Non-pharmacological heart failure therapies : evaluation by ventricular pressure-volume loops

Tulner, Sven Arjen Friso

CHAPTER 11

Sustained left ventricular reverse remodeling, improved systolic function and unchanged diastolic function six months after surgical ventricular restoration
-Analysis by pressure-volume loops-

S.A.F. Tulner
P. Steendijk
J.J. Bax
R.J.M. Klautz
J.W. Jukema
D.E. Atsma
H.F. Verwey
M.J. Schalij
R.A.E. Dion
E.E. van der Wall

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ABSTRACT

Background. Previous studies have demonstrated that surgical ventricular restoration (SVR) has acute beneficial effects on mechanical dyssynchrony and left ventricular (LV) systolic function. However, chronic effects on systolic and diastolic function are largely unknown.

Methods. We studied 8 patients with ischemic dilated cardiomyopathy who underwent SVR, restrictive mitral annuloplasty and coronary artery bypass grafting. In all patients, invasive hemodynamic measurements by the conductance catheter were performed before and six months after surgery. In addition, NYHA classification, six-minute walk-test, Minnesota Living with Heart failure questionnaire were assessed at the same time-points.

Results. At six months follow-up, all patients were alive and clinically improved significantly (NYHA from 3.6±0.5 to 1.5±0.5, Minnesota-score from 45±23 to 16±16, and six-minute walking distance from 300±133 to 442±89 m). Hemodynamic data showed significantly improved LV ejection fraction (from 31±8 to 40±14%), LV reverse remodeling (end-diastolic volume from 214±57 to 173±46 mL, end-systolic volume from 146±46 to 100±41 mL), and significantly improved intrinsic systolic function (end-systolic elastance from 0.98±0.31 to 1.51±0.82 mmHg/mL). In addition, mechanical efficiency significantly improved (0.40±0.12 to 0.55±0.13) with significant reduction of mechanical dyssynchrony (30±4 to 26±3%). However, parameters of diastolic function were unchanged six months after surgery (end-diastolic pressure: 20±9 to 18±7 mmHg; dP/dt_{MIN}: -1149±233 to –1189±307 mmHg/s; tau: 80±14 to 81±17 ms; chamber stiffness constant: 0.097±0.037 to 0.104±0.037 mmHg/mL).

Conclusion. Surgical ventricular restoration leads to clinical improvement with sustained LV reverse remodeling, improved global and intrinsic systolic function and unchanged diastolic function. The improved clinical status after six months may be related to improved mechanical efficiency, intrinsic systolic function and reduced mechanical dyssynchrony.

INTRODUCTION

Chronic heart failure is one of the leading causes of morbidity and mortality in the Western world.[1] In the majority of cases, the etiology in these patients is ischemic heart disease. More specific in patients after anteroseptal infarction, left ventricular (LV) aneurysm is a frequently observed complication. It leads to ineffective wall motion during the cardiac cycle and LV geometric shape changes resulting in inefficient LV pump function and adverse effects on remote myocardium.[2] These changes will increase the systolic workload in the remote myocardium, which may contribute to progressive heart failure.[3] Despite optimal medical treatment, patients with LV aneurysm often remain symptomatic and surgery may be indicated. Surgical ventricular restoration (SVR) by endoventricular circular patch plasty is increasingly performed in these patients. This technique can exclude akinetic or dyskinetic portions of the anterior wall and septum, reshapes the LV by the use of a patch to re-establishes the ventricular wall continuity.[4] Long-term studies have been demonstrated that SVR is safe and highly effective in the treatment of ischemic cardiomyopathy with reduction of end-systolic volume and favorable five-year outcome.[5]

Currently, little is known about the mechanisms of SVR on long-term LV systolic and diastolic function. Recent hemodynamic studies have demonstrated that SVR acutely reduces LV mechanical dyssynchrony with acute improvement of intrinsic LV systolic function.[6,7] In these studies, no data is available about the acute effects on diastolic function while some studies suggest that SVR may induce diastolic dysfunction.[8,9] Furthermore, limited data are available regarding chronic hemodynamic effects of SVR on LV function. Therefore, the purpose of this study is to evaluate these effects by use of invasive hemodynamic measurements derived by the conductance catheter before and six months after surgery.

