Hemodynamic folluw-up after heart failure surgery : systolic and diastolic function

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CHAPTER 6

Long-term effects of surgical ventricular restoration with additional restrictive mitral annuloplasty and/or coronary artery bypass grafting on left ventricular function: Six-month follow-up by pressure-volume loops

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ABSTRACT

Background: Previous studies demonstrated beneficial short-term effects of surgical ventricular restoration on mechanical dyssynchrony and left ventricular function, and improved midterm and long-term clinical parameters. However, long-term effects on systolic and diastolic left ventricular function are still largely unknown.

Methods: We studied 9 patients with ischemic dilated cardiomyopathy who underwent surgical ventricular restoration with additional restrictive mitral annuloplasty and/or coronary artery bypass grafting. Invasive hemodynamic measurements by conductance catheter (pressure-volume loops) were obtained before and 6 months after surgery. In addition, New York Heart Association classification, quality-of-life score and 6-minute hall-walk test were assessed.

Results: At 6 months' follow-up, all patients were alive and clinically in improved condition: New York Heart Association class from 3.3±0.5 to 1.4±0.7, quality-of-life score from 46±22 to 15±15 and 6-minute hall-walk test from 302±123 to 444±78m (all $p<0.01$). Hemodynamic data showed improved cardiac output (4.8±1.4 to 5.6±1.1L/min), stroke work (6.5±1.9 to 7.1±1.4mmHg×L, $p=0.05$) and left ventricular ejection fraction (36%±10% to 46%±10%, $p<0.001$). Left ventricular surgical remodeling was sustained at 6 months: end-diastolic volume decreased from 246±70 to 180±48mL and end-systolic volume from 173±77 to 103±40mL (both $p<0.001$). Left ventricular dyssynchrony decreased from 29%±6% to 26%±3% ($p<0.001$) and ineffective internal flow fraction decreased from 58%±30% to 42%±18% ($p<0.005$). Early relaxation (Tau, minimal rate of pressure change) was unchanged, but diastolic stiffness constant increased from 0.012±0.003 to 0.023±0.007mL^{-1} ($p<0.001$).

Conclusion: Surgical ventricular restoration with additional restrictive mitral annuloplasty and/or coronary artery bypass grafting leads to sustained left ventricular volume reduction at 6-months' follow-up. We observed improved systolic function and unchanged early diastolic function, but impaired passive diastolic properties. Clinical improvement, supported by decreased New York Heart Association class, improved quality-of-life score and improved 6-minute hall-walk test may be related to improved systolic function, reduced mechanical dyssynchrony and reduced wall stress.

INTRODUCTION

Chronic heart failure is a leading cause of morbidity and mortality. Most affected patients have an ischemic etiology and in case of anteroseptal infarction, left ventricular (LV) aneurysm is a frequent complication. Abnormal LV geometry and dyscoordinate wall motion may cause a highly inefficient pump function. Ultimately, adverse effects on the remote myocardium, which is exposed to increased workload at enhanced wall stress despite compensatory hypertrophy, may lead to cardiac failure. Patients with LV aneurysm often remain symptomatic despite optimal medical treatment, and surgery may be indicated. Surgical ventricular restoration (SVR) by means of endoventricular circular patch plasty is increasingly performed. With this procedure, akinetic or dyskinetic sections of the anterior wall and septum are excluded to normalize cavity volume and to reshape an elliptical LV, using a Dacron patch to establish wall continuity and ensure adequate residual volume. Studies have shown that SVR is effective and relatively safe with a favorable 5-year outcome,[1 2] although the additional effect of SVR to coronary artery bypass grafting (CABG) remains debated.[3 4] SVR is also frequently combined with mitral valve repair and the impact of that procedure in patients with heart failure has been the subject of several recent studies.[5] Recent hemodynamic studies demonstrated that SVR may acutely reduce LV mechanical dyssynchrony and wall stress and improve LV systolic function.[6] However, as predicted by theoretical studies SVR may be associated with diastolic dysfunction limiting the overall beneficial effects on cardiac pump function. Adverse effects on diastolic function were previously demonstrated in the acute phase,[6] but accurate long-term human data of the potentially differential effects of SVR on systolic and diastolic function are lacking. Therefore we studied the long-term hemodynamic effects in patients with heart failure and ischemic dilated cardiomyopathy treated with SVR. Additional surgery included restrictive mitral annuloplasty (RMA) and/or CABG. Global, systolic and diastolic LV function were assessed invasively using conductance catheter-derived pressure-volume loops before surgery and at 6 months' follow-up.

