Mitral valve reconstruction in Barlow disease: Long-term echographic results and implications for surgical management

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Objective: Owing to the complexity of the underlying lesions, Barlow disease remains a challenge for surgeons performing mitral valve repair. We aimed to assess whether our most recent results involving several surgeons were comparable with those of a previous experience in which mitral valve repair was performed by a more limited group of surgeons.

Methods: From September 2000 to January 2007, 200 patients with Barlow disease (135 men and 65 women; mean age, 56 ± 13 years) were referred to our institution for surgical treatment of their mitral regurgitation. We retrospectively analysed the mitral lesions characteristics, the surgical techniques used, and clinical outcomes. Follow-up echocardiograms were biannually reviewed.

Results: Lesions comprised annular dilatation, excess tissue, and leaflet prolapse in all cases. The most frequent prolapsed segments were P2 (88.5%; $n = 177$) and A2 (55.5%; $n = 111$). Annular calcifications and restrictive valvular motion were associated in 20% ($n = 40$). Repair was feasible in 94.7% ($n = 179/189$) of non-redo interventions. Immediate postoperative echocardiography showed residual mitral regurgitation greater than 1+ in 6 cases; these patients were all reoperated on within the next months. Operative mortality was 1.5% ($n = 3$). Mean follow-up was 77.5 ± 25.6 months. At 8 years postoperatively, overall survival was $88.6\% \pm 3.1\%$, freedom from reintervention was $95.3\% \pm 1.7\%$, and freedom from late recurrent moderate mitral regurgitation ($>2+$) was $90.2\% \pm 3.1\%$

Conclusions: Provided that the fundamental principles of mitral valve reconstruction are respected, the surgical techniques are highly reproducible with good long-term results, similar to those published during the pioneering phase of this surgery. (J Thorac Cardiovasc Surg 2012;143:S17-20)

Barlow disease or billowing mitral valve (MV) syndrome accounts for approximately 30% of the patients undergoing MV repair for degenerative disease.¹ Multiple confusing terminologies have been used to describe it in the literature, including floppy valve, myxomatous valve, and MV prolapse, whereas leaflet prolapse should refer only to a nonspecific dysfunction in which the free edge of the leaflet overrides the annular plane. Within the group of degenerative diseases, 2 distinctive entities should be distinguished: fibroelastic deficiency and Barlow disease.² The distinction is based on population characteristics,

valve structure, and microscopic lesions. As opposed to fibroelastic deficiency, Barlow disease is characterized by excess of thickened leaflet as a result of myxoid degeneration.³ It is typically observed in a patient under 60 years of age with complex MV lesions including severe annular dilatation, generalized excess of tissue, leaflet billowing, and multiple sites of leaflet prolapse.² In forme fruste of Barlow disease, the excess of tissue involves only a part of the valve. Microscopically, myxoid infiltrations are associated with alterations predominantly involving collagen fibers rather than elastic fibers.¹ Nevertheless, the distinction between Barlow disease and fibroelastic deficiency is seldom made in the literature and the results of complex MV repair in Barlow disease are still not very widely known.

The long-term superiority of MV repair over replacement in severe mitral regurgitation (MR) has been well established.^{4,5} A better understanding of the mechanisms of MR and improvements in echocardiography have both allowed surgeons to perform more complex MV reconstruction.⁶ Still, among degenerative MV diseases, Barlow disease remains a challenge for surgeons.

Following the evolution of Carpentier's techniques over the years, our institution has been implicated in understanding and treating Barlow disease by reconstructive valve

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Abbreviations and Acronyms

LCOS	= low cardiac output syndrome
MR	= mitral regurgitation
MV	= mitral valve
SAM	= systolic anterior motion
TEE	= transesophageal echocardiography

surgery. We report our latest results with MV repair in Barlow disease with a critical analysis of the surgical problems that have been encountered and report postoperative mid-term results.

PATIENTS AND METHODS

Between September 2000 and January 2007, a total of 453 patients underwent MV surgery at our institution for degenerative disease; Barlow disease was identified in 200 cases.

The diagnosis of Barlow disease was based on the patient's medical history and preoperative 2-dimensional echocardiography showing dilatation of the annulus, excess valvular tissue with billowing leaflets, and leaflet thickening. The diagnosis was confirmed, at the time of surgery, by gross examination and by histologic examination of the resected tissue specimen, attesting global myxomatous proliferation. Formes frustes with excess tissue localized onto several segments of the posterior leaflet and commissures were also included.

There were 135 men and 65 women with a mean age of 56.0 ± 13.4 years. Fifty-one (25.5%) patients were in New York Heart Association class III or IV and 25 (12.5%) had preoperative atrial fibrillation.

Preoperative 2-dimensional echocardiography showed an ejection fraction of less than 50% in 26 (13%) patients and an end-systolic left ventricle diameter over 45 mm in 36 (18%) patients.

Nine (4.5%) patients had deterioration of a previous MV repair performed in another institution. Twenty-seven (13.5%) patients needed a concomitant procedure: Cox maze, tricuspid valve annuloplasty, coronary artery bypass, or aortic valve replacement.