METHODS

Patients

In this study we included 8 patients with ischemic dilated cardiomyopathy (NYHA class III/IV, LVEF < 35%) who underwent SVR. All patients underwent restrictive mitral annuloplasty for at least moderate to severe mitral regurgitation (grade ≥ 2) and all underwent additional CABG. All patients received stable medical therapy for chronic

heart failure, including diuretics (n=7), spironolactone (n=5), β-blockers (n=6), and ACE inhibitors (n=6). All patients gave informed consent and procedures were conducted in accordance with institutional guidelines. Patient characteristics are summarized in table 1.

Table 1. Patient characteristics

Number of patients (n)	8
Male / Female	6/2
Age (years)	62±7
NYHA class	3.6± 0.5
LVEF (%)	27±8
Angina (n)	5
Mean stenosed coronary arteries	2.3±0.9
Duration of symptoms (median, months)	8 (2-14)
Post-MI time (median, months)	3 (8-144)

NYHA: New York Heart Association, MI: myocardial infarction

Study protocol

All patients underwent routine right and left heart catheterization at baseline (i.e. pre-surgery) and six months after surgery, including thermodilution cardiac output, left ventriculography, and coronary angiography. In addition, a conductance catheter was placed in the LV via the femoral artery, and a temporary pacing lead was positioned in the right atrium.

Hemodynamic measurements. The conductance catheter enables on-line measurement of multiple segmental volume slices perpendicular to the LV long axis. We used 7F combined pressure-conductance catheters with 1-cm interelectrode spacing (CD Leycom, Zoetermeer, The Netherlands). The catheter was connected to a Cardiac Function Lab (CD Leycom) for on-line display and acquisition (sample frequency 250Hz) of segmental and total LV volumes, LV pressure and ECG. Total LV volume (V_{LV}) is obtained as the instantaneous sum of the segmental volumes. V_{LV} was calibrated using thermodilution and hypertonic saline dilution as previously described.[10] Right atrial pacing was performed at 80 beats/min. All measurements were repeated during re-catheterization at least six months after surgery.

Clinical evaluation. Evaluation of clinical status included assessment of NYHA functional class, quality-of-life score (using the Minnesota quality-of-life questionnaire) and six-minute hall-walk test.

Echocardiography. In patients with moderate to severe mitral regurgitation (grade ≥2) on transthoracic echocardiography (TTE), additional transesophageal echocardiography (TEE) was performed within 5 days before surgery. The TTE and TEE were performed without general anesthesia to avoid underestimation of the severity of mitral regurgitation. The severity of mitral regurgitation was graded semi-quantitatively from color-flow Doppler in the conventional parasternal long-axis and apical 4-chamber images.[11,12] When the severity of mitral regurgitation was less than 3+, a loading test (as described previously[13,14]) was performed during anesthesia just before surgery. During these provocative tests, the severity of mitral regurgitation is followed, and patients who deteriorate to grade 3 or 4+ mitral regurgitation underwent restrictive mitral annuloplasty. Immediately after surgery, TEE was repeated to assess residual mitral regurgitation, transmitral diastolic gradient (determined from continuous-wave Doppler), and length of coaptation of the mitral leaflets (ideally ≥ 8 mm). Six months after surgery, TTE was performed to assess the severity of mitral regurgitation. All TTE measurements were analyzed in random order by two independent observers without knowledge of the clinical status of the patient and the timing of the echocardiogram.

Surgical procedures

SVR was performed by the endoventricular circular patch plasty as previously described by Dor.[4,15] Briefly, the left ventricle was opened through the infarcted area. An endocardial encircling suture (Fontan Stitch) was placed at the transitional zone between scarred and normal tissue. A balloon containing 55mL/m^2 body surface area saline was introduced into the LV and the Fontan stitch was tightened to approximate the ventricular wall to the balloon. An oval dacron patch was tailored and used to close the residual orifice. The excluded scar tissue was closed over the patch to ensure hemostasis. Care was taken to eliminate all septal scar and to delineate a new LV apex with the goal to restore the normal elliptical shape. After completion of the LV restoration, a stringent restrictive mitral annuloplasty (2 sizes smaller than measured) was performed in these patients via an atrial transseptal approach using a Carpentier Edwards Physio ring (Edwards Lifesciences, USA).