METHODS

Patients

The study group consisted of 9 patients with ischemic dilated cardiomyopathy, New York Heart Association (NYHA) class III/IV, and LV ejection fraction less than 35% who underwent SVR. In 8 patients with moderate-to-severe mitral regurgitation (MR grade ≥2) additional RMA was performed. All patients underwent additional CABG (CABG,

n=8) or had recent percutaneous coronary interventions (n=1). The protocol was approved by our institutional ethics committee and all patients gave informed consent. Patient characteristics, medication, and surgical data are summarized in Table 1.

Table 1. Patient Characteristics

	Baseline	6-months follow-up
Patients (n)	9	
Male (female) (n)	7(2)	
Age (y)	62±6	
Mean No. stenosed coronary arteries	2.0±1.0	
QRS duration (ms)	109±19	112±15
Clinical characteristics		
NYHA class	3.3±0.5	1.4±0.7*
6-min hall-walk test (m)	302±123	444±78*
Quality-of-Life score	46±22	15±15*
Medication		
Diuretics	6 (67%)	7 (78%)
Beta-blockers	7 (78%)	6 (67%)
ACE inhibitors/AT antagonists	8 (89%)	6 (67%)
Cholesterol inhibitors	8 (89%)	8 (89%)
Vasodilators	2 (22%)	1 (11%)
Aspirin/anticoagulants	8 (89%)	6 (67%)
Surgical data		
Surgical intervention:		
SVR + RMA + CABG	7 (78%)	
SVR + RMA	1 (11%)	
SVR + CABG	1 (11%)	
Ring size (RMA)	25±1	
Mitral regurgitation grade	2.0±1.2	0.3±0.5*
No. of distal anastomoses	3±1	
Cardiopulmonary bypass (min)	222±46	
Aorta crossclamping (min)	153±28	
Intensive care unit stay (d)	4±2	
Hospital stay (d)	16±5	
Intra-aortic balloon pump	2 (22%)	
Inotropic support# >24h	6 (66%)	

NYHA, New York Heart Association; ACE, angiotensin-converting enzyme; AT, angiotensin; SVR, surgical ventricular restoration; RMA, restrictive mitral annuloplasty; CABG, coronary artery bypass grafting. Data are presented as number of patients involved and percent of the total group or as mean±SD. * $p<0.01$. # Dobutamine >2μg × kg^{-1} × min^{-1}

Study protocol

Baseline hemodynamic data were obtained during diagnostic catheterization, 25±18 days before surgery, including thermodilution cardiac output, ventriculography, and coronary angiography. In addition, a 7F conductance catheter (CD-Leycom, Zoetermeer, The Netherlands) was placed in the LV via the femoral artery and a temporary pacing lead in the right atrium to obtain pressure-volume loops at fixed incremental (80, 100, 120beats/min) heart rates (HRs). LV volume was calibrated by thermodilution and hypertonic saline dilution. Data were acquired at least 1 minute after changing to a higher HR and periods of ~20 seconds were selected for offline analysis. All measurements were repeated after SVR during recatheterization at 6.5±0.8 months' follow-up.