All procedures were performed in the same institution by 8 surgeons having different levels of expertise in MV repair but using Carpentier's techniques.

Postoperative transesophageal echocardiography (TEE) was performed in all cases before chest closure. A predischarge transthoracic echocardiogram was also performed to confirm the results of the surgical procedure.

Follow-up

The mean follow-up was 77.5 ± 25.6 months. Follow-up was complete in 97% of the cases. It was done by contact with each patient and the referring cardiologist. Late echocardiograms were obtained from the referring cardiologists and reviewed every 2 years.

Statistical Analysis

Data analyses were performed with SPSS software (SPSS, Inc, Chicago, Ill) and SAS software (SAS Institute, Inc, Cary, NC). Descriptive statistics were expressed as mean $\pm$ standard deviation for continuous variables and percentage and/or frequencies for categorical variables. Estimates for long-term survival and freedom from adverse events were made by the Kaplan-Meier method.

Preoperative patient variables were entered into a binary logistic regression analysis to highlight independent predictors of immediate adverse outcomes. The appropriateness of tested variables was first determined by univariate analysis using a χ^2 or Fisher exact test for categorical data and the Student *t* test for continuous data. Finally, the Kaplan-Meier method

was used to determine univariate predictors of late adverse outcomes. Every variable with a *P* value $< .2$ was entered into a Cox regression multivariate model to identify independent multivariate predictors.

RESULTS

Intraoperative functional MV analysis revealed a dilated annulus and a prolapse (type II) in all cases. The site of mitral prolapse is detailed in Table 1. A restrictive leaflet motion (type IIIa) was associated with leaflet prolapse in 7 (3.5%) patients and was the consequence of the fibrous scar of a previous MV repair. Calcification of the annulus was present in 40 (20%) patients.

Repair was feasible in 182 (91%) patients. In the remaining 18 patients, the MV was judged unsuitable for repair and was therefore replaced. Seven of these patients had been previously operated on for their MV disease. Thus, the feasibility of MV reconstruction in initial surgery was 94.7%. Mean bypass time was 147 ± 64 minutes. The surgical reconstructive techniques used at each level of the MV apparatus are summarized in Table 1. Quadrangular resection of the posterior leaflet was performed without sliding plasty in 54 (29.7%) patients and was associated with a sliding plasty in 127 (69.8%). Commissural or paracommissural prolapse was addressed by localized edge-to-edge technique, also called commissuroplasty, in 10 (5.5%) patients. The prosthetic rings used in MV repairs were 34 mm in 54 (29.7%) patients, 36 mm in 84 (46.1%), 38 mm in 24 (13.2%), and 40 mm in 20 (11%) patients. After the patients had been weaned from bypass and had reached optimal hemodynamic conditions, intraoperative TEE showed residual MR ($>1+$) in 6 patients. This problem was addressed by MV replacement in 1 patient, insertion of a more adapted ring in 1 patient, a complementary MV repair procedure in 2 patients, and abstention in 2 patients. A systolic anterior motion (SAM) of the anterior leaflet was detected in 6 patients and was resolved by increased left ventricular filling in 3 patients; in the remaining 3, the problem was fixed by insertion of a larger prosthetic ring, reduction of the height of the posterior leaflet, and MV replacement.

In-hospital mortality was 1.5% ($n = 3$). Complications during intensive care unit stay were as follows: low cardiac output syndrome (LCOS) in 25 (12.5%) patients, prolonged intubation over 48 hours and/or acute respiratory distress syndrome in 10 (5%) patients, and postoperative hemorrhage requiring surgical reintervention in 3 (1.5%) patients.

LCOS was defined by the association of the following criteria: (1) arterial systolic blood pressure less than 90 mm Hg, (2) central venous pressure greater than 12 mm Hg, (3) globally hypokinetic left ventricle (ejection fraction $< 50\%$) on intraoperative TEE (after weaning from cardiopulmonary bypass) or on postoperative transthoracic echocardiography, and (4) need for inotropic support for at least

TABLE 1. Sites of mitral leaflet prolapse and surgical techniques used for repair according to the level of the lesion

Sites of leaflet prolapse	Value (%)	No. of patients
Posterior leaflet		
P1	28	56
P2	88.5	177
P3	40	80
Anterior leaflet		
A1	17	34
A2	55.5	111
A3	37.5	75
Commissures		
Posterior	20.5	41
Anterior	6.5	13

Level	Type	Value (%)	No. of patients
Annulus	Ring annuloplasty	100	182
	Decalcification	8.8	16
Posterior leaflet	Resection	29.7	54
	Sliding plasty	69.8	127
	Chordal transfer	7.7	14
	Resection	3.8	7
Anterior leaflet	Chordal transfer	25.3	46
	Neochordae	4.4	8
	Edge-to-edge	5.5	10
Commissure	Edge-to-edge	5.5	10
Papillary muscle	PM shortening	25.3	46
	PM sliding plasty	10.4	19
	Chordal shortening	4.4	8

PM, Papillary muscle.

6 hours or for mechanical support (intra-aortic balloon counterpulsation).

