A standardized repair-oriented strategy for mitral insufficiency in infants and children: Midterm functional outcomes and predictors of adverse events

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Objective: Surgical management of mitral regurgitation (MR) in children remains a challenge because of the heterogeneity of the anatomy, growth potential, and necessity to avoid valve replacement. Our objective was to assess the functional outcomes and prognostic factors of a standardized strategy of mitral valve (MV) repair for children with MR.

Methods: Consecutive patients aged <18 years who had undergone surgery for severe MR from 2001 to 2012 were studied retrospectively. The standardized repair strategy mainly included leaflet debridement, annuloplasty, and leaflet augmentation. Multivariable risk analyses for recurrent MR (grade > II), transmural mean echocardiographic gradient > 5 mm Hg, MV reoperation, replacement, and mortality were performed.

Results: A total of 106 patients were included (median age, 5.1 years; range, 11 days to 18 years). The mean follow-up period was 3.9 ± 3.2 years (range, 2 months to 11 years). The proportion of congenital and left heart obstruction-related (left ventricular outflow tract obstruction) etiology was 49% (n = 52) and 11% (n = 12), respectively. MV repair was performed primarily in 97% of the patients. The mortality, reoperation, replacement, and MR rate at the last follow-up visit was 4.5% (n = 5), 23% (n = 24), 5.5% (n = 6), and 17% (n = 18), respectively. Actuarial survival was 93% ± 2% at 10 years. Freedom from MV replacement was 95% ± 2% and 86% ± 7% at 5 and 15 years, respectively. Native valve preservation was obtained in 85% of the infants and 94% beyond infancy. Independent predictors of recurrent MR, MV reoperation, and replacement included left ventricular outflow tract obstruction etiology (hazard ratio, 45; P = .004), associated preoperative mitral stenosis (hazard ratio, 21; P = .03), and young age (hazard ratio, 1.2; P = .04).

Conclusions: A standardized and reproducible MV repair strategy can achieve satisfactory functional results in infants and children with severe MR, allowing native valve preservation. The left ventricular outflow tract obstruction-related etiology was the main independent predictor of recurrent MR, MV reoperation, and MV replacement. (J Thorac Cardiovasc Surg 2014;148:1459-66)
Abbreviations and Acronyms

CI = confidence interval
HR = hazard ratio
LV = left ventricular
LVOTO = left ventricular outflow tract obstruction
MI = mitral insufficiency
MR = mitral regurgitation
MV = mitral valve

Of the 106 patients, 30 (25%) were <1 year and 41 (38.6%) were <2 years old (Figure 1). All patients presented with symptoms, including failure to thrive and intolerance to feeding in infants and young children, and New York Heart Association class III-IV in the older patients. The 4 most frequent etiologies of MR were congenital (n = 52; 49%), including the presence of a mitral leaflet cleft (n = 15; 14%), rheumatic (n = 13; 12%), related to left ventricular (LV) outflow tract obstruction (LVOTO; n = 12; 11%), and ischemic (n = 11; 10%; in 10, an anomalous left coronary artery arising from the pulmonary artery, and in 1, atresia of the left coronary ostium). Twelve patients (11%) had associated mitral stenosis, defined by a mean echocardiographic gradient of >10 mm Hg. Most patients had an associated lesion in addition to MR. Patients presenting with repaired atrioventricular septal defect were excluded. The patient and mitral valve anatomic and functional characteristics are listed in Table 1 and the functional classification in Table 2.

Echocardiographic Evaluation

All 106 patients had undergone an echocardiographic examination before surgery, during surgery (control transesophageal echocardiography), at discharge from the hospital, and annually during the follow-up visits. Preoperative MV function was assessed by transthoracic echocardiography according to the European Association of Echocardiography guidelines. In brief, the echocardiographic examinations were used to assess the MV anatomy and function (ie, annulus, leaflet, subvalvar apparatus), quantified the MR (ie, size of the left cavities using M mode, reverse flow in the pulmonary veins using pulsed Doppler, and proximal isovelocity surface area), and evaluate the consequences of MR (ie, LV ejection fraction using Simpson’s method, systolic arterial pressure calculated from the tricuspid regurgitation flow velocity, mean pulmonary arterial pressure calculated from the pulmonary regurgitation flow velocity). A multimodality approach combining all these parameters was used to separate MR into 4 classes from I to IV. Preoperatively, 54 patients (51%) had moderate to severe MR (grade III) and 44 (42%) had severe (grade IV) MR.