Echocardiography

Additional transesophageal echocardiography (TEE) was performed within 5 days before surgery on patients with moderate-to-severe MR (grade ≥2) seen on transthoracic echocardiography (TTE). TEE was done without general anesthesia to avoid underestimation of MR. Severity was graded semi-quantitatively from color Doppler in conventional parasternal long-axis and apical 4-chamber images. Immediately after surgery, TEE was repeated to exclude residual MR. At 6 months' follow-up, repeat TTE assessed possible recurrent MR. All TTE measurements were analyzed in random order by two independent observers without knowledge of the clinical status of the patient.

Surgical procedures

Surgical procedures were performed using normothermic cardiopulmonary bypass with intermittent antegrade warm blood cardioplegia. After median sternotomy, patients underwent conventional CABG, using internal thoracic arteries when possible. Next, SVR was performed by an endoventricular circular patch plasty as previously described by Dor [7] Briefly, the LV 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 55 mL of saline per square meter of body surface area was introduced into the LV. 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 en to delineate a new LV apex with the goal to restore the normal elliptical shape. After completion of the LV restoration, a stringent RMA (2 sizes smaller than the measured size) was performed by the atrial transseptal approach using a Carpentier-Edwards Physio ring (Edwards Lifesciences, Irvine, Calif, USA).

Data analysis

Hemodynamic indexes were calculated with custom-made software as the mean of all beats during a steady state period of ~20 seconds at each paced HR level. LV function was quantified by cardiac output (CO), LV ejection fraction (LVEF), stroke volume (SV), end-diastolic and end-systolic volume (EDV, ESV) and pressure (EDP, ESP), and maximal and minimal rate of LV pressure change (dP/dt_{MAX}, $-dP/dt_{MIN}$). Stroke work (SW) was calculated as the pressure-volume loop area. Afterload (effective arterial elastance E_A) was calculated as ESP/SV, mechanical efficiency (ME) as the ratio of SW and pressure-volume area (PVA): ME = SW/PVA.[8] To determine peak wall stress (PWS), time-varying wall stress was calculated from LV pressure and volume, P(t) and V(t), and LV mass as described by Arts et al.[9]: $WS(t) = P(t)\cdot(1+3\cdot V(t)/LV\ mass)$. LV mass was based on diastolic posterior wall thickness derived from M-mode echocardiography. The end-systolic pressure-volume relation (ESPVR) was determined by single-beat analysis and quantified by its slope E_{ES} (end-systolic elastance) and volume intercept at 125 mmHg (ESV_{125}) as detailed elsewhere.[10] The preload recruitable stroke work relation (PRSW) was determined as described by Lee et al. and characterized by slope M_W and volume axes intercept V_W.[11] The time constant of relaxation (Tau) was determined by phase-plot analysis. The end-diastolic pressure-volume relation (EDPVR) was derived from the filling phase trajectory of the pressure-volume loop including all data points between the moments of minimal pressure and maximal volume. LV diastolic stiffness (E_{ED}) was determined as the linear slope of the EDPVR, the stiffness constant (K_{ED}), from an exponential fit ($EDP = A\cdot\exp(K_{ED}\cdot EDV)$). EDPVR position was defined by the intercept at 18 mmHg (EDV_{18}). LV mechanical dyssynchrony (DYS) was determined from the segmental conductance signals.[12] In addition, we calculated internal flow fraction (IFF) to quantify the ineffective shifting of blood volume within the LV due to nonuniform contraction and relaxation.[12]

Statistical analysis

We used a linear mixed-effects model with patients included as random effects and conditions (baseline, 6-months' follow-up), pacing (80, 100 and 120beats/min), and their interaction as fixed effects. This model accounts for correlation between repeated measurements. Data are presented as mean±SD. All analyses were performed using the statistical software program SPSS 16.0 (SPSS, Inc, Chicago, Ill, USA). The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.

RESULTS

Patient clinical characteristics and medication are reported in Table 1. Note that in the present study we included a selected group of patients with complete hemodynamic follow-up by pressure-volume loops. In the associated 2-year interval, a total of 39 patients with NYHA III/IV underwent SVR in our center. The operative mortality in this entire group was 10.3%, and 6-months' survival was 87%.

