Mitral valve surgery for mitral regurgitation in patients with advanced dilated cardiomyopathy

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Key words:
Dilated cardiomyopathy; Mitral regurgitation; Mitral valve surgery.

Background. **Unfortunately, mitral valve surgery for mitral regurgitation (MR) in patients with advanced dilated cardiomyopathy is generally associated with a high operative risk and a poor outcome. Some authors believe that only heart transplantation is the really effective surgical treatment. We analyzed our clinical and echocardiographic results after mitral repair or replacement in this difficult subset of patients.**

Methods. **From September 1998 to May 2001, 24 consecutive patients (mean age 65.7 ± 11.0 years) with MR > 2+ and advanced dilated cardiomyopathy (left ventricular ejection fraction < 0.35) underwent mitral repair (n = 11) or replacement (n = 13). The cause of left ventricular dysfunction was ischemic in 17 patients and idiopathic in 7. Myocardial revascularization was performed in all patients with ischemic disease. NYHA functional class IV was present in 21 patients (87.5%) and urgent surgical priority in 14 (58.3%). The mean follow-up was 26.7 ± 11.8 months.**

Results. **One patient died (4.2%) of myocardial infarction 5 days after operation. The mean hospital stay was 10.6 ± 3.7 days. During follow-up, two deaths (8.7%) due to heart failure occurred. In survivors, NYHA functional class improved from 3.9 ± 0.4 preoperatively to 2.2 ± 0.4 at follow-up (p = 0.0037) and left ventricular ejection fraction from 0.24 ± 0.05 to 0.30 ± 0.05 (p = 0.0035) in patients with ischemic dilated cardiomyopathy, and from 0.23 ± 0.04 to 0.26 ± 0.05 (p = NS) in patients with idiopathic dilated cardiomyopathy.**

Conclusions. **Mitral surgery in advanced left ventricular dysfunction can be accomplished with an acceptable operative risk. It offers a durable functional improvement. In ischemic dilated cardiomyopathy concomitant myocardial revascularization procures a significant amelioration in the left ventricular performance as evaluated at echocardiography.**

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Introduction

Dilated cardiomyopathy is the most common cause of the clinical syndrome of chronic heart failure. Because of its high prevalence (1.0 to 1.5% of the adult population) and morbidity, chronic heart failure is among the most costly health problems in developed countries. Despite improvements in the treatment of heart failure introduced in the last 10 years, including the widespread availability of heart transplantation and better medical treatment (use of angiotensin-converting enzyme inhibitors and beta-adrenergic blocking agents), the clinical outcome has not changed substantially[1,2].

In patients with dilated cardiomyopathy, functional mitral regurgitation (MR), i.e. secondary to left ventricular dilation and dysfunction, is a frequent serious complication that makes the prognosis worse, causing more frequent and more severe episodes of congestive heart failure[3]. The appropriate management of these patients is controversial[4-8].

We analyzed our more recent experience in the surgical correction of functional MR in severe left ventricular dilation and dysfunction. The aim of this study was to present the clinical and echocardiographic results of our patient-adjusted surgical strategy for the management of functional MR in a selected subset of high-risk patients with dilated cardiomyopathy.

Methods

Study patients. From September 1998 to May 2001, 24 consecutive patients with severe MR and advanced dilated cardiomyopathy underwent primary mitral valve surgery at our Department.

The inclusion echocardiographic criteria were: functional MR > 2+, left ventricular ejection fraction (LVEF) < 0.35, left ventricular end-diastolic diameter > 30 mm/m^2, and left ventricular end-diastolic volume > 100 ml/m^2. Since one objective of this study was to examine the impact of

the correction of MR with or without myocardial revascularization on the left ventricular dimensions and function, the study population was further refined excluding those patients who were submitted to concomitant aortic valve surgery or left ventricular remodeling operations. On the other hand, those patients who were submitted to concomitant tricuspid valve repair or ascending aorta replacement were retained.

