Functional capacity late after partial left ventriculectomy: relation to ventricular geometry and performance

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Abstract

Objectives: While partial left ventriculectomy (PLV) may improve functional status, the duration and determinants of this improvement are poorly known. This study sought to assess the relationship between left ventricular (LV) shape and function and functional status in late survivors after PLV for non-ischemic dilated cardiomyopathy (DCM).

Methods: We assessed the relations between LV shape and function and functional status in 17 consecutive patients who survived >12 months after PLV for non-ischemic DCM. Invasive diagnostic studies were performed before, early after, at mid-term after, and late after PLV. According to their functional status after >12 months of follow-up, patients were divided into responders (n = 10) or non-responders (n = 7).

Results: After PLV, the LV systolic major-to-minor axis ratio was higher in responders at early, mid-, and late follow-up (P < 0.003, P < 0.008 and P < 0.04, respectively). LV circumferential end-diastolic stress decreased early after PLV, but increased afterwards in non-responders only (P < 0.049). LV ejection fraction was similar in the two groups at baseline, and at early and mid-follow-up, but was lower in non-responders at late follow-up (P < 0.006). However, LV end-diastolic and end-systolic volumes, and LV end-systolic circumferential stress showed no difference between the two groups.

Conclusions: It appears that poor functional capacity in late post-PLV survivors is related to postoperative LV geometry.

Keywords: Heart failure; Partial left ventriculectomy; Left ventricular performance

1. Introduction

It has been shown that partial left ventriculectomy (PLV) decreases left ventricular (LV) volumes and increases the LV ejection fraction in patients with dilated cardiomyopathy (DCM) [1–3]. These initial beneficial effects are marred by a high early (3–6 months) mortality [3–7]. On the other hand, those patients who survive usually have improved functional status [3–5]. Some survivors may even experience that this improvement, evidenced by both subjective and objective measures of functional capacity, may remain stable through a prolonged period of time [3–7]. Unfortunately, some patients, after satisfactory post-operative outcome and an initial improvement of functional status, may show a progressive downhill course marked by an increase of LV filling pressures and frequent hospitalization for heart failure. Although this delayed separation of responders and non-responders has been noted previously [6], the mechanisms and underlying hemodynamics that are responsible for, or herald, the occurrence of heart failure are poorly understood. In order to elucidate these important issues, we have performed a sequential invasive assessment of LV performance in a consecutive series of patients with non-ischemic DCM who underwent a PLV procedure at our institution.

2. Materials and methods

2.1. Patients

During the period from October 1996 to December 1997, we performed PLV in 25 patients. All patients had normal coronary anatomy and normal valve morphology [4], without histopathologic signs of lymphocytic myocarditis.

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Eight of these patients died during the 12 months after PLV due to a cerebrovascular incident (three patients), sudden death (two patients), sepsis (two patients), and post-operative low cardiac output syndrome (one patient). Seventeen patients survived for more than 12 months, and they represent the study group (15 men, mean age 47 ± 13 years). All patients were receiving standardized medical heart failure treatment consisting of captopril ≥75 mg/day, digoxin, furosemide, amiodarone, and oral anticoagulant throughout follow-up. The study protocol was approved by the hospital’s Human Research Committee. The investigational status of PLV was explained to all patients, who gave informed consent both for the catheterization studies and for the operation.

Patients were classified as non-responders (7/17 patients) if they met all three of the following criteria: hospitalization for heart failure during follow-up, furosemide dosage ≥80 mg/day at a last control, and inability to tolerate a workload of more than 25 W. One of these patients died during follow-up because of refractory heart failure; three others were placed on a heart transplant list, while three were considered unsuitable for heart transplantation (one due to advanced age, and two because of a high transpulmonary gradient). The remaining 10 patients were classified as responders; none of them were hospitalized for heart failure during follow-up, all were receiving <80 mg furosemide daily, and all were able to tolerate a workload of >25 W. None of them died during the follow-up (mean 27 months, range 19–33 months). All 17 patients met no, or all, of three criteria for classification.