Surgical Technique

After median sternotomy and pericardotomy, cardiopulmonary bypass was established using standard aortic and bivacal cannulation, antegrade intermittent warm blood cardioplegia, and normothermia. A patch of pericardium was prepared free from adipose and extrapleural tissue and treated in glutaraldehyde for 7 minutes in the primary procedures.

After dissection of Sondergaard’s groove, a left atriotomy was performed. Annular stay stitches were placed on both trigones and posterior part of the annulus to expose the MV. Direct and systematic inspection of the MV apparatus (ie, papillary muscles, chordae, leaflets, and annulus) using nerve hooks allowed us to confirm the echocardiographic findings and completely assess the valve pathologic condition and MR mechanism and etiology.

A 3-step standardized repair strategy was then applied, leading to surgical interventions according to the MR mechanism and etiology and MV anatomy. The final objective of this standardized repair strategy was to restore the functional MV anatomy to as close as possible to the normal functional anatomy.

Step A. The first step consisted of subvalvular apparatus rehabilitation, mainly to increase the leaflet mobility through extensive leaflet debridement. This step, involving both leaflets and using nerve hooks to expose the lesions, required

1. Searching for and cutting all useless and restrictive secondary chordae tendineae
2. Splitting the papillary muscles in the case of shortened leaflets or “papillary muscle–leaflet fusion”
3. In the case of leaflet prolapse, shortening the papillary muscle, directly or by intraventricular repositioning, chordae transfer, and/or the use of artificial PTFE chordae or resection of redundant anterior leaflet tissue associated with repositioning of a native chordae coming from the anterior or posterior leaflet

Twenty patients (19%) benefited from the latter technique. The treatment of posterior leaflet prolapse was performed by quadrangular resection of the posterior leaflet associated with sliding plasty of each hemileaflet (n = 9; 8%). Step A was required in more than two thirds of the patients (n = 75; 71%).

Step B. Step B consisted of plication and reinforcement of the mitral annulus. The 3 tools were used to meet this aim were as follows:

1. Commissural and posterior annuloplasty stitches, in younger patients and larger patients, in the case of insignificant annular dilatation. This procedure was used in 15 patients (14%).
2. Posterior annuloplasty, using a Gore-Tex Accuseal interrupted strip (W. L. Gore & Associates, Inc, Flagstaff, Ariz), in the case of severe annular dilatation in growing children. This strip should be sutured to the posterior annulus using mattress sutures, extending a few millimeters over each trigon. Stitches placed on the annulus will unequally plicate different segments of the posterior annulus, especially at the level of each trigone and the level of P3 in LVOTO-related and ischemic MR. The Accuseal strip should be cut in a semicircular fashion, with a length corresponding to approximately two thirds of the Rowlatt table-based indexed annulus size. Additional resorbable polydioxanone annuloplasty sutures to allow further growth of the annulus at a distance from the surgery has also been occasionally used. Posterior annuloplasty was used in 50 patients (47%).
3. Complete annuloplasty, using a prosthetic ring, in the case of severe dilatation when a ≥28 mm prosthetic ring was suitable. The ring should

FIGURE 1. Age at surgery stratified by the number of patients.
Mechanisms of MR (Carpentier’s functional classification)

Preoperative cardiac functional status
- NYHA class III-IV: 106 (100)
- Preoperative LV dysfunction (EF < 50%): 24 (22)
- Preoperative artificial ventilation: 6 (6)
- Previous cardiac surgery in another hospital: 22 (21)