The mean age of the patients at the time of operation was 65.7 ± 11.0 years (20 to 76 years). Six patients (25.0%) were female.

On the basis of both the preoperative echocardiographic examinations and of the operative findings, it was determined that the etiology of functional MR was ischemic in 17 patients (70.8%) and secondary to an idiopathic dilated cardiomyopathy in 7 (29.2%). All patients with ischemic MR had a history of remote myocardial infarction; 3 patients had had previous coronary artery bypass grafting and 2 previous percutaneous transluminal coronary angioplasty.

In all patients MR was the result of severe global left ventricular dilation and dysfunction, with or without regional left ventricular wall motion abnormalities and/or a restricted leaflet motion. The mitral valves were structurally normal.

All patients had severe ongoing symptoms of dyspnea, edema and fatigue on minimal exertion (NYHA functional class III, 3 patients – 12.5%) or at rest (NYHA functional class IV, 21 patients – 87.5%). All patients were receiving maximized medical therapy for chronic heart failure, including angiotensin-converting enzyme inhibitors, diuretics, and beta-adrenergic blocking agents. Seven patients (29.2%) were initially referred in order to be evaluated for heart transplantation. Fourteen patients (58.3%) were operated on an urgent basis: 13 after decompensated episodes of heart failure and 1 for refractory ventricular tachycardia; among these, a preoperative intra-aortic balloon pump was used in 7 (29.2%) ischemic patients.

The preoperative heart rhythm was atrial fibrillation in 14 patients (58.3%) and sinus rhythm in 9 (37.5%); 1 patient (4.2%) was on permanent pacing. Three patients had a preoperative history of ventricular tachycardia or fibrillation, with one requiring the placement of an internal cardioverter-defibrillator.

The operative risk was evaluated according to the European System for Cardiac Operative Risk Evaluation (EuroSCORE). The EuroSCORE was 8.5 ± 3.4 (95% confidence interval for the expected mortality, 10.93 to 11.54%)[9].

Echocardiographic examination. All preoperative and postoperative echocardiographic transthoracic examinations were performed at our Department by one experienced observer, with preoperative examinations within 1 month of surgery.

The measurements of the left ventricular dimensions were determined on the basis of two-dimensional echocardiographic images taken in the parasternal long-axis view at M-mode echocardiography. The left ventricular volumes were calculated by using a modification of the Simpson's method with two apical views. The left ventricular stroke volume was calculated as the difference between the left ventricular end-diastolic volume and the left ventricular end-systolic volume, and the LVEF was calculated as the ratio of the left ventricular stroke volume to the left ventricular end-diastolic volume. Mitral and tricuspid regurgitation were assessed with color flow Doppler; the severity was graded as mild (1+), moderate (2+), moderate-severe (3+), and severe (4+). Eighteen (75.0%) patients had 4+ and 6 (25.0%) patients 3+ MR. Mean MR for the 24 patients was 3.7 ± 0.5. In the presence of trivial to severe tricuspid valve regurgitation, the systolic pulmonary artery pressure was calculated at Doppler echocardiography[10] (Table I).

In all patients with ischemic dilated cardiomyopathy, preoperative echocardiography during infusion of dobutamine was used in order to determine myocardial viability[11].

Surgical techniques. Mitral valve repair was performed in all patients with idiopathic dilated cardiomyopathy and in the 5 patients with ischemic dilated cardiomyopathy and myocardial viability in the infero-lateral segments. All repairs were carried out according to the Bolling undersized annuloplasty technique[12], using the Cosgrove-Edwards band (Edwards Lifesciences, Irvine, CA, USA) as an annuloplasty system[13]. Conventional mitral valve replacement was adopted in the patients with ischemic dilated cardiomyopathy without myocardial viability in the infero-lateral segments.

Myocardial revascularization was performed in all patients with ischemic heart dysfunction, with a mean number of grafts per patient of 2.1. Concomitant tricuspid valve repair was performed in 3 (12.5%) patients and ascending aorta replacement in 1 patient.