Surgical and clinical data

Surgery was associated with an aortic crossclamping time of 153±28 minutes and a total cardiopulmonary bypass (CPB) duration of 222±46 minutes. In all cases, intra-operative TEE excluded residual MR. Two patients needed an intra-aortic balloon pump to wean from CPB and 6 patients needed inotropic support (dobutamine $>2\mu g \times kg^{-1} \times min^{-1}$) more than 24 hours postoperatively. Hospital stay was 16±15 days with an intensive care stay of 4±2 days. All patients were discharged from the hospital in good clinical condition. At 6 months' follow-up, QRS duration was unchanged and the clinical status of the patients showed significant improvements (Table 1).

Hemodynamic data

Hemodynamic data are summarized in Table 2. The statistical model tested differences between conditions (baseline, 6 months' follow-up), effect of HR (pacing), and the interaction between conditions and pacing. The latter would indicate whether effects of pacing were different between both conditions; however none of the variables showed significant interaction. At follow-up, global LV function was improved as evidenced by significantly increased SW ($p=0.05$), a tendency for increased CO and SV ($p=0.09$, $p=0.06$) and reduced PWS ($p<0.001$). ESV and EDV were significantly reduced (both $p<0.001$) with respectively -40% and -27% (at 80 beats/min), indicating substantial persistent reverse LV remodeling. The significant increase in SW combined with unchanged PVA resulted in an improved ME, which however did not reach statistical significance ($p=0.113$). Systolic function was improved as evidenced by a significantly increased slope and leftward shift of the PRSW relation ($p=0.004$, $p<0.001$). Furthermore we observed an increased LVEF and reduced ESV_{125} (both $p<0.001$). E_{ES} and the arterial/ventricular coupling ratio (E_A/E_{ES}) did not change significantly, although afterload (E_A) decreased significantly ($p=0.013$). Passive diastolic function showed impairment indicated by increased E_{ED} and K_{ED} (both $p<0.001$). However, early, active relaxation indexed by Tau and $-dP/dt_{MIN}$ was unaltered after SVR. EDV, calculated from the EDPVR at 18 mmHg was significantly reduced, reflecting lower operating volumes consistent with

Table 2. Hemodynamics by pressure-volume loops at baseline and 6 months' follow-up after SVR