Mechanisms of MR (Carpenter’s functional classification)
- Type I, normal leaflet motion (isolated cleft): 47 (44)
- Type II, enhanced leaflet motion (isolated leaflet prolapse): 24 (23)
- Type III, restricted leaflet motion: 35 (33)
  - Restricted leaflet motion with normal papillary muscles: 27
  - Short chordae: 25
  - Thickened leaflets: 22
  - Fused commissures: 18
  - Papillary muscle-commissural fusion: 12
  - Accessory MV tissue: 7
  - Valvar ring: 1
  - Restricted leaflet motion with abnormal papillary muscles: 8
    - Papillary muscle hypoplasia: 4
    - Hammock valve: 3
    - Parachute valve: 1
    - Associated stenotic component: 12

MR etiology
- Congenital, other than isolated anterior mitral leaflet cleft: 37 (35)
- Isolated anterior mitral leaflet cleft: 15 (14)
- Rheumatismal: 13 (12)
- Left heart obstruction-related: 12 (11)
- Ischemic: 11 (10)
- Other
  - Marfan syndrome: 5
  - Endocarditis: 5
  - Iatrogenic: 5
  - Barlow disease: 2
  - Dilated cardiomyopathy: 1

Associated lesions addressed at procedure
- LVOTO: 9 (8)
- Anomalous left coronary artery from pulmonary artery: 9 (8)
- Atrial septal defect: 7 (7)
- Complex cyanotic cardiac defects: 7 (7)
- Tricuspid regurgitation: 6 (6)
- Aortic regurgitation: 6 (6)
- Other: 8 (8)
- Marfan syndrome: 5 (5)

Data presented as n (%), unless otherwise noted. NYHA, New York Heart Association; LV, left ventricular; EF, ejection fraction (Simpson); MR, mitral regurgitation; MV, mitral valve; LVOTO, LV outflow tract obstruction.
Kaplan-Meier estimates with 95% confidence intervals. Univariate analysis of time-related events was achieved using the log-rank test and the univariate Cox model, which allowed the selection of variables \( P < .10 \) for inclusion in the multivariate analysis. The multivariate analysis was performed using a logistic regression model to estimate the risk factors for recurrent MR and transmitral gradient and a Cox model to estimate the risk factors for MV reoperation, MV replacement, and mortality. The variables were included in the model by backward elimination if \( P < .05 \).

**RESULTS**

**Mortality, Reoperations, Replacements, and MV Functional Status**

Four patients underwent revision of the initial MV repair in the same anesthetic session after transesophageal echocardiography. Three in-hospital deaths (3%) occurred. A 10-month-old boy died of multiorgan failure after 1 MV repair for MV endocarditis. A newborn girl with severe congenital MR, severe LV dysfunction, and preoperative artificial ventilation died of low cardiac output after 2 attempts at MV repair. A 4-month-old boy initially had congenital stenosis of the main left coronary artery. He had undergone coronary artery bypass grafting at another institution but then presented with severe MR and LV dysfunction requiring 3 consecutive MV replacements. He finally died of prosthetic valve dysfunction.

At discharge, 4 patients had residual moderate-to-severe (grade III) MR; all others had no MR or grade I-II MR. Three patients required a definitive pacemaker because of associated non–MV-related surgical procedures. During the follow-up period, 24 patients (23%) underwent 31 MV reoperations (25 repairs and 6 replacements). The indications for MV reoperation were progressive MR \( (n = 16) \), progressive mitral stenosis \( (n = 4) \), severe valve-related hemolysis \( (n = 3) \), repair rupture \( (n = 2) \), late reopening of a mitral cleft \( (n = 2) \), endocarditis \( (n = 2) \), iatrogenic catheter-induced MV perforation \( (n = 1) \), and severe calcification of the anterior leaflet augmentation patch \( (n = 1) \). Six of these patients (6%) finally required MV replacement with 17-mm \( (n = 1) \), 19-mm \( (n = 1) \), 23-mm \( (n = 2) \), 25-mm \( (n = 1) \), or 29-mm \( (n = 1) \) mechanical prosthesis.