Table I. Preoperative echocardiographic data.

	Mean ± SD	Range
Mitral regurgitation	3.7 ± 0.5	3+-4+
Left ventricle		
End-diastolic diameter (mm/m^2)	40.9 ± 4.0	32.1-47.6
End-diastolic volume (ml/m^2)	148.6 ± 21.6	100.5-195.4
End-systolic diameter (mm/m^2)	36.3 ± 3.7	27.6-42.1
End-systolic volume (ml/m^2)	113.5 ± 19.2	72.1-162.5
Ejection fraction	0.24 ± 0.05	0.13-0.32
Stroke volume (ml/m^2)	34.7 ± 7.4	17.5-46.2
Left atrium		
Transversal diameter (mm/m^2)	29.2 ± 5.6	19.7-40.1
Tricuspid regurgitation	1.0 ± 0.6	0-3+
Right ventricle/Pulmonary artery		
Systolic pulmonary artery pressure (mmHg)*	44.4 ± 8.9	31-65

* in the 21 (87.5%) patients with trivial to severe combined tricuspid valve regurgitation.

A median sternotomy was always the surgical approach used. Normothermic cardiopulmonary bypass with crystalloid priming and antegrade cold blood cardioplegia were used. The mean duration of cardiopulmonary bypass was 105.4 ± 39.3 min (45 to 180 min), with a mean aortic cross-clamping time of 62.6 ± 39.3 min (24 to 109 min).

Follow-up. Complete follow-up information was available in all 23 hospital survivors. Patients were followed up for a total of 46.7 patient-years, with a mean follow-up among survivors of 26.7 ± 11.8 months, ranging from 13.9 to 45.7 months. All cases of postoperative hospital readmission for congestive heart failure as well as the date and cause of death were documented.

Statistical analysis. All data are expressed as the mean ± SD or as percentage. The echocardiographic measurements of the left ventricular dimensions were normalized for the patient body surface area. Paired Student's t-tests were used for comparison of the preoperative and postoperative echocardiographic data. The postoperative change in NYHA functional class was assessed by means of the sign rank test. Because of the small sample size, statistical significance was assumed for a p value < 0.01. Non-parametric estimates of survival and freedom from hospital readmission for heart failure were obtained by the Kaplan-Meier method. Statistical analysis was performed using the MINITAB release 13 statistical software (MINITAB Inc., State College, PA, USA).

Results

In-hospital mortality and morbidity. All patients survived the procedure and were weaned off cardiopulmonary bypass with moderate doses of inotropes. One patient (4.2%) died of myocardial infarction with low cardiac output syndrome 5 days after mitral repair and myocardial revascularization. Significant morbidity was observed in 5 patients (20.8%). The mean length of hospital stay was 10.6 ± 3.7 days (6 to 18 days) (Table II).

Survival. Two late deaths (8.7%) occurred during follow-up, for an over 3.5-year actuarial survival of 78.3%. Heart failure was the cause of death in both patients (one patient was afflicted with an advanced malignant disease) (Fig. 1).

Freedom from hospital readmission for heart failure. Freedom from hospital readmission for heart failure occurred in 19 patients (82.6%), for an over 3.5-year actuarial rate of 71.1% (Fig. 2).

NYHA functional class. For all the 21 survivors, the NYHA functional class improved from 3.9 ± 0.4 preoperatively to 2.2 ± 0.4 at follow-up (p = 0.0037) (Fig. 3).

In the 15 survivors with ischemic dilated cardiomyopathy, the NYHA functional class improved from 3.9 ± 0.3 to 2.3 ± 0.6 (p = 0.0070). In the 6 survivors with idiopathic dilated cardiomyopathy, the NYHA func-

Table II. In-hospital outcome.