Data-analysis

LV function was quantified by cardiac output (CO), LV ejection fraction (LVEF) and stroke volume (SV), end-diastolic and end-systolic volume (EDV, ESV), end-systolic and end-diastolic pressure (ESP, EDP), maximal and minimal rate of LV pressure change (dP/dt_{MAX}, dP/dt_{MIN}). The time constant of relaxation (τ) was determined using phase-plot analysis.[16] Stroke work (SW) was calculated as the area of the pressure-volume loop. Mechanical efficiency (ME) was calculated as the ratio of external stroke work and pressure-volume area (PVA) as a measure of total mechanical work: ME=SW/PVA[17]. LV end-systolic elastance (Ees) was estimated by ESP/ESV as relatively load-independent indexes of systolic function. LV end-diastolic chamber stiffness (CS) was estimated by EDP/EDV to characterize passive late diastolic function. Nonuniform LV performance was determined from the segmental LV conductance signals and quantified by calculating the percentage of time within the cardiac cycle that a specific segment is dyssynchronous (i.e. opposite in phase with the global LV volume signal). Overall LV dyssynchrony (DYS) was determined as the mean of the segmental dyssynchronies. In addition, we calculated the internal flow fraction (IFF), which quantifies the ineffective shifting of blood volume within the LV due to nonuniform contraction and filling[18].

Statistics

Pre- and post data were compared with paired t-tests. Statistical significance was assumed at $p < 0.05$. All data are presented as the mean value ± SD.

RESULTS

There were no peri-operative or hospital deaths and all patients were alive at six months follow-up. After surgery, two patients needed intra-aortic balloon pump to wean from cardiopulmonary bypass and six patients needed inotropic support (dobutamine > 2 µg/kg/min) more than 24 hours postoperatively. Immediate after surgery, transesophageal echocardiography was performed and showed restored leaflet coaptation with no residual mitral regurgitation. Surgical details are summarized in table 2.

Table 2. Surgical data

CPB (minutes)	228±46
Aox (minutes)	155±29
Number of distal anastomosis	3±1
Ring size	25± 1
Pre-operative TEE	
-MR-grade	2.5± 0.9
-AML (cm)	2.88± 0.11
-MA (cm)	3.81± 0.64
-MA/AML-ratio	1.32± 0.22
-Coaptation	0.21±0.07
Post-operative TEE	
-MR-grade	0.1±0.4
-Coaptation (cm)	0.78±0.13
-MV-gradient (mmHg)	2.57±1.02
ICU-stay (days)	5±2
Hospital stay (days)	16±5

CPB, Cardiopulmonary bypass; AoX, Aortic cross clamping time; TEE, Transesophageal echocardiography; MR, Mitral regurgitation; AML, Anterior mitral leaflet; MA, Mitral annulus MV, Mitral valve; ICU: Intensive care unit

Clinical and hemodynamic data. Clinical parameters as NYHA functional class, quality-of-life score (using the Minnesota quality-of-life questionnaire) and 6-minute hall-walk test significantly improved from baseline to six months follow-up (Table 3). QRS duration was unchanged and mitral valve repair was successful in all cases with no recurrence of mitral regurgitation at six months follow-up.

The chronic effects of surgery on LV function are summarized in detail in table 3. LVEF improved significantly, whereas EDV and ESV were significantly reduced at six months follow-up, indicating substantial reversed remodeling. Stroke volume was unchanged at six months follow-up. Improved intrinsic systolic function was evidenced by the significant increase in the end-systolic elastance (Ees). End-diastolic pressure, active relaxation (τ), dP/dt_{MIN}, and CS, all parameters of diastolic function, were unchanged, indicating unchanged LV diastolic function six months after SVR. Furthermore, at six month follow-up, mechanical dyssynchrony was reduced as shown by significantly reduced DYS, whereas IFF showed a clear tendency to be reduced. Mechanical efficiency was significantly improved at six months follow-up, resulting from a significant increase of SW in combination with a significant decrease of PVA.