	Baseline (beats/min)			6-month follow-up (beats/min)			P-values		
	80	100	120	80	100	120	Condition	Pacing	Interaction
General									
HR (beats/min)	79.5±2.9	99.3±2.8	121.9±2.6	82.6±2.0	101.7±1.4	122.0±2.1	0.003	<0.001	0.145
CO (L/min)	4.8±1.4	4.7±2.3	5.8±2.5	5.6±1.1	5.7±1.7	5.3±2.3	0.090	0.528	0.229
SV (mL)	60±17	47±23	48±21	68±13	56±16	43±19	0.060	<0.001	0.271
SW (mmHg · L)	6.5±1.9	4.9±1.9	4.9±2.1	7.1±1.4	6.0±1.1	4.4±1.3	0.050	<0.001	0.296
E_A (mmHg/mL)	2.5±1.1	3.9±2.3	3.2±2.0	2.0±0.7	2.4±1.0	3.3±1.6	0.013	0.011	0.227
E_A/E_{ES}	2.24±1.17	2.19±1.10	2.60±1.36	1.93±0.61	2.16±0.66	2.64±1.18	0.163	0.045	0.793
ME	0.49±0.12	0.48±0.11	0.45±0.15	0.53±0.11	0.51±0.10	0.47±0.13	0.113	0.078	0.964
PVA (mmHg·L)	14.1±6.6	10.5±4.1	11.0±3.3	14.0±4.1	12.1±3.1	9.4±1.7	0.763	0.003	0.511
PWS (mmHg)	431±177	434±188	465±240	310±125	307±118	285±115	<0.001	0.988	0.836
Systole									
ESV (mL)	173±77	180±87	184±93	103±40	105±44	100±51	<0.001	0.958	0.940
ESP (mmHg)	133±32	129±29	122±25	126±27	123±25	114±22	0.088	0.140	0.958
EF (%)	36±10	33±12	32±11	46±10	42±12	40±13	<0.001	0.121	0.865
dP/dt_{MAX} (mmHg/s)	1291±274	1368±261	1424±324	1291±225	1384±209	1384±224	0.919	0.138	0.932
E_{ES} (mmHg/mL)	1.2±0.6	1.6±0.7	1.5±0.7	1.1±0.5	1.2±0.4	1.3±0.6	0.087	0.378	0.792
ESV_{125} (mL)	165±96	178±91	187±101	103±51	111±57	114±65	<0.001	0.820	0.968
M_W (mmHg)	38±15	29±15	31±16	48±7	42±8	32±11	0.004	0.003	0.415
V_W (mL)	79±85	76±91	91±86	29±51	23±52	9±54	<0.001	0.772	0.802
Diastole									
EDV (mL)	246±70	241±78	243±86	180±48	171±49	151±52	<0.001	0.527	0.823
EDP (mmHg)	19.8±8.6	19.8±10.0	19.7±9.3	19.0±7.6	15.6±8.1	11.2±6.1	0.021	0.118	0.262
$-dP/dt_{MIN}$ (mmHg/s)	1166±238	1180±213	1180±232	1187±287	1211±250	1180±229	0.685	0.857	0.901
Tau (ms)	80±14	74±14	67±16	82±17	76±14	70±12	0.351	0.003	0.895
E_{ED} (mmHg/mL)	0.15±0.08	0.14±0.08	0.14±0.07	0.24±0.11	0.24±0.16	0.23±0.18	<0.001	0.821	0.960
K_{ED} (mL^{-1})	0.012±0.003	0.010±0.006	0.012±0.012	0.023±0.007	0.026±0.017	0.035±0.032	<0.001	0.434	0.530
EDV_{18} (mL)	261±93	248±102	266±115	198±40	190±56	194±62	<0.001	0.860	0.994
Dyssynchrony									
DYS (%)	29.3±5.5	29.4±6.1	29.0±6.3	26.3±3.4	25.9±3.4	25.4±2.7	<0.001	0.800	0.912
IFF (%)	58±30	62±35	60±34	42±18	41±15	39±15	0.004	0.856	0.959

SVR, surgical ventricular restoration; HR, heart rate; CO, cardiac output; SV, stroke volume; SW, stroke work; E_A, arterial elastance; E_{ES}, end-systolic elastance (slope of ESPVR, end-systolic pressure-volume relation); ME, mechanical efficiency; PVA, pressure-volume area; PWS, peak wall stress; ESV, end-systolic volume; ESP, end-systolic pressure; EF, ejection fraction; $dPdt_{MAX}$, maximal rate of pressure change; ESV_{125}, ESPVR intercept at 125mmHg; M_W, slope of PRSW (preload recruitable stroke work relation); V_W, intercept of PRSW; EDV, end-diastolic volume; EDP, end-diastolic pressure; $-dPdt_{MIN}$, minimum rate of pressure change; Tau, pressure relaxation time constant; E_{ED}, diastolic stiffness; K_{ED}, diastolic stiffness constant; EDV_{18}, intercept of EDPVR (end-diastolic pressure-volume relation) at 18mmHg; DYS, mechanical dyssynchrony; IFF, internal flow fraction.

a leftward shift of the pressure-volume loop. DYS and IFF were significantly ($p<0.001$, $p=0.004$) reduced with -10% and -28%, respectively, indicating substantially reduced dyssynchrony.

