CARDIOTHORACIC TRANSPLANTATION

PARTIAL LEFT VENTRICULECTOMY FOR DILATED CARDIOMYOPATHY: IS THIS AN ALTERNATIVE TO TRANSPLANTATION?

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Objective: To determine the late effectiveness of partial left ventriculectomy and risk factors for failure.

Methods: Between May 1996 and December 1998, partial left ventriculectomy and concomitant mitral valve surgery were performed in 62 patients (95% transplant candidates) with a mean age of 54 years (range 17-72 years). All patients were in New York Heart Association functional class III (38%) or IV (62%) because of idiopathic dilated cardiomyopathy (59 patients) or ischemic, valvular, or familial cardiomyopathy (1 patient each). Outcomes considered for multivariable analysis included implantation of left ventricular assist device, return to class IV heart failure, relisting for transplantation, and death.

Results: Partial left ventriculectomy reduced the left ventricular end-diastolic diameter immediately preoperatively to immediately postoperatively (from 8.4 ± 1.1 cm to 5.92 ± 0.8 cm; $P = .01$), reduced the left ventricular end-diastolic volume index (from 133 ± 48.6 mL to 64.1 ± 26 mL; $P < .0001$), and increased the left ventricular ejection fraction (from 16 ± 7.6 to 31.5 ± 10.9 ; $P < .0001$). Survival was 80% and 60% at 1 and 3 years after surgery and freedom from failure was 49% and 26%, respectively. Increased systolic pulmonary artery pressure, decreased maximum exercise oxygen consumption, and increased left atrial pressure were associated with failure and/or death. The degree of preoperative mitral regurgitation did not correlate with clinical outcome.

Conclusions: Early and late failures preclude the widespread use of partial left ventriculectomy. However, in view of its sometimes beneficial effect, use in situations that do not allow for transplantation or as a biologic bridge to transplantation may be appropriate. (J Thorac Cardiovasc Surg 2001;121:879-93)

Despite marked improvement in the pharmacologic treatment of end-stage heart failure, the prognosis is still poor with a high mortality rate especially for those who have a dilated heart.¹ Because heart transplantation is limited and expensive, alternate surgical procedures have been investigated for these patients.²⁻⁴ Partial left ventriculectomy (PLV) with reduction of left ventricular (LV)

volume leads to reduced wall tension, aims to restore the normal mass/volume ratio, and has been proposed as a treatment modality for heart failure resulting from dilated cardiomyopathy.⁵⁻⁷ Although early data have been encouraging, with improvement of LV function and reversal of congestive heart failure, patient outcomes have been variable, different surgical techniques have been used, and long-term survival and prolonged beneficial effects have yet to be evaluated.^{6,8-12} Furthermore, patient selection criteria remain unclear.¹³⁻¹⁵

The Cleveland Clinic, therefore, prospectively evaluated this operation as a surgical option for patients with advanced heart failure resulting from dilated cardiomyopathy. In the initial publication from that series, we made several positive observations, including acute improvement in LV function, mitral regurgitation, and

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Table I. Variables considered in risk analysis

Baseline		Evaluation	Preop		
			In operating room	Operative	Postop
Demographic	Clinical status	Hemodynamics	Hemodynamics	Operative	Postop
Age, BSA, sex, race	Duration of HF, preop inotropes	BP (diastolic, systolic, mean [mm Hg]), exercise maximum MVO_2 ($\text{mL} \cdot \text{min}^{-1} \cdot \text{kg}^{-1}$), HR (beats/min), CO ($\text{L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$), indexed LV internal diameter (mm/m^2)	BP (diastolic, systolic, mean [mm Hg]), PAP (diastolic, systolic, mean [mm Hg]), HR (beats/min), CO (L/min), CI ($\text{L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$), RAP, LAP (mm Hg)	Papillary resection (anterior, posterior), MV annuloplasty with ring, TV repair, LV mass resected (g)	
		LV function	LV function	LV function	LV function
		LVEF, LVEDV (mL), LV internal diameter (mm), indexed LVEDV (mL/m^2), indexed LV internal diameter (mm/m^2), 0-4+ MR	LVEF, LVEDV (mL), LV diameter (mm), indexed LVEDV (mL/m^2), indexed LV internal diameter (mm/m^2), 0-4+ MR, SV	LVEF, LVEDV (mL), LV internal diameter (mm), indexed LVEDV (mL/m^2), indexed LV internal diameter (mm/m^2), differences in preop and postop measures of LVEDV and LVEDD	0-4+ MR