Table 3. Clinical and hemodynamic data

Parameter	Baseline	6 months follow-up	P-value
NYHA class	3.6±0.5	1.5±0.5	<0.001
QoL-test	45±23	16±16	0.028
6-minute HWT (m)	300±133	442±89	0.003
QRS-duration (ms)	103± 19	109± 15	0.348
MR-TTE (grade)	2.1±0.7	0.4±0.5	0.001
HR (bpm)	80±2	83±2	0.059
SV (mL)	64±17	65±12	0.619
CO (L/min)	5±1	5±1	0.270
ESV (mL)	146±46	100±41	0.014
EDV (mL)	214±57	173±46	0.034
EF (%)	31±8	40±14	0.032
ESP (mmHg)	133±33	124±28	0.319
EDP (mmHg)	20±9	18±8	0.435
dPdtMax (mmHg/s)	1270±254	1283±240	0.906
dPdtMin (mmHg/s)	-1149±233	-1189±307	0.577
SW (mmHg.mL)	5971±1749	6878±1266	0.062
Tau (ms)	80±15	81±18	0.966
Ees (mmHg/mL)	0.98±0.31	1.51±0.82	0.049
CS (1/mmHg)	0.097±0.037	0.104±0.037	0.667
ME	0.40±0.12	0.55±0.13	0.020
PVA (mmHg.mL)	16000±5160	13047±3407	0.044
DYS (%)	30±5	26±3	0.058
IFF (%)	61±25	41±19	0.169

NYHA, New York Heart Association; QoL, Quality of life; HWT, Hall walk test; MR-TTE, Mitral regurgitation on transthoracic echocardiography; HR, Heart rate; CO, Cardiac output; ESV,End-systolic volume; EDV, End-diastolic volume; EF; Ejection fraction; ESP, End systolic pressure; EDP, End-diastolic pressure; SW, Stroke work; Ees, End-systolic elastance; CS, Chamber stiffness ;ME, Mechanical efficiency; DYS, Dyssynchrony; IFF, Internal flow fraction

DISCUSSION

SVR by endoventricular circular patch plasty has been applied in patients with ischemic dilated cardiomyopathy complicated by an apicoseptal LV aneurysm. The short-term effects of this procedure on LV function are beneficial and consists of acute LV volume reduction with a decrease of mechanical dyssynchrony and improved LV systolic

function.[6,19] The purpose of the present study was to quantify chronic hemodynamic effects of SVR and in particular the effects on diastolic function.

The results of this study demonstrate that SVR leads to clinical improvement with improved LV hemodynamics. At six months follow-up, sustained LV reverse remodeling and improved global and intrinsic systolic function were observed. Furthermore, mechanical dyssynchrony was significantly reduced with significantly improved mechanical efficiency of the LV. Parameters of early (dP/dtmin, tau) and late diastolic function (EDP, CS) were unchanged six months after surgery, indicating that volume reduction and patch insertion did not compromise LV diastolic function.

LV reverse remodeling. Our results demonstrated a 20% and 31% reduction of EDV and ESV respectively at six months follow-up. The observed decrease in EDV and ESV is consistent with the findings of Qin et al. showing similar reductions of EDV (25%) and ESV (35%) at six months follow-up in 30 patients who underwent SVR and mitral valve repair.[20]

Somewhat larger reductions in LV volumes were reported in studies by Schreuder et al. and Di Donato et al.[6,7] These larger reductions may be due to a more extensive surgical volume reduction related to larger pre-operative LV volumes. Alternatively, these differences may reflect redilation, because ours and Qin's studies were done at six months follow-up, whereas the studies by Schreuder and Di Donato were performed acutely after surgery. Findings of a later study by Di Donato et al., showing a reduction in EDV and ESV of 31% and 44% respectively at 12 months follow-up, may suggest some redilation at late follow-up.[21]