Two late heart-related deaths occurred. A 2-year-old girl with severe congenital MR underwent 2 MV repairs but finally required implantation of a mechanical prosthesis and died of valve thrombosis 1 year after MV replacement. A 12-month-old boy had had LVOTO-related MV disease. He had first undergone MV repair associated with aortic valvotomy. Four months later, he underwent a second MV repair associated with a complicated Ross procedure that required extracorporeal membrane oxygenation. He died of extracorporeal membrane oxygenation complications.

At the last follow-up visit, 15 patients (14%) had moderate MR and 3 had moderate-to-severe or severe MR. Five patients (4%) had a mean echocardiographic gradient > 10 mm Hg. All but 1 patient were New York Heart Association class I-II. Native valve preservation was obtained for 85% of the infants and 94% of those beyond infancy. The actuarial survival and actuarial

![FIGURE 2. Subtotal posterior leaflet augmentation, avoiding the “gutter” effect, and interrupted annuloplasty.](image-url)
freedom from MV reoperation and MV replacement according to MR etiology are presented in Figures 2 and 3. The actuarial survival, freedom from MV reoperation, and freedom from MV replacement rate was 93% ± 2% at 10 years (Figure 2, A), 67% ± 7% at 8 years (Figure 2, B), and 86% ± 7% at 10 years (Figure 3, A), respectively. An LVOTO-related MR etiology was significantly associated with decreased actuarial freedom from MV reoperation and replacement (log-rank, P < .001; Figures 3, C, and 4, B).

Outcomes and Etiologies

The outcomes according to the mechanism and etiology of MI are summarized in Table 2. A Carpentier classification type III MI mechanism was significantly associated with an increased risk of MV replacement (P = .02) and a postoperative transmitral mean echocardiographic gradient > 5 mm Hg (P = .02). An LVOTO-related MI etiology was statistically associated with MV reoperation (P < .001), MV replacement (P = .01), residual MI (P < .001), and a postoperative transmural mean echocardiographic gradient > 5 mm Hg (P = .005). In contrast, the presence of a mitral cleft seemed to be less prone to developing postoperative MR (P = .04).

Risk Analysis

The results of the univariate and multivariate analyses are presented in Table 3. An LVOTO-related etiology was an independent predictor of recurrent MR (odds ratio, 33; 95% confidence interval [CI], 1.2-956; P = .04), MV reoperation (hazard ratio [HR], 45; 95% CI, 3-624; P = .004), and MV replacement (HR, 30; 95% CI, 1.2-731; P = .03). The other independent predictors of MV reoperation were an associated preoperative transmural mean echocardiographic gradient > 5 mm Hg (HR, 21; 95% CI, 1.3-341; P = .03) and young age at surgery (HR, 1.21; 95% CI, 1.1-1.4; P = .04). The MR grade did not significantly increase the risk of MV reoperation. However, MV reoperation, MV replacement, and young age at surgery were significantly associated with an increased risk of mortality on univariate analysis (Table 3).

DISCUSSION

The surgical options for MR in children include MV repair and MV replacement with mechanical prostheses.
MV mechanical replacement in children has had numerous major drawbacks, including the absence of annular growth and the subsequent need for mitral reoperation, difficult management of anticoagulant therapy for children, a potential patient–prosthesis mismatch exposing patients to high early and late mortality in children, and the deleterious effect of a mechanical MV prosthesis on LV function. To avoid mechanical prostheses and their poor outcomes, we considered MV repair as the reference standard, aiming more for the restoration of a durable functional anatomy than a time gain. The “nothing else but repair” strategy was adopted and showed, usually at the cost of a considerable rate of reoperation, promising outcomes with a preserved native valve.

