired valves had no or only mild mitral regurgitation.

Our series include three Marfan patients who underwent successful minimally invasive MVR through lateral minithoracotomies despite severe chest deformities. All three patients had good results in the echocardiographic follow-up examination. In these patients, aortic diameters were normal. Previous median sternotomy is an independent risk factor for perioperative mortality in reoperations.[17] The operative risk for later aortic surgery might be decreased after minimal access MV surgery because of fewer adhesions compared with reoperations after conventional median sternotomy. Thus, this surgical approach may be used more often in MFS patients in the future.

We performed chordal replacement in three patients with anterior leaflet prolapse, which was not reported previously

Table 3 Postoperative characteristics of patients with Marfan syndrome who underwent mitral valve repair

	Mitral valve repair ($n = 12$)
Mean follow-up (months)	60.1 (48–72)
30-day mortality	0
Mortality (> 30 d)	1 (8.3%)
Mean ejection fraction (%)	52 (43–60)
No mitral regurgitation	11 (91.7%)
Mild mitral regurgitation	1 (8.3%)
NYHA class $\geq$ 3	2 (16.6%)
Endocarditis	0
Reoperation	0
Stroke	0
Re-exploration for bleeding	0
Permanent pacemaker implantation	0

Abbreviations: NYHA, New York Heart Association.
Note: Means and 95% confidence intervals are shown.

Table 4 Surgical strategies in 12 patients with Marfan syndrome

	Indication	Surgical access	Techniques	Concomitant procedure
1	Previous aortic root replacement and mitral valve repair, AML prolapse, severe decreased LV Fx, CAD	Median resternotomy	Neochord to AML, edge-to-edge stitch, annuloplasty	CABG
2	PML prolapse, aortic root aneurysm, ASD, good LV Fx	Median sternotomy	Triangular resection, annuloplasty	ASD closure by direct suture, aortic root replacement according to David et al[25]
3	Previous aortic root replacement with mechanical CVG, bileaflet prolapse, good LV Fx	Median resternotomy	Quadrangular resection, slidingplasty, annuloplasty	None
4	Previous aortic root replacement with biological CVG, moderate prolapse of AML, annulus dilatation, good LV Fx	Median resternotomy	Annuloplasty, neochord insertion to AML	None
5	Previous aortic root replacement with mechanical CVG, moderate impaired LV Fx, annulus dilatation	Median resternotomy	Annuloplasty	None
6	PML prolapse, good LV Fx, aortic root dilatation	Median sternotomy	Quadrangular resection, annuloplasty	Aortic root replacement according to David et al[25]
7	Bileaflet prolapse, annulus calcification, good LV Fx,	Median sternotomy	Triangular resection, anuloplasty	None
8	Bileaflet prolapse, aortic root aneurysm, good LV Fx	Median sternotomy	Quadranguar resection, slidingplasty, annuloplasty	Aortic root replacement with biological CVG
9	Annulus dilatation, aortic root aneurysm, good LV Fx	Median sternotomy	Annuloplasty	Aortic root replacement according to David et al[25]
10	PML Prolapse, Good LV Fx, severe kyphoscoliosis	Lateral thoracotomy	Quadrangular resection, slidingplasty, anuloplasty	None
11	Severe bileaflet prolapse, PML cleft, annulus calcification, good LV Fx,	Lateral thoracotomy	Triangular resection, suture of PML cleft, PML patch plasty with autologous pericardium, anuloplasty, neochord insertion to AML, edge-to-edge stitch	None
12	Severe bileaflet prolapse, AML cleft, good LV Fx, young female	Lateral thoracotomy	Quadrangular resection, suture of AML cleft, neochord insertion to AML, anuloplasty	None

Abbreviations: AML, anterior mitral leaflet; ASD, atrial septal defect; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CVG, composite valve grafting; Mic MVR, minimally invasive mitral valve repair; LV Fx, left ventricular function; PML, posterior mitral leaflet.

in Marfan patients. Long-term results in myxomatous mitral disease showed that established techniques for posterior leaflets repair are particularly effective with excellent results. However, repair of the anterior leaflet remains challenging. Feasibility and durability of anterior leaflet repair is inferior to that of posterior leaflet repair in myxomatous MV disease.[25] Chordal replacement by artificial chordae is indicated in cases of extensive anterior or posterior leaflet prolapse, circumstances that are more common in mitral disease of MFS than in myxomatous mitral disease. Application of artificial chordae might improve the feasibility and durability of MVR. We believe that the use of artificial chordae is also justified in MFS patients (►**Table 4**).

Anterior displacement of the leaflet coaptation line and redundant posterior leaflet tissue, just as relationship of anterior and posterior leaflet surface area to the normal annular dimension cause SAM.[28,29] SAM is described in up to 5% after MVRs.[30–32] We did not observe any episodes of postrepair SAM. However, as MV morphology is one risk factor for postoperative SAM, some authors indicate a high posterior leaflet height a risk factor, whereas other authors highlight the length of anterior leaflet for the postoperative occurrence of SAM.[33,34] A recent study suggested that the selection of ring size plays a crucial role in development of SAM.[35] We try to avoid too extensive downsizing of the mitral annuloplasty to prevent SAM.

Quadrangular resection of the posterior leaflet of the MV is an established technique for MVP.[9] The traditional plication of the annulus in a single location, as described in the original quadrangular resection, may contribute to SAM. This

encouraged the development of the sliding leaflet technique defined by Carpentier.[36] But in case of extensive P2-prolapse, the sliding technique may also lead to posterior leaflet tension and leaflet-annulus mismatch, and therefore, causing SAM.[37] Our strategy is insertion of artificial chordae in this scenario. In recent years, MVR techniques changed toward less leaflet resection in favor of leaflet preservation using artificial chordae for correction of prolapse in our cohort.

There is evidence of low morbidity and mortality after MVR in asymptomatic patients with severe mitral regurgitation.[23] Therefore, guidelines of the American Heart Association and the American College of Cardiology recommend MVR for such patients if the probability of repair is expected to exceed 90%.[17] Our series provides further evidence that these criteria can be fulfilled in the majority of MFS patients with severe MV regurgitation.

Limitations

The limitations of this study are as follows: a relatively short follow-up period and the relative small number of Marfan patients who underwent MV surgery.

Conclusion

With increasing preservation of the aortic valve, avoiding anticoagulation by repairing the MV early has become increasingly important. Minimally invasive MVRs and the usage of neochordae are feasible in MFS patients even in deformed chests—lowering the risk for future aortic surgery. MVR has a low-mortality rate and a low rate of complications and reoperations. Because of excellent mid-term to long-term results MVR may also be justified in asymptomatic Marfan patients.

Conflict of Interest
None declared.

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Preparation of the manuscript was a true team effort involving both first authors on an equal level not only with regards to data acquisition but also in data interpretation and manuscript writing. Involvement concerned:

Alexander Bernhardt: Manuscript planning, Data collection, Manuscript preparation.
Hendrik Treede: Surgery, Manuscript planning, Data collection, Manuscript preparation.

Although both authors had a slightly different impact on above mentioned parts of the whole work, their overall impact for this manuscript has to be seen as equal.

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