A possible explanation for redilation in the study of Di Donato is the high recurrence of mitral regurgitation (38%) at 12 months follow-up. Qin et al. emphasized the importance of effective mitral valve repair in SVR patients as a pronounced redilation was occurred in patients with recurrence of mitral regurgitation.[20] However, in our study no recurrence of mitral regurgitation occurred after six months follow-up. Therefore, it may be suggested that the smaller volume reduction at six months in our study may be result from less extensive resection in the acute phase due to smaller pre-operative LV volumes. Long-term sustained volume reduction has been confirmed by a recent study by Fujii et al. reporting 33% reduction in EDV after isolated SVR at 23 days, which was unchanged at 32 months follow-up.[22]

Systolic function. Our data confirm previous findings regarding improved LVEF, unchanged SV and reduced LV volumes after SVR.[23,24] However, to our best knowledge, the present study is the first study with invasive hemodynamic measurements before and six months after SVR. At six months follow-up, a significant increase in Ees (from 0.98±0.31 mmHg/mL to 1.51±0.82 mmHg/mL) was observed in our study, indicating improved long-term intrinsic systolic function. Furthermore, mechanical efficiency was significantly improved with a significant reduction in mechanical dyssynchrony. These results are in line with previous findings by Schreuder et al. reporting a significant acute increase in Ees (from 1.2±0.6 mmHg/mL to 2.2±1.0 mmHg/mL), reduced mechanical dyssynchrony and improved LV mechanical efficiency.[7] Similarly, Tanoue et al. reported a similar significant increase in Ees (from 1.15±0.6 mmHg/mL to 1.86±0.84 mmHg/mL) and improvement of ventricular efficiency derived by LV angiography 3 to 4 weeks postoperatively.[25] However, these previous findings merely reflect acute changes of SVR on LV systolic function. Our study demonstrated that the increase in Ees is sustained after six months follow-up. Therefore, the improvement of intrinsic systolic function immediate after SVR is sustained on the long-term. These chronic effects are possibly due to positive acute effects on the remote myocardium by reduction of mechanical dyssynchrony, improvement of mechanical efficiency and reduction in LV wall stress. Schreuder et al. found that changes in Ees are inversely related to parameters of mechanical dyssynchrony and energy efficiency. Presumably, the chronic beneficial effects on Ees found in our study are mainly related to acute beneficial effects.

Diastolic function. In this study, both early and late diastolic function were unchanged at six months follow-up. This is an important finding as endoventricular circular patch plasty may induce diastolic filling abnormalities with a restrictive pattern.[9]

Previous acute studies reported altered early diastolic function after SVR with improved active relaxation (τ).[6,7] These acute effects may be related to direct effects of revascularization[26,27] and effects of cardiopulmonary bypass.[28,29] Schreuder et al.[7] found an increase in EDP (from 9.4±3 to 13.8±3 mmHg) after SVR, however these changes may be due to effects of postoperative edema.[30] Di Donato et al. recently demonstrated that EDP was unchanged (from 20±12 to 17±8 mmHg) 10 days after SVR. These findings are in line with ours as EDP was unchanged (from 20±9 to 18±8 mmHg) after SVR at six months follow-up. In addition, diastolic chamber stiffness was unchanged after six months follow-up, indicating that volume reduction and insertion of patch

plasty does not increase diastolic chamber stiffness. These data imply that SVR does not alter diastolic function six months after surgery.

In conclusion, surgical ventricular restoration leads to clinical improvement with sustained LV reverse remodeling, improved global and intrinsic systolic function and unchanged diastolic function. The improved clinical status after six months may be related to improved mechanical efficiency, intrinsic systolic function and reduced mechanical dyssynchrony.