Outcome	No.
Atrial fibrillation	6/9* (66.7%)
Bleeding requiring re-exploration of the chest	2 (8.3%)
Re-intubation and re-admission to the intensive care unit because of respiratory problems	1 (4.2%)
Myocardial infarction	1 (4.2%)
Postoperative creatinine concentration > 2.0 mg/dl	1 (4.2%)

* patients with preoperative sinus rhythm.

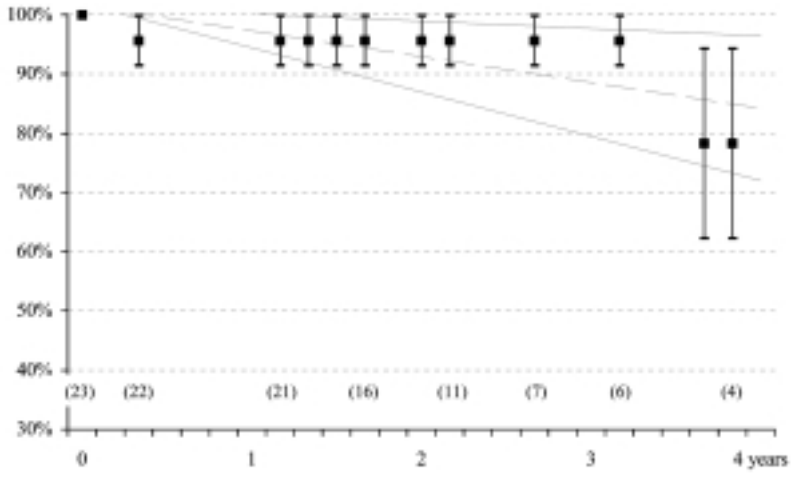

Figure 1. *Survival. The* squares *correspond to the non-parametric estimates of survival. The* vertical bars *correspond to the asymmetric confidence limits equivalent to one standard error. Trend lines are also shown. The number of patients remaining at risk at various intervals is in parenthesis.*

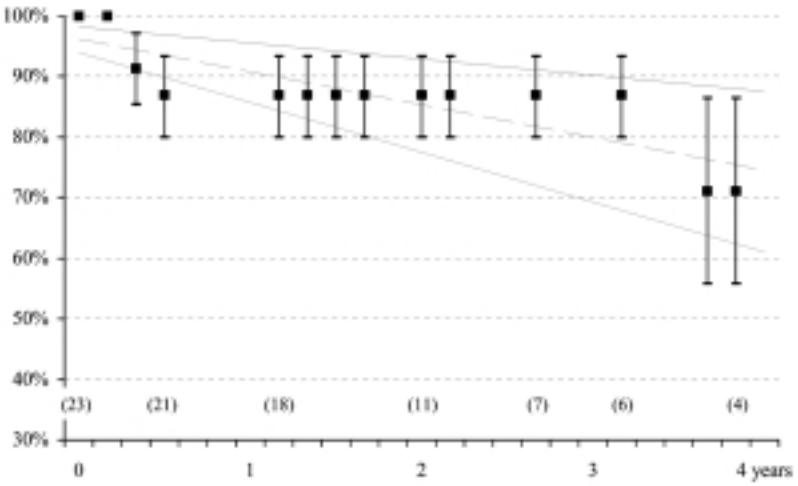

Figure 2. *Hospital readmission for heart failure. The* squares *correspond to the non-parametric estimates of hospital readmission for heart failure. The* vertical bars *correspond to the asymmetric confidence limits equivalent to one standard error. Trend lines are also shown. The number of patients remaining at risk at various intervals is in parenthesis.*