MV repair in children has been considered one of the least reproducible and most difficult to teach cardiac surgical procedures. This has been because of the high variability in MV anatomy, MV dysfunctional mechanisms, lesion etiology, the unavailability of prosthetic ring devices, and differing surgical indications and techniques. We have reported, through this relatively significant series, our repair-oriented strategy in a standardized manner for pedagogic purposes and reproducibility. The tools we have described, with their own indication, represent the true skeleton of the strategy supported by the reported outcomes. Improving the leaflet mobility through aggressive subvalvular apparatus debridement is of major importance and will determine the success of the repair in many cases. Annuloplasty, whose role is to segmentally reduce the dilated annulus, stabilize the repair, and differing surgical indications and techniques. We have reported, through this relatively significant series, our repair-oriented strategy in a standardized manner for pedagogic purposes and reproducibility. The tools we have described, with their own indication, represent the true skeleton of the strategy supported by the reported outcomes. Improving the leaflet mobility through aggressive subvalvular apparatus debridement is of major importance and will determine the success of the repair in many cases. Annuloplasty, whose role is to segmentally reduce the dilated annulus, stabilize the repair, and increase the height of the posterior leaflet coaptation surface area, seems mandatory for all MV repairs for MR, even in patients with an isolated mitral cleft. Pericardial patch augmentation of the leaflets had been demonstrated as a simple, safe, and efficient technique in MV reconstruction by Carpentier’s group, in both adult

### TABLE 3. Univariate and multivariate risk analyses for recurrent mitral regurgitation, transmitral gradient, reoperation, replacement, and mortality

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<thead>
<tr>
<th>Endpoint</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
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<tbody>
<tr>
<td>MR (grade II-III)</td>
<td>Left heart obstruction-related MR ($P &lt; .001$)</td>
<td>Left heart obstruction-related MR ($P = .04$; OR, 33; 95% CI, 1.2-956)</td>
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<td></td>
<td>Associated mitral cleft ($P = .04$) (protective factor*)</td>
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<td></td>
<td>Associated preoperative transmitral gradient $&gt; 5$ mm Hg ($P = .02$)</td>
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<td></td>
<td>Nonoptimal immediate result ($P = .01$)</td>
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<td></td>
<td>Young age ($P &lt; .001$)</td>
<td></td>
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<tr>
<td>Transmitral mean echocardiographic gradient $&gt; 5$ mm Hg</td>
<td>Left heart obstruction-related MR ($P = .005$)</td>
<td>None</td>
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<tr>
<td></td>
<td>Associated preoperative transmitral gradient $&gt; 5$ mm Hg ($P = .004$)</td>
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<td></td>
<td>Type III MR mechanism ($P = .02$)</td>
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<td>Nonoptimal immediate result ($P = .007$)</td>
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<td></td>
<td>Young age ($P &lt; .001$)</td>
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<td></td>
<td>Male gender ($P = .03$)</td>
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<td>MV replacement</td>
<td>Left heart obstruction-related MR ($P &lt; .001$)</td>
<td>Left heart obstruction-related MR ($P = .004$; HR, 45; 95% CI, 3-624)</td>
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<td></td>
<td>Nonoptimal immediate result ($P = .01$)</td>
<td>Associated preoperative transmitral gradient $&gt; 5$ mm Hg ($P = .03$; HR, 21; 95% CI, 1.3-341)</td>
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<tr>
<td></td>
<td>Young age ($P &lt; .001$)</td>
<td>Young age ($P = .04$; HR, 1.21; 95% CI, 1.1-1.4)</td>
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<tr>
<td>Mortality</td>
<td>Preoperative NYHA class ($P = .001$)</td>
<td>Left heart obstruction-related MR ($P = .03$; HR, 30; 95% CI, 1.2-731)</td>
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<tr>
<td></td>
<td>Papillary muscle hypoplasia ($P = .01$)</td>
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<td></td>
<td>Immediate postoperative severe MR ($P = .001$)</td>
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<tr>
<td></td>
<td>MV reoperation ($P = .03$)</td>
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<td></td>
<td>MV replacement ($P = .02$)</td>
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<td></td>
<td>Long stay in ICU ($P &lt; .001$)</td>
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<td></td>
<td>Young age ($P &lt; .001$)</td>
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MR, Mitral regurgitation; OR, odds ratio; CI, confidence interval; MV, mitral valve; HR, hazard ratio; NYHA, New York Heart Association; TMG, trans-mitral gradient; ICU, intensive care unit. *Isolated mitral cleft was a protective factor; all other factors were risk factors. |
and pediatric patients. In addition to increasing the leaflet surface and improving leaflet coaptation in patients with MR with valvular tissue lacking, this surgical technique also allows one to limit the need for excessive annular plication in young patients. In the beginning of our experience, posterior leaflet augmentation appeared to be more appropriate. However, the commissure-to-commissure enlargement of the posterior leaflet resulted in significant postoperative transvalvular gradients, particularly in younger patients. The cause of this complication was obviously the “gutter” effect created by the disappearance of both scallops of the posterior leaflet. Preservation of at least 1 (the anterior would seem to be more appropriate) of these would seem mandatory if the repair should include posterior leaflet augmentation. The patch used was almost always autologous pericardium. Glutaraldehyde treatment was performed in primary procedures, with fresh pericardium preferred in reoperations because of the fibrous thickening in the latter. In 2 patients, heterologous glutaraldehyde-treated pericardium was used because autologous pericardium was unavailable. The behavior of autologous pericardium as leaflet tissue was satisfactory in most patients; however, the anterior leaflet augmentation patch composed of glutaraldehyde-treated autologous pericardium led to significant fibrocalcifications requiring a reoperation in 1 of 23 patients (4%).