2.2. Surgery

Operations were performed using cardiopulmonary bypass [4]. In 6/17 patients the beating heart technique was used, while in 11/17 patients surgery was performed during cardioplegic arrest. Mitral valve replacement with mechanical prosthesis was performed by transventricular approach in five patients. Mitral repair was performed in the remaining 12 patients, with a commissural stitch placed in all of them, and additional mitral repair procedures were performed using a previously described modification in six patients [4], de Vega tricuspid annuloplasty was performed in five patients.

2.3. Cardiac catheterization

Hemodynamic studies before, early after (mean 14 ± 4 days, range 10–29 days) and at mid-term after (7.1 ± 1.6 months, range 6–10 months) surgery were performed in all patients. In 14/17 patients a hemodynamic study was also performed late after (15.7 ± 4.3 months, range 12–24 months) surgery. In two patients (non-responders), hemodynamic studies late after surgery were not performed because of end-stage heart failure with fluid retention refractory to intravenous diuretics, while in a third patient (responder) a hemodynamic study was not performed due to technical reasons. The detailed protocol has been described elsewhere [1]. Briefly, we performed RAO 30° single plane left ventriculography with simultaneous recording of arterial pressures. Temporary right heart pacing was used to keep a constant heart rate in all four studies. From these data, LV volumes [8], LV major-to-minor axis ratio [1], LV mass [9–11], and LV mid-wall circumferential stress (Mirskey’s thick wall model) [12] were calculated.

2.4. Post-operative exercise capacity

All patients, unless contraindicated [13], performed symptom-limited incremental supine bicycle ergometry, with invasive hemodynamic measurements obtained using a Swan-Ganz thermodilution catheter 13–24 months after surgery. Tests were repeated if functional deterioration occurred; if more than one test was performed, the results of the last one were reported. Stages were 2 min in duration, with the initial workload of 15 W increased to 25 W at the second level, and continued with 25 W increments. The LV stroke work index was calculated using standard equations. Peak oxygen consumption was calculated by multiplying the arterio-venous oxygen difference by the thermodilution cardiac output [14].

2.5. Morphometric analysis

Myocardial specimens, embedded in paraffin and cut in semithin sections, were stained with Masson-trichrome. At least three biopsy specimens were analyzed per patient. A single microscopic field (400× magnification) per biopsy specimen was digitized via a light microscope (Olympus, Japan) coupled to a color camera interfaced with a Pentium computer. Myocyte diameters were measured at the level of the nucleus of all longitudinally cut myocytes [15] using ImageTool 2.0 software (University of Texas Health Science Center, San Antonio, TX, USA). The myocardial fibrosis percentage was quantified by a previously described method using LeicaQwin software (Leica Corporation, St. Galen, Switzerland) [15].

2.6. Statistical analysis

Data are presented as the mean ± SD. The Mann–Whitney U-test and Fisher exact tests were used to assess differences between the two groups for clinical, morphometric and baseline hemodynamic data. Repeated measures analysis of variance was used to assess the effects of time and groups on LV function and shape, with post-hoc testing using Scheffe tests when appropriate. Repeated measures analysis of covariance with circumferential end-systolic stress as a covariate was used in order to obtain the end-systolic stress-adjusted LV ejection fraction [16]. The association of clinical (age, sex, New York Heart Association class and symptom duration), histomorphometric (myocardial fibrosis percentage and myocyte diameter), and baseline and early postoperative hemodynamic variables (LV
circular end-diastolic and end-systolic stress, end-
end-diastolic and end-systolic volume index, cardiac index,
diastolic and systolic major-to-minor axis ratio, and LV
ejection fraction) with response to PLV was tested using
univariate logistic regression. Variables for which the
P values were <0.05 were then entered into a multiple step-
wise logistic regression model. A P value of <0.05 was
considered significant.

3. Results

3.1. Patient characteristics

Table 1 shows baseline clinical, hemodynamic, operative,
and morphometric characteristics of the responders and
non-responders. Responders tended to have a higher cardiac
index (P = 0.04) and more frequently had mitral valve
replacement (P = 0.044). Postoperative exercise capacity
data are presented in Table 2.