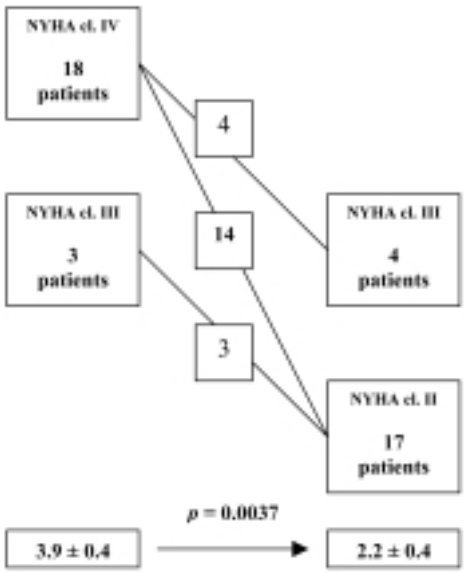

Figure 3. *Change in the NYHA functional class in the 21 survivors at follow-up. The NYHA functional class decreased in all patients.*

tional class improved from 3.8 ± 0.4 to 2.2 ± 0.4 (p = 0.0022).

The decrease in NYHA functional class was more evident when reconstructive mitral valve surgery was used: 3.9 ± 0.3 to 2.3 ± 0.5 in mitral repair (p = 0.00012) vs 3.8 ± 0.4 to 2.4 ± 0.6 in mitral valve replacement (p = 0.0074).

Echocardiographic follow-up. Echocardiography was performed in all 21 survivors. These were compared with the matched preoperative echocardiographic examinations. MR improved from 3.7 ± 0.5 preoperatively to 0.8 ± 0.8 at follow-up (p = 0.0059). The decrease in left ventricular end-systolic volume was greater than that in left ventricular end-diastolic volume; this resulted in a significant increase in left ventricular stroke volume (p = 0.0057) and in LVEF (p = 0.0029). The left atrial transversal diameter and the systolic pulmonary artery pressure decreased, but not significantly (Table III).

These results were confirmed in the 15 survivors with ischemic dilated cardiomyopathy: LVEF improved from 0.24 ± 0.05 to 0.30 ± 0.05 (p = 0.0035). In the 6 survivors with idiopathic dilated cardiomyopathy, although there was a significant improvement in the NYHA functional class, mitral valve repair procured a slight and not significant increase in left ventricular stroke volume and LVEF (from 0.23 ± 0.04 to 0.26 ± 0.05, p = 0.095).

Obviously, mitral valve replacement completely resolved the MR. In 3 patients who underwent mitral valve repair, the residual MR was mild in one, moderate in the second and moderate-severe in the third. However, there were no important differences in the echocardiographic changes in the survivors who underwent mitral repair versus those who underwent mitral replacement.

Discussion

The frequent onset of functional MR in dilated cardiomyopathy aggravates left ventricular volume overload, contributes to the symptoms of congestive heart failure and is associated with a poor prognosis[3].

In the past, patients with advanced dilated cardiomyopathy complicated by severe functional MR were not considered candidates for conventional mitral valve surgery because of the prohibitive operative mortality[4]. Heart transplantation was the standard treatment for this subset of patients. However, besides a shortage of donor hearts, the outcome in heart transplantation is

Table III. Changes in echocardiographic data in the 21 survivors.

	Preoperative	Postoperative	p
Mitral regurgitation	3.7 ± 0.5	0.8 ± 0.8	0.0059
Left ventricle			
End-diastolic diameter (mm/m^2)	40.7 ± 4.1	40.3 ± 4.3	0.79
End-diastolic volume (ml/m^2)	147.7 ± 22.6	144.9 ± 24.2	0.70
End-systolic diameter (mm/m^2)	36.1 ± 3.8	34.8 ± 4.3	0.31
End-systolic volume (ml/m^2)	112.5 ± 20.4	103.9 ± 23.1	0.21
Stroke volume (ml/m^2)	35.2 ± 7.2	41.0 ± 5.7	0.0057
Ejection fraction	0.24 ± 0.05	0.29 ± 0.05	0.0029
Left atrium			
Transversal diameter (mm/m^2)	29.5 ± 5.6	28.5 ± 4.6	0.52
Tricuspid regurgitation	1.0 ± 0.6	0.5 ± 0.5	0.0011
Right ventricle/pulmonary artery			
Systolic pulmonary artery pressure (mmHg)*	42.6 ± 7.7	36.4 ± 7.0	0.059

* in the 15 patients with trivial to moderate postoperative residual tricuspid regurgitation.

limited by the serious consequences of immunosuppression and by transplant coronary artery disease.