REFERENCES

1. Nohria A, Lewis E, Stevenson LW. Medical management of advanced heart failure. *JAMA*. 2002;287:628-640.
2. Bogaert J, Bosmans H, Maes A, Suetens P, Marchal G, Rademakers FE. Remote myocardial dysfunction after acute anterior myocardial infarction: impact of left ventricular shape on regional function: a magnetic resonance myocardial tagging study. *J Am Coll Cardiol*. 2000;35:1525-1534.
3. Homans DC, Sublett E, Elsperger KJ, Schwartz JS, Bache RJ. Mechanisms of remote myocardial dysfunction during coronary artery occlusion in the presence of multivessel disease. *Circulation*. 1986;74:588-596.
4. Dor V, Saab M, Coste P, Kornaszewska M, Montiglio F. Left ventricular aneurysm: a new surgical approach. *Thorac Cardiovasc Surg*. 1989;37:11-19.
5. Athanasuleas CL, Buckberg GD, Stanley AW, Siler W, Dor V, Di Donato M, Menicanti L, Almeida dO, Beyersdorf F, Kron IL, Suma H, Kouchoukos NT, Moore W, McCarthy PM, Oz MC, Fontan F, Scott ML, Accola KA. Surgical ventricular restoration in the treatment of congestive heart failure due to post-infarction ventricular dilation. *J Am Coll Cardiol*. 2004;44:1439-1445.
6. Di Donato M, Toso A, Dor V, Sabatier M, Barletta G, Menicanti L, Fantini F. Surgical ventricular restoration improves mechanical intraventricular dyssynchrony in ischemic cardiomyopathy. *Circulation*. 2004;109:2536-2543.
7. Schreuder JJ, Castiglioni A, Maisano F, Steendijk P, Donelli A, Baan J, Alfieri O. Acute decrease of left ventricular mechanical dyssynchrony and improvement of contractile state and energy efficiency after left ventricular restoration. *J Thorac Cardiovasc Surg*. 2005;129:138-145.
8. Ratcliffe MB, Wallace AW, Salahieh A, Hong J, Ruch S, Hall TS. Ventricular volume, chamber stiffness, and function after anteroapical aneurysm plication in the sheep. *J Thorac Cardiovasc Surg*. 2000;119:115-124.
9. Salati M, Paje A, Di Biasi P, Fundaro P, Cialfi A, Santoli C. Severe diastolic dysfunction after endoventriculoplasty. *J Thorac Cardiovasc Surg*. 1995;109:694-701.
10. Baan J, van der Velde ET, de Bruin HG, Smeenk GJ, Koops J, van Dijk AD, Temmerman D, Senden J, Buis B. Continuous measurement of left ventricular volume in animals and humans by conductance catheter. *Circulation*. 1984;70:812-823.
11. Fisher EA, Goldman ME. Simple, rapid method for quantification of tricuspid regurgitation by two-dimensional echocardiography. *Am J Cardiol*. 1989;63:1375-1378.
12. Thomas JD. How leaky is that mitral valve? Simplified Doppler methods to measure regurgitant orifice area. *Circulation*. 1997;95:548-550.
13. Byrne JG, Aklog L, Adams DH. Assessment and management of functional or ischaemic mitral regurgitation. *Lancet*. 2000;355:1743-1744.
14. Dion R, Benetis R, Elias B, Guennaoui T, Raphael D, Van Dyck M, Noirhomme P, Van Overschelde JL. Mitral valve procedures in ischemic regurgitation. *J Heart Valve Dis*. 1995;4 Suppl 2:S124-S129.
15. Dor V, Sabatier M, Di Donato M, Montiglio F, Toso A, Maioli M. Efficacy of endoventricular patch plasty in large postinfarction akinetic scar and severe left ventricular dysfunction: comparison with a series of large dyskinetic scars. *J Thorac Cardiovasc Surg*. 1998;116:50-59.
16. Langer SF. Differential laws of left ventricular isovolumic pressure fall. *Physiol Res*. 2002;51:1-15.