3.2. Catheterization studies

PLV decreased LV end-diastolic and end-systolic volume
indices in both groups (responders: P < 0.001 at all time
points versus baseline for both end-systolic and end-diastolic
volume indices; non-responders: P < 0.05 for all time
points versus baseline for both end-systolic and end-diastolic
volume indices) (Fig. 1A,B). LV volume indices were
similar among the groups throughout the study. When the
two groups were merged, an increase of LV end-diastolic and
end-systolic volume indices was noticed between early
and late follow-up (P = 0.031 and P = 0.023, respectively).

Following PLV, LV circumferential end-diastolic stress in
responders decreased at mid- and late follow-up (P = 0.04
and P = 0.05, respectively) (Fig. 2A). In non-responders, LV
circumferential end-diastolic stress decreased at early
follow-up (P = 0.017), but increased afterwards at mid-
and late follow-up (P = 0.019 and P = 0.014 versus early,
respectively). While the group-by-time interaction was
significant (P = 0.049), no difference between groups was

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Table 1
Preoperative clinical, hemodynamic and histomorphometric data

<table>
<thead>
<tr>
<th></th>
<th>Responders (n = 10)</th>
<th>Non-responders (n = 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>49 ± 9</td>
<td>43 ± 17</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>9/1</td>
<td>6/1</td>
</tr>
<tr>
<td>Symptom duration (months)</td>
<td>23.4 ± 12.8</td>
<td>39.9 ± 40.6</td>
</tr>
<tr>
<td>NSR/atrial fibrillation</td>
<td>7/3</td>
<td>6/1</td>
</tr>
<tr>
<td>NYHA class (III/IV)</td>
<td>4/6</td>
<td>0/7</td>
</tr>
<tr>
<td>LV EDVI (mL/m²)</td>
<td>181 ± 41</td>
<td>160 ± 24</td>
</tr>
<tr>
<td>LV EF (%)</td>
<td>22 ± 8</td>
<td>22 ± 9</td>
</tr>
<tr>
<td>LV EDP (mmHg)</td>
<td>21 ± 11</td>
<td>28 ± 13</td>
</tr>
<tr>
<td>Cardiac index (mL/m²)</td>
<td>2.6 ± 0.8</td>
<td>1.9 ± 0.8</td>
</tr>
<tr>
<td>Preoperative MR grade</td>
<td>1.7 ± 1.0</td>
<td>2.1 ± 1.6</td>
</tr>
<tr>
<td>MV/MVR</td>
<td>5/5</td>
<td>7/0</td>
</tr>
<tr>
<td>de Vega TA</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Myocardial fibrosis (%)</td>
<td>18.2 ± 3.1</td>
<td>21.4 ± 4.6</td>
</tr>
<tr>
<td>Myocyte diameter (μm)</td>
<td>23.0 ± 0.6</td>
<td>24.5 ± 2.3</td>
</tr>
</tbody>
</table>

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Table 2
Exercise capacity data

<table>
<thead>
<tr>
<th></th>
<th>Responders (n = 10)</th>
<th>Non-responders (n = 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise time (s)</td>
<td>335 ± 104</td>
<td>168 ± 17</td>
</tr>
<tr>
<td>Peak workload (W)</td>
<td>100 ± 43</td>
<td>20 ± 7</td>
</tr>
<tr>
<td>Rest LV SWI (gm/m²)</td>
<td>41 ± 15</td>
<td>22 ± 11</td>
</tr>
<tr>
<td>Peak LV SWI (gm/m²)</td>
<td>49 ± 24</td>
<td>22 ± 4</td>
</tr>
<tr>
<td>Peak VO₂ (ml/kg per min)</td>
<td>17.8 ± 6.4</td>
<td>8.3 ± 1.3</td>
</tr>
</tbody>
</table>

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*EDP, end-diastolic pressure; EDVI, end-diastolic volume index; EF, ejection fraction; LV, left ventricular; MR, mitral regurgitation; MV, mitral
valvoplasty; MVR, mitral valve replacement; NSR, normal sinus rhythm; NYHA, New York Heart Association; TA, tricuspid annuloplasty.

b P < 0.05, between groups.
detected at any specific time point. However, a cutoff value of end-diastolic stress of 78 gm/cm\(^2\) separated responders and non-responders with no error at mid-term, and with only one error at late follow-up.