In an effort to address this problem, newer and alternative mitral valve surgical approaches such as the Bolling undersized mitral annuloplasty[12] and mitral subvalvar apparatus preserving techniques of mitral replacement are being investigated[14]. Furthermore, emerging left ventricular remodeling techniques, such as the Batista[15] and the Dor[16] procedures often employ mitral surgery as an integral part of the treatment of MR associated with dilated cardiomyopathy. When these operative techniques which improve the left ventricular geometry are utilized (always in combination with optimal medical management), the survival is acceptable and patients can postpone or quite often even avoid transplantation.

However, the choice of the treatment for the patient with severe MR and advanced dilated cardiomyopathy remains controversial[4-8]. Part of this controversy arises from the difficulty encountered when characterizing the left ventricular function in the setting of MR. The favorable unloading effect of the regurgitation into the left atrium on the left ventricular work must be taken into consideration. Hence, virtually all measurements of left ventricular function, including the LVEF, tend to overestimate the true level of ventricular performance[17]. Despite this, the LVEF is one of the most important predictors of the outcome after mitral valve surgery for MR, especially in case of left ventricular dysfunction: patients with a moderately to severely reduced LVEF are at considerable risk[18].

In this study, the cause of left ventricular dysfunction and secondary MR was ischemic or idiopathic. According to the literature, the mortality associated with mitral surgery for ischemic MR is higher than for other forms of MR, particularly when regurgitation is due to left ventricular impairment; the presence of MR in patients with idiopathic dilated cardiomyopathy is a marker of a poor prognosis. Therefore, the patients of this study represent a high-predicted-mortality population. However, all patients survived the surgical procedure, with only one hospital death in the group of patients with ischemic dilated cardiomyopathy. The over 3.5-year survival and the freedom from hospital readmission for congestive heart failure were good. The NYHA functional class decreased in all survivors. Its decrease after mitral repair was greater than that observed after mitral replacement. The echocardiographic data improved both after mitral repair and after mitral replacement regardless of whether the etiology of the dilated cardiomyopathy was ischemic or idiopathic. The increase in left ventricular performance in ischemic dilated cardiomyopathy was greater (and significantly so) than that observed for idiopathic dilated cardiomyopathy. The significant increase in the left ventricular stroke volume and LVEF in patients with ischemic dilated cardiomyopathy may be secondary both to the surgical correction of MR (regardless of whether mitral repair or mitral replacement was performed) and to the myocardial revascularization. This finding confirms the usefulness of echocardiography during infusion of dobutamine for the detection of reversible ischemic myocardial dysfunction. The lack of significant change in the left ventricular function in patients with idiopathic dilated cardiomyopathy after mitral valve repair could depend on a preoperative overestimation of the LVEF secondary to MR. In effect, there was a significant symptomatic improvement that is notoriously more sensitive than the variations in the echocardiographic measurements. Moreover, the persistence of residual MR could have contributed to slow down the regression in left ventricular dilation.

Study limitations. The main limitation of this study is that the number of patients is small. For this reason, great care must be employed when interpreting the results. Because deaths and cases of hospital readmission for heart failure were rare, it was impossible to identify their risk factors.

This series included patients undergoing mitral surgery in association with myocardial revascularize-

tion. If myocardial revascularization is simultaneously performed, it is hard to resolve whether the improvement in dimensions and function is due to the reperfusion of the ischemic myocardium or to the correction of the left ventricular volume overload. However, the primary objective of this study was to verify whether mitral surgery in advanced dilated cardiomyopathy can achieve good results and whether it may constitute an effective surgical alternative to transplantation.

In all the patients of our study, mitral surgery was performed for moderate-severe or severe MR only. In moderate MR, the indication for mitral surgery is debatable: the benefits are uncertain, but the operative risk is certainly high.