BSA, Body surface area; HF, heart failure; BP, blood pressure; MVO_2 , oxygen consumption; HR, heart rate; CO, cardiac output; LV, left ventricular; PAP, pulmonary artery pressure; CI, cardiac index; RAP, right atrial pressure; LAP, left atrial pressure; MV, mitral valve; TV, tricuspid valve; LVEF, left ventricular ejection fraction; LVEDV, left ventricular end-diastolic volume; MR, mitral regurgitation; SV, stroke volume; LVEDD, left ventricular end-diastolic diameter.

clinical functional class during early follow-up (mean 5 months).⁸ We also noted, however, the occurrence of unpredictable early failures (22%) and concluded that the operation warranted investigation, but not widespread dissemination, as an alternative to transplantation until several issues were studied.^{8,16} Those issues included long-term durability, the role of associated mitral valve repair, and risk factors that could be useful to determine candidate selection.

The purpose of this article is to assess the later effects of PLV in terms of (1) clinical time-related outcomes, (2) factors predictive of these outcomes with specific attention to the influence of preoperative mitral regurgitation, and (3) assessment of the durability of acute improvement in LV function and mitral valve competence.

Patients and methods

Patients. Sixty-two patients (76% male; 54 ± 14 years, range 17-72 years) underwent PLV between May 1996 and December 1998. All patients were in New York Heart Association functional class III (38%) or IV (62%). All but 3 were transplant candidates and listed as United Network for Organ Sharing status 1 ($n = 23$) or status 2 ($n = 36$). Inotropic support preoperatively included inotropic agents in 23 patients, intra-aortic balloon counterpulsation in 3 patients, and an LV assist device (LVAD) in 1 patient (HeartMate LVAD; Thermo Cardiosystems, Inc, Woburn, Mass).

Patient selection was based on the hypothesis that patients with dilated cardiomyopathy without extensive areas of scar

would benefit from the procedure.⁸ An LV end-diastolic dimension (LVEDD) of more than 7.0 cm as determined by echocardiography was a prerequisite. All but 3 patients were evaluated and accepted as transplant candidates should mechanical circulatory support or cardiac transplantation be necessary after the PLV surgery.

Informed consent was obtained from all patients after verbal and written discussion of risks, alternatives, and perceived benefits of the operation were discussed by the cardiologists, surgeon, and other members of the heart failure/transplant team. The 62 patients were chosen from approximately 3000 referrals. Most often patients were turned down for medical reasons or because the patient was too well, but other patients refused PLV after informed consent discussions and continued toward transplantation or with medical therapy. Patients were reviewed at the weekly heart failure/transplant team meeting as part of the Kaufman Center for Heart Failure. The Cleveland Clinic Institutional Review Board was notified of this prospective study and reviewed and approved protocols regarding blood samples for neurohormones and a study of amiodarone use.

At the time of preoperative evaluation all patients had heart failure. Only patients with heart failure of at least 6 months' duration were eligible (range 6-240 months). All patients referred for surgery were evaluated by at least one heart failure cardiologist from The Cleveland Clinic Foundation and had been optimized with medical therapy. Medications at the time of surgery in the 62 patients were angiotensin-converting enzyme inhibitor, 47 (76%); β -blocker, 10 (16%); digitalis, 45 (73%); loop diuretic, 50 (81%); metolazone, 6 (10%); amiodarone, 10 (16%); dobutamine or milrinone, 23 (37%); and warfarin, 16 (26%).