DISCUSSION

Previous research has shown that SVR is an effective therapy for patients with end-stage ischemic heart failure according to acceptable survival rates, improved clinical performance, and sustained LV reverse remodeling diagnosed by echocardiography at midterm and long-term follow-up.[13 14] Several previous studies examined the *acute* hemodynamic status after SVR showing the expected volume reductions, a decrease of mechanical dyssynchrony, improved systolic function and impaired diastolic function, which effects however could be partly transient.[6] The present study therefore was designed to analyze the long-term effects of SVR with additional RMA and/or CABG on several aspects of LV function including chronotropic responses, at 6 months' follow-up. To our knowledge, long-term follow-up data including invasive pressure-volume indices, have not been published previously for this patient group.

Global LV function

Our results demonstrate sustained reverse LV remodeling with reduced ESV (-40%) and EDV (-27%) at 6 months' follow-up, exceeding the previously reported ~25% acute volume reductions.[6] In line with other studies, CO and SV showed a tendency to increase but did not reach statistical significance, whereas SW increased significantly after SVR.[14 15] Afterload (E_A) decreased significantly which was also observed by Fantini et al.,[16] whereas ME and PVA did not change significantly. Consequently, calculated wall stress, an important determinant of myocardial oxygen consumption, decreased substantially (-28%), which may partly explain improved clinical performance. Our results regarding long-term relative volume reduction are in line with most previous studies, at midterm follow-up (4-12 months).[1 17-19] Likewise, the mean ESV index obtained at 6 months after SVR (53±21mL/m^2) is in the same range as follow-up values reported in larger series by, for example, the RESTORE group[1] (57±34mL/m^2), Dor et al.[18] (51±18mL/m^2), and Di Donato et al.[17] (average of 3 groups: 44±20mL/m^2).

Systolic LV function

Our data confirm previous findings regarding significantly improved LVEF after SVR. However this may be partly due to reduced afterload and, more in general, the relevance

of increased LVEF after SVR has been questioned. Therefore, additional systolic indices derived from load-independent pressure-volume relations ESPVR and PRSW were investigated. ESPVR showed a leftward shift evidenced by reduced ESV_{125}, indicating improved systolic function, but the slope E_{ES} was not significantly altered. E_{ES} is often used to index systolic function; however, in case of regional dysfunction, the ESPVR may primarily show parallel shifts rather than a decreased slope presumably because at systolic pressure levels the aneurysm is very stiff.[20] The PRSW relation showed a leftward shift (reduced intercept of PRSW) and increased slope of PRSW, both indicating improved systolic function. Although PRSW is predominantly a measure of systolic function, alterations in diastolic function also affect this relation. However, the negative effects on diastolic function in this case would tend to decrease the PRSW slope and thus partly mask even more positive systolic effects. The improved global systolic function presumably was related to improved functioning of the remote myocardium by reduced wall stress and reduced mechanical dyssynchrony.

Diastolic function

Early active relaxation ($-dP/dt_{MIN}$, Tau) was unchanged after SVR, but passive diastolic stiffness was significantly increased. The fact that $-dP/dt_{MIN}$ and Tau did not change, despite the substantial volume reduction, could result from negative effects due to a distortion of the normal myocardial fiber orientation.[21] Apparently, increased diastolic stiffness observed *acutely* after SVR[6] which, however, did not reach significance (pre-SVR: K_{ED} 0.021±0.009mL^{-1} , post-SVR: K_{ED} 0.037±0.02 mL^{-1}, p=0.147) is still present at 6 months and thus not merely a transient effect of cardioplegic arrest. The significantly increased K_{ED} in the present study cannot be directly compared with the results of the previous short-term study performed in the operating room,[6] because other effects related to the perioperative conditions may also play a role.[10] To put these values into perspective, Kasner et al.[22] recently reported K_{ED} to be approximately 0.010 mL^{-1} in normals and 0.029 mL^{-1} in patients with heart failure and normal ejection fraction, whereas in patients with hypertrophic obstructive cardiomyopathy a value of 0.025 mL^{-1} was found by Steendijk et al.[23] Thus, the baseline values for K_{ED} in the present study of 0.012±0.003 mL^{-1} appear to be in the normal range, whereas 0.023±0.007 mL^{-1} observed 6 months after surgery is close to values observed in patient groups with diastolic dysfunction. A study by Zhang et al. in sheep also reported a tendency for increased diastolic stiffness up to 6 weeks after SVR.[24] Furthermore, a few other studies have reported filling abnormalities after SVR and suggested that a marked reduction of LV size may result in a restrictive LV filling pattern.[25 26] In our data set we also found a correlation between the reduction in EDV and the increase in diastolic stiffness constant ($\%\Delta K_{ED} = 41.9 - 3.0 \cdot \%\Delta EDV$, $r^2=0.55$, $p<0.01$). This finding suggests that a restriction in the amount of LV volume reduction