17. Nozawa T, Yasumura Y, Futaki S, Tanaka N, Uenishi M, Suga H. Efficiency of energy transfer from pressure-volume area to external mechanical work increases with contractile state and decreases with afterload in the left ventricle of the anesthetized closed-chest dog. *Circulation*. 1988;77:1116-1124.
18. Steendijk P, Tulner SA, Schreuder JJ, Bax JJ, Van Erven L, van der Wall EE, Dion RA, Schalij MJ, Baan J. Quantification of left ventricular mechanical dyssynchrony by conductance catheter in heart failure patients. *Am J Physiol Heart Circ Physiol*. 2004;286:H723-H730.
19. Schreuder JJ, Steendijk P, van der Veen FH, Alfieri O, van der NT, Lorusso R, van Dantzig JM, Prenger KB, Baan J, Wellens HJ, Batista RJ. Acute and short-term effects of partial left ventriculectomy in dilated cardiomyopathy: assessment by pressure-volume loops. *J Am Coll Cardiol*. 2000;36:2104-2114.
20. Qin JX, Shiota T, McCarthy PM, Asher CR, Hail M, Agler DA, Popovic ZB, Greenberg NL, Smedira NG, Starling RC, Young JB, Thomas JD. Importance of mitral valve repair associated with left ventricular reconstruction for patients with ischemic cardiomyopathy: a real-time three-dimensional echocardiographic study. *Circulation*. 2003;108 Suppl 1:II241-II246.
21. Di Donato M, Sabatier M, Dor V, Gensini GF, Toso A, Maioli M, Stanley AW, Athanasuleas C, Buckberg G. Effects of the Dor procedure on left ventricular dimension and shape and geometric correlates of mitral regurgitation one year after surgery. *J Thorac Cardiovasc Surg*. 2001;121:91-96.
22. Fujii H, Ohashi H, Tsutsumi Y, Kawai T, Iino K, Onaka M. Radionuclide study of mid-term left ventricular function after endoventricular circular patch plasty. *Eur J Cardiothorac Surg*. 2004;26:125-128.
23. Dor V, Sabatier M, Di Donato M, Maioli M, Toso A, Montiglio F. Late hemodynamic results after left ventricular patch repair associated with coronary grafting in patients with postinfarction akinetic or dyskinetic aneurysm of the left ventricle. *J Thorac Cardiovasc Surg*. 1995;110:1291-1299.
24. Suma H, Isomura T, Horii T, Sato T, Kikuchi N, Iwahashi K, Hosokawa J. Nontransplant cardiac surgery for end-stage cardiomyopathy. *J Thorac Cardiovasc Surg*. 2000;119:1233-1244.
25. Tanoue Y, Ando H, Fukumura F, Umesue M, Uchida T, Taniguchi K, Tanaka J. Ventricular energetics in endoventricular circular patch plasty for dyskinetic anterior left ventricular aneurysm. *Ann Thorac Surg*. 2003;75:1205-1208.
26. Humphrey LS, Topol EJ, Rosenfeld GI, Borkon AM, Baumgartner WA, Gardner TJ, Maruschak G, Weiss JL. Immediate enhancement of left ventricular relaxation by coronary artery bypass grafting: intraoperative assessment. *Circulation*. 1988;77:886-896.
27. Halow JM, Figueredo VM, Shames DM, Camacho SA, Baker AJ. Role of slowed Ca(2+) transient decline in slowed relaxation during myocardial ischemia. *J Mol Cell Cardiol*. 1999;31:1739-1748.
28. Brutsaert DL, Sys SU, Gillebert TC. Diastolic dysfunction in post-cardiac surgical management. *J Cardiothorac Vasc Anesth*. 1993;7:18-20.
29. Zile MR, Brutsaert DL. New concepts in diastolic dysfunction and diastolic heart failure: Part II: causal mechanisms and treatment. *Circulation*. 2002;105:1503-1508.
30. Tulner SA, Klautz RJ, Engbers FH, Bax JJ, Baan J, van der Wall EE, Dion RA, Steendijk P. Left ventricular function and chronotropic responses after normothermic cardiopulmonary bypass with intermittent antegrade warm blood cardioplegia in patients undergoing coronary artery bypass grafting. *Eur J Cardiothorac Surg*. 2005;27:599-605.