PLV decreased LV circumferential end-systolic stress in responders at all three time points (\(P < 0.0005\) for all versus baseline), and in non-responders at early and mid-term follow-up (\(P = 0.02\) and \(P = 0.004\), respectively). Late after surgery, the LV ejection fraction was lower in non-responders than in responders (\(P = 0.006\)) (Fig. 4A). There was no overall difference between the two groups for the LV end-systolic stress-adjusted ejection fraction (\(P = 0.08\)). However, a significant treatment-by-group interaction (\(P = 0.008\)) showed that the end-systolic stress-adjusted ejection fraction behaved differently in the two groups, with responders showing a slight increase and non-responders showing a late decrease during follow-up (Fig. 4B).

The mean mitral regurgitation grade in non-responders was 0.57 ± 0.79, 1.00 ± 0.58 and 1.60 ± 0.55 early, at mid-term, and late after PLV and mitral valve repair, respectively. The

Fig. 2. (A) Serial changes of left ventricular end-diastolic stress (LV EDS) in responders and non-responders after PLV. (B) Serial changes of left ventricular end-systolic stress (LV ESS) in responders and non-responders after PLV. *\(P < 0.05\) vs. baseline; †\(P < 0.001\) vs. baseline; ‡\(P < 0.05\) versus early; §\(P < 0.01\) versus early, Scheffe post-hoc testing.

Fig. 3. (A) Serial changes of left ventricular diastolic major-to-minor (L/D) axis ratio in responders and non-responders after PLV. (B) Serial changes of left ventricular systolic major-to-minor (L/D) axis ratio in responders and non-responders after PLV. *\(P < 0.001\) versus baseline, Scheffe post-hoc testing.

Following PLV, the LV diastolic major-to-minor axis ratio in responders was higher at all three time points \(P \leq 0.0003\) versus baseline for all versus baseline), with no change in non-responders (Fig. 3A). The two groups showed a group-by-treatment interaction \(P = 0.005\), with-
mean mitral regurgitation grade in responders was 0.40 ± 0.89, 0.40 ± 0.55 and 0.60 ± 1.34 early, at mid-term, and late after PLV and mitral valve repair, respectively. While there was no difference between the groups (P = 0.14, repeated measures ANOVA) and no interaction between groups and the time (P = 0.14), there was an apparent trend of non-responders to increase mitral regurgitation over time.

3.3. Predictors of response to PLV

Univariate logistic regression identified that the lower early postoperative LV systolic major-to-minor axis ratio (P = 0.024) and lower early postoperative end-systolic stress (P = 0.030) predicted an unfavorable outcome late after PLV. Multivariate logistic regression analysis identified both an early LV systolic major-to-minor axis ratio and early LV end-systolic stress as independent predictors of late heart failure after PLV (P = 0.0005).

4. Discussion

PLV was introduced as an option for the treatment of end-stage heart failure [17]. However, data are scarce on how long the initial LV volume reduction lasts, and how it affects functional capacity [18]. A previous study reported long-term effects of PLV on LV volumes and the ejection fraction [19]. However, there is no information on the long-term effects of PLV on the reduction of LV wall stress, a stated goal of this procedure [17].

4.1. Hemodynamic data and suggested mechanisms leading to overt heart failure following PLV

We confirmed that after PLV ventricular redilation occurs in all patients, irrespective of their functional status [19]. On the other hand, we found a gradual increase of end-systolic stress in non-responders only, in whom it returned almost to baseline values at late follow-up. Interestingly, higher early postoperative end-systolic stress was associated with a better outcome. It appears that this association was not the result of the elimination of patients who died within 12 months. It is possible that high early end-systolic stress reflected a better LV pressure generating capacity in responders. Importantly, the increase of LV end-systolic stress in non-responders was preceded by an increase of end-diastolic stress at mid-term follow-up.