could be relevant to avoid diastolic dysfunction. However, the number of patients is too small to draw firm conclusions and further studies are needed to address this issue.

Dyssynchrony

Mechanical dyssynchrony is increasingly recognized as an important factor explaining LV dysfunction. Earlier studies[6] demonstrated an immediate improvement in dyssynchrony after SVR and the present data indicate persistent improvement at 6 months. The reduced dyssynchrony presumably underlies the improved systolic function whereas the reduced intraventricular shifting of blood volume indexed by IFF will contribute to a more efficient pump function.

Heart rate effect

We performed measurements during pacing to exclude bias by altered HR and to investigate HR dependencies before and after SVR. Statistical analysis showed that CO tended (p=0.09) to be higher after SVR (+18% at 80 beats/min) but the effect of pacing on CO was unaltered, indicating a remaining lack of chronotropic reserve. As shown in Figure 1, SV (width of pressure-volume loop) gradually decreased at higher HR, limiting the CO increase. Interestingly, it appeared that the reduction in SV was mainly due to an increase in ESV at baseline, but due to a decrease in EDV at 6 months' follow-up, suggesting that the resolved contractile problem is partly biased by a filling abnormality. However, these pacing effects did not reach statistical significance and thus remain

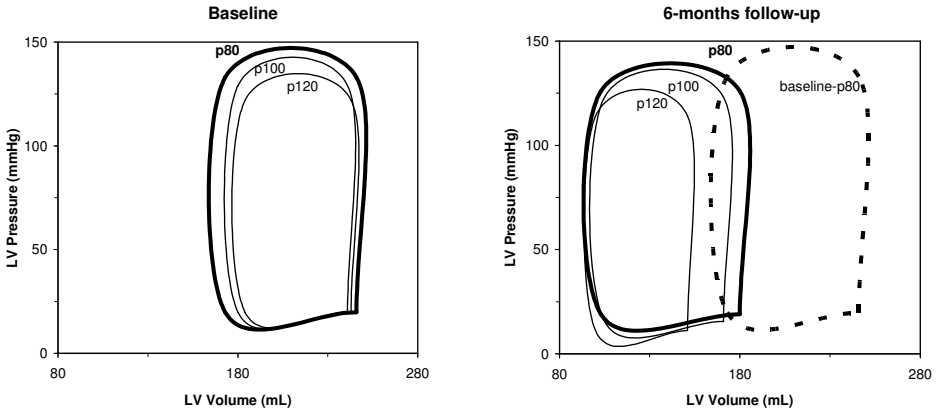

Figure 1. Schematic pressure-volume loops (based on mean end-diastolic and end-systolic pressures and volumes) at baseline *(left panel)* and at 6 months after surgical ventricular restoration (SVR) *(right panel)*. Loops are shown during pacing at 80, 100 and 120 beats/min (p80, p100, p120). Baseline p80 data are repeated in the right panel *(dotted lines)* to illustrate the substantial volume reduction induced by SVR. LV, left ventricular.