The echocardiographic measurements used could be too simple and insufficient for the identification of small changes in the left ventricular function in advanced dilated cardiomyopathy. Furthermore, the left ventricular end-diastolic diameter and volume are load-dependent and changes in arterial or filling pressure could confound the data.

References

1. Massie BM, Shah NB. The heart failure epidemic: magnitude of the problem and potential mitigating approaches. Curr Opin Cardiol 1996; 11: 221-6.
2. Sharpe N, Doughty R. Epidemiology of heart failure and ventricular dysfunction. Lancet 1998; 352: S13-S17.
3. Kono T, Sabbah HN, Rosman H, et al. Left ventricular shape is the primary determinant of functional mitral regurgitation in heart failure. J Am Coll Cardiol 1992; 20: 1594-8.
4. Rothlin ME. Severe mitral regurgitation with ejection fraction below 40%: pharmacological therapy is the treatment of choice. Schweiz Med Wochenschr 1997; 127: 2035-9.
5. Calafiore AM, Gallina S, Di Mauro M, et al. Mitral valve procedure in dilated cardiomyopathy: repair or replacement? Ann Thorac Surg 2001; 71: 1146-52.
6. Calafiore AM, Gallina S, Contini M, et al. Surgical treatment of dilated cardiomyopathy with conventional techniques. Eur J Cardiothorac Surg 1999; 16: S73-S78.
7. Bishay ES, McCarthy PM, Cosgrove DM, et al. Mitral valve surgery in patients with severe left ventricular dysfunction. Eur J Cardiothorac Surg 2000; 17: 213-21.
8. Cope JT, Kaza AK, Reade CC, et al. A cost comparison of heart transplantation versus alternative operations for cardiomyopathy. Ann Thorac Surg 2001; 72: 1298-305.
9. Nashef SAM, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R. European system for cardiac operative risk evaluation (EuroSCORE). Eur J Cardiothorac Surg 1999, 16: 9-13.
10. Weyman AE. Principles and practice of echocardiography, Philadelphia, PA: Lea & Febiger, 1994: 575-624.
11. La Canna G, Alfieri O, Giubbini R, Gargano M, Ferrari R, Visioli O. Echocardiography during infusion of dobutamine for identification of reversibly dysfunction in patients with chronic coronary artery disease. J Am Coll Cardiol 1994; 23: 617-26.
12. Badwar V, Bolling SF. Mitral valve surgery in the patient with left ventricular dysfunction. Semin Thorac Cardiovasc Surg 2002; 14: 133-6.
13. Gillinov AM, Cosgrove DM III, Shiota T, et al. Cosgrove-Edwards annuloplasty system: midterm results. Ann Thorac Surg 2000; 69: 717-21.
14. Rozich JD, Carabello BA, Usher BW, Kratz JM, Bell AE, Zile MR. Mitral valve replacement with and without chordal preservation in patients with chronic mitral regurgitation: mechanisms for differences in postoperative ejection performance. Circulation 1992, 86: 1718-26.
15. Batista RJ, Verde J, Nery P, et al. Partial left ventriculectomy to treat end-stage heart disease. Ann Thorac Surg 1997; 64: 634-8.
16. Dor V. Left ventricular aneurysms: the endoventricular circular patch plasty. Semin Thorac Cardiovasc Surg 1997; 9: 123-30.
17. Cohn JN, Johnson GR, Shabetai R, et al, for the V-HeFT VA Cooperative Studies Group. Ejection fraction peak exercise oxygen consumption, cardiothoracic ratio, ventricular arrhythmias, and plasma norepinephrine as determinants of prognosis in heart failure. Circulation 1993; 87: VI5-VI16.
18. Enriquez-Sarano M, Tajik AJ, Schaff HV, Orszulak TA, Bailey KR, Frye RL. Echocardiographic prediction of survival after surgical correction of organic mitral regurgitation. Circulation 1994; 90: 830-7.