Only systolic LV geometry separated patients as responders and non-responders early after PLV, with diastolic LV geometry showing a similar trend. Interestingly, the postoperative LV geometry in the two groups of patients was different despite the fact that in all of them the same type of reconstruction was attempted. Since all relevant preoperative characteristics were similar, it appears that the reason for this variability is probably the form of resection. The form of resection is affected by patient factors, such as actual coronary anatomy and papillary muscle position [5]. It is possible that it may also be influenced by the surgical technique.

In contrast to changes in LV geometry and end-diastolic stress, the decline of the LV ejection fraction in non-responders occurred only late after PLV. These observations are supported by the analysis of LV ejection fraction changes after adjustment for end-systolic stress. This is important as the increase of the LV ejection fraction following PLV is mediated by a decrease of end-systolic stress [1]. Although, as expected, there was no overall effect of PLV on the end-systolic stress-adjusted LV ejection fraction, it also showed a separation of the two groups at late follow-up.

These findings suggest a possible association between early unfavorable postoperative LV geometry, a delayed increase of LV preload and a late decrease of the LV ejection fraction. As the two patient groups showed early separation according to systolic geometry, it may imply that worse geometry forces the left ventricle to perform its work on a rightward (high-preload) portion of the Frank–Starling curve [1]. Excessive preload may depress LV ejection performance [20], while its normalization may improve ejection [21]. Our data on changes of the LV ejection frac-
tion are in line with these findings, showing its late decrease in a high-preload group of non-responders, and its preservation in a low-preload group of responders.

4.2. Previous studies

Studies that evaluated predictors of survival following PLV [4–7,19] indicated the importance of preoperative histology. It has been shown that the myocyte diameter was the only predictor of mid-term outcome following PLV [19] and that myocardial fibrosis was inversely correlated with postoperative LV elastance [22]. However, we did not find an association between preoperative histology and either outcome or LV function. It is possible that this may be due to a very narrow distribution of values of percentage fibrosis and myocyte diameter.

4.3. Clinical implications

Patients with refractory heart failure remain a clinical challenge even in a contemporary era as newer treatment modalities may provoke side effects [23]. However, PLV is done with little consensus about patients who may benefit [18], how large the LV resection should be [24], and into what shape LV should be remodeled [25]. Our data suggest that the refinement of the surgical technique is desirable, with the goal of making LV as elongated as possible. Interestingly, a computer simulation study noted a greater effect of lateral (ventricle more elongated) as opposed to apical ventriculectomy (ventricle less elongated) [25]. Our data strongly indicate that early postoperative LV geometry has a major impact on LV function and clinical status [1].

4.4. Study limitations

First, the present study focuses on the behavior of LV performance after a successful PLV procedure. The utility of this information is limited, since the issue of patients’ selection was not addressed. However, we analyzed ‘the best-case-scenario’, that is, what one should expect from PLV when possible complications of the early postoperative period are resolved.

Second, all patients in this study had either mitral valve repair or replacement, which is a mandatory part of a PLV. Thus, changes induced by elimination of mitral regurgitation cannot be separated from changes induced by ventricular remodeling. However, the degree of preoperative mitral regurgitation was similar in the two groups.

Finally, it is possible that factors other than geometry may have influenced the outcome of PLV, such as preoperative hemodynamics, postoperative mitral regurgitation, diastolic dysfunction or neurohormonal activation. Besides having a lower cardiac index, non-responders tended to be more frequently in a higher preoperative functional class, with longer symptom duration and higher LV end-diastolic pressure. Despite that, the major prognostic factor was early postoperative LV systolic geometry. There was a trend to increase mitral regurgitation over time in non-responders. However, since the degree of mitral regurgitation early postoperatively was similar in responders and non-responders, it seems that its presence postoperatively was not related to PLV failure during follow-up. It is possible that the use of an annuloplasty ring may prevent the appearance of mitral regurgitation. Similarly, diastolic dysfunction (defined as increased end-diastolic stress and/or increased end-diastolic pressure) was not present early after the operation, but developed afterwards in non-responders.

In conclusion, beneficial effects of PLV on patients’ functional status are preserved for at least 12 months after surgery in a moderate number of survivors. As our data indicate that the functional status late after PLV is affected by early postoperative LV geometry, it is possible that the refinement of the surgical technique may confer these beneficial effects to a larger proportion of patients.

References