speculative. Interestingly, the response to pacing after SVR appears to be similar to that observed in patients with heart failure and preserved ejection fraction.[27] It should be noted that increased HR by pacing only partly mimics the effects of exercise. Given the drop in EDP during pacing after SVR, sympathetic stimulation and volume recruitment during true exercise may lead to a more positive effect on CO by maintaining or even increasing normal filling pressures.[27]

Additional surgery

In this study SVR was the primary indication for surgery, but additional CABG and/or RMA was performed in all patients. Therefore, the reported effects can not be attributed to SVR alone. Revascularization has been shown to have beneficial effects in patients with ischemic dilated cardiomyopathy.[28] Moreover, a recent randomized trial concluded that adding SVR to CABG in patients eligible for both procedures was not associated with greater clinical benefits than CABG alone, despite the fact that a larger reduction in ESV index was obtained (19% vs. 6%).[3] However, this trial is currently strongly debated, in particular because the SVR-related volume reductions were much smaller than in other SVR trials (typically ~40%).[29] Likewise, beneficial clinical effects and significant long-term volume reductions have been reported for RMA with or without CABG.[30 31] Pressure-volume loop studies in patients with RMA alone are in progress, but comparison with the present study will remain difficult because studies are not randomized and baseline characteristics of patients groups are different.

Study limitations

In addition to the potentially confounding effects of additional surgery, the study is limited by a small sample size. However, by using each patient as his or her own control, statistical power was optimized. Moreover, we used invasive pressure-volume measurements, which are generally regarded as highly accurate and the gold standard for LV function assessments.

Conclusion

Our findings provide insight in the long-term effects of SVR on systolic and diastolic LV function and reveal that the clinical improvements presumably are due to improved systolic function and reduced dyssynchrony and wall stress, leading to more efficient global pump function. However, the surgical intervention may be associated with an adverse effect on diastolic function limiting its full potential (Figure 2). Further research is needed to investigate this issue and whether patients who are prone to the devel-

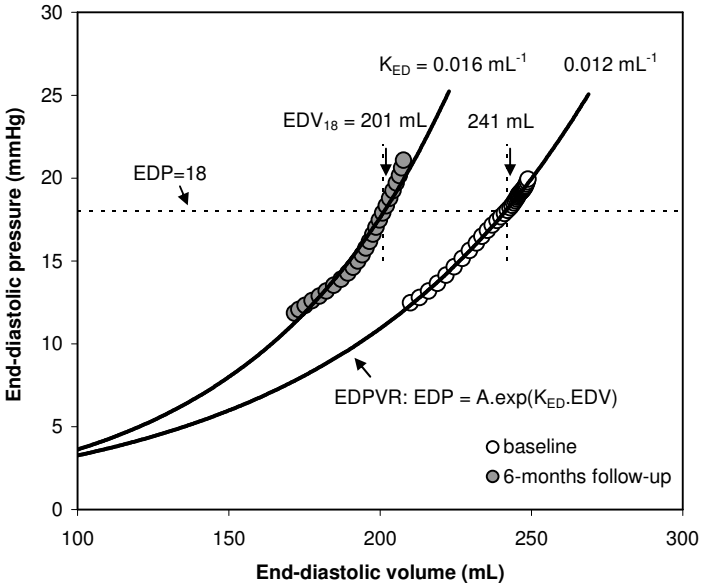

Figure 2. Typical examples of end-diastolic pressure-volume relationships (EDPVR) at baseline and 6 months after surgical ventricular restoration (SVR) illustrating increased diastolic stiffness constant (K_{ED}) and reduced LV volume. EDPVR intercepts at 18 mmHg (EDV_{18}) are indicated. EDP, end-diastolic pressure; EDV, end-diastolic volume.

opment of diastolic dysfunction should be excluded or whether modifications in the procedure such as an adaptation of the target cavity volume should be considered. However, considering the positive net effect of the surgical procedure on improved clinical outcome it is clear that the effect of SVR on systolic function, dyssynchrony, and wall stress is more prominent than the possible adverse effect on diastolic function.

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