By univariate analysis, predictors of operative mortality were chronic obstructive pulmonary disease ($P = .005$) and MV replacement ($P = .004$). Predictors of LCOS were preoperative left ventricular ejection fraction less than 60% ($P = .03$) and total bypass time ($P < .001$).

By multivariate analysis, chronic obstructive pulmonary disease and total bypass time were independent predictors of operative mortality and LCOS, respectively.

At 8 years postoperatively, overall survival was 88.6% $\pm$ 3.1% and freedom from cardiac death was 93.6% $\pm$ 2.3% (Figure 1, A). Predictive factors of late cardiac death were MV replacement ($P = .003$), redo surgery ($P = .006$), LCOS ($P = .002$), and preoperative New York Heart Association class III/IV ($P = .001$). By multivariate analysis, LCOS and MV replacement were independent predictors of late cardiac death ($P = .032$ and $P = .003$, respectively).

Freedom from reintervention was 95.3% $\pm$ 1.7% at 8 years. The 7 patients who required reoperation at the time of follow-up were distributed as follows: (1) Three patients had a new chordal rupture at 1, 10, and 42 months; 2 of these patients underwent MV rerepair and 1 patient underwent MV replacement. (2) Two patients had more than mild

residual MR on postoperative TEE; they eventually needed MV replacement within the first month. (3) One patient had acute endocarditis develop on a bioprosthesis at 2 months. (4) One patient had a fibrous restrictive posterior leaflet scar develop and had an MV replacement at 11 months.

Freedom from late moderate recurrent MR ($>2+$) was 90.2% $\pm$ 3.1% at 8 years (Figure 1, B).

DISCUSSION

MV reconstruction in Barlow disease respecting the fundamental principles of Carpentier's techniques provided a high proportion of repair feasibility and good long-term results. These results of MV obtained by 8 surgeons were similar to those of the pioneering phase of MV repair for degenerative disease of our institution, which was essentially based on the experience of a more limited number of surgeons, thereby reflecting the high reproducibility of the surgical techniques used.⁴

One of the most challenging aspects of surgical repair in Barlow disease is obviously the presence of an anterior leaflet billowing, frequently associated with prolapse. Extensive billowing hampers the surgical segmental MV analysis. Preoperative TEE plays a major role in pointing out the prolapsed areas. Nevertheless, anterior leaflet prolapse clearly jeopardizes the results of MV repair.⁷ Our approach for this lesion has evolved during the past decade. Chordal shortening should no longer be used, as advocated by others,⁸ and papillary muscle plasty is currently preferred to chordal transposition in the setting of large prolapsed areas without chordal rupture. These technical evolutions, as noted by others, have improved the results of MV reconstruction in Barlow disease.⁹ "Edge-to-edge" repair, even though immediately satisfactory, produces uncertain midterm results and some degree of valve stenosis,¹⁰ which could be questionable for patients under the age of 60 years.

Preoperative TEE is also of utmost importance in the prevention of SAM. It allows measurements of the height of the leaflets and calculation of the aorta-mitral angle and estimates the volume of the left outflow tract. This information helps in predicting the risk of postoperative SAM and guides the surgeon in the MV reconstruction. Our policy is to perform a sliding plasty when the height of the posterior leaflet is greater than 15 mm or greater than one third the height of the anterior leaflet. Careful measurement of the height of the anterior leaflet and subsequent ring selection significantly reduced the risk of SAM.¹¹ In our series, more than 20% of patients required a prosthetic ring of 38 or 40 mm. Such a policy has permitted us to reduce the number of cases of SAM in the past decade of our experience, and in the present series only 3 cases of significant SAM remained after adequate left ventricular filling.

Although not frequently reported in the literature, LCOS was the most frequent complication encountered in this

FIGURE 1. Kaplan-Meier survival curves. A, Global survival and freedom from cardiac death of the whole population (n = 200). B, Freedom from recurrent moderate (>2+) mitral regurgitation (MR) of patients undergoing mitral valve repair (n = 182).

study. Preoperative left ventricular dysfunction and complex MV lesions requiring longer bypass times were both predictive factors of LCOS. Owing to the specific characteristics of patients with Barlow disease, other frequently reported predictive factors of LCOS, such as age and female gender, were not identified in this series. Interestingly, LCOS was predictive of rather than an immediate cause of cardiac death. This argues for an optimal intraoperative management of patients with risk factors of LCOS. Valve replacement and coronary artery disease were the other 2 factors influencing late mortality. This finding is consistent with the common idea that MV repair has a better long-term prognosis than MV replacement, even in the setting of complex valve lesions.^{7,9} It also emphasizes the importance of referring patients with Barlow disease to centers experienced in MV repair, as suggested by the recent guidelines of the American Heart Association and American College of Cardiology.

CONCLUSIONS

Barlow disease is a specific degenerative process leading to extensive lesions of the MV. Despite its complexity, MV reconstruction is most often possible and should be preferred in this young population. The long-term results are good, provided that surgeons use reproducible techniques and do not accept more than mild MR on the postoperative control echocardiogram. However, owing to the possible progression of this degenerative process, close follow-up has to be achieved after surgery.

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