We have also demonstrated that young age at surgery was the main independent predictor of recurrent MR, and MV replacement. Other independent predictors of MV reoperation were associated preoperative mitral stenosis and young age at surgery. To our knowledge, only 1 previous study had tried to determine the multivariate risk factors for pejorative outcomes after MV repair in children. However, that study, which included 71 patients, only suggested that residual postoperative valvular dysfunction could lead to an increased risk of reoperation ($P = .07$).

In infants born with subaortic-aortic valvular stenosis, with or without aortic arch obstruction, MV dysfunction is not uncommon, resulting in a clinical and surgical challenge. The major pejorative role played by the LVOTO-related etiology of MR could be because the MR in this pathologic condition is only the marker of a global disease of the left heart. Even if the LVOTO has been treated surgically, the spontaneous evolution of the ventricular geometry would negatively affect the outcome of the MV repair: the deterioration of good early functional results at midterm follow-up was not uncommon. Nevertheless, we have continued to advocate the use of our strategy for this challenging subgroup in lieu of a more satisfactory alternative.

We have also demonstrated that young age at surgery was an independent predictor of MV reoperation. This finding has been suggested but not proved by previous studies.

**Study Limitations**

The major limitation of the present study was its retrospective design. The possible bias related to the effect of the surgical era on the evaluation of outcomes was very limited, because the surgical strategy was quite constant during the study period. The heterogeneity of the patients and their anatomic variants were taken into account in the multivariate risk analysis. A low cutoff of 5 mm Hg was chosen for evaluation of the transmitral mean echocardiographic gradient in the risk analysis to detect the risk factors for early postoperative mitral stenosis. The bias owing to a very small number of patients with extremely unfavorable anatomy and/or clinical condition who underwent valve replacement with poor outcomes should also be considered.

**CONCLUSIONS**

The present 3-step standardized and reproducible MV repair strategy achieved satisfactory functional results in infants and children with severe MR, avoiding MV replacement, but at the cost of reoperations. Mortality, MV reoperation, MV replacement, and recurrent MR rates at the last follow-up examination was 4%, 23%, 5%, and 17%, respectively. The actuarial survival and freedom from MV replacement was 93% ± 2% and 86% ± 7% at 10 years, respectively. An LVOTO-related etiology was the main independent predictor of recurrent MR, MV reoperation, and MV replacement. Other independent
predictors of MV reoperation were associated preoperative mitral stenosis and young age at surgery. Additional follow-up data appear mandatory, in particular to investigate the outcomes of the autologous pericardium substituting for the lacking leaflet tissue.

References