Fig 1. Time-related survival after PLV. Also shown in the figure is the hazard function analysis for risk of death depicted enlarged for clarification (scale is 0%-25%). Numbers within parentheses represent patients.

Optimal medical therapy for heart failure was reinstituted as soon as possible after surgery, including angiotensin-converting enzyme inhibitors, diuretics, digoxin, and amiodarone.^{7,8} β -Blockers, including carvedilol, were added as tolerated. Beginning in 1997 implantable defibrillators were implanted for most patients before hospital discharge.

Surgical technique. The surgical technique used is a modification of that originally described by Batista and associates⁶ and has been published earlier.⁸ In brief, a wedge-shaped portion of the left ventricle supplied by the circumflex artery was resected. If possible, the papillary muscles were left intact ($n = 29$; 47%), but if needed to obtain normal LVEDD, one or both papillary muscles were resected and transferred to an adjoining site on the ventricular wall ($n = 33$; 53%). A mitral annuloplasty was performed using the Cosgrove-Edwards annuloplasty system (Baxter Healthcare Corp, Edwards Division, Irvine, Calif). In addition, the free edges of the anterior and posterior mitral leaflets were approximated (Alfieri stitch). Due to residual 2+ mitral regurgitation at the end of the operation, 2 patients underwent intraoperative mitral valve replacement. Papillary muscle resection and reimplantation was performed as described⁸ in 33 patients (53%); 10 of them (16% of total cases) had both anterior and posterior resections, 3 had only anterior resection, and 20 had only posterior resection. Concomitant surgical procedures included tricuspid valve repair (36 patients), coronary artery bypass grafting (5 patients), and aortic valve repair (1 patient).

Time-related outcomes

End points. The end points were (1) all cause mortality, (2) implantation of an LVAD, (3) return to class IV heart failure (including relisting for transplantation), (4) use of an implantable defibrillator, and (5) the earliest of these end points (event-free survival).

Clinical follow-up. None of the patients were lost to follow-up, which was performed at The Cleveland Clinic when-

ever possible. Patients were asked to return to The Cleveland Clinic at 3, 6, and 12 months and annually thereafter. Because many patients resided far away, they were not always able to return. Patients unable to return for follow-up were contacted by telephone for determination of clinical events and functional capacity. Referring physicians were also contacted for follow-up, including echocardiograms and functional studies.

Mean follow-up was 24 ± 12 months and encompasses 76 patient-years. The longest follow-up extends to 3.5 years. Among surviving patients, 10% have been followed up for 3 or more years, 73% have been followed up for 2 or more years, and 94% for more than 1 year.

Time-related estimates and their predictors. Non-parametric estimates of outcomes were obtained by the method of Kaplan and Meier.¹⁷ A parametric method was used to resolve the number of phases of instantaneous risks of each event (hazard function) and to estimate their shaping parameters.¹⁸

The multivariable analyses of outcomes were preceded by exploratory analysis of the variables in Table I, including correlation analysis, stratified life-table analyses, and decile risk analysis of ordinal and continuous variables to determine possible transformations of scale needed to calibrate properly the variables to each outcome. Among the potential risk factors screened were several measurements obtained across time preoperatively for each patient, including hemodynamic measures and echocardiographic LV function. In addition, echocardiographic assessments of mitral valve regurgitation required incorporation with an analysis of a time-varying covariable. Thereafter, multivariable analyses were performed sequentially, first considering baseline and demographic variables, then preoperative measures, then immediate postoperative measures, and finally, the sequence of postoperative estimates of mitral valve regurgitation. The analysis used a directed

Fig 2. Time-related freedom from implantation of LVAD after PLV. Numbers within *parentheses* represent patients. Also shown in the figure is the hazard-function analysis for risk of LVAD implantation, depicted enlarged for clarification (scale is 0%-25%).

Table II. Predictors of time related outcomes

Risk factors	Coefficient $\pm$ SD	P value
Death	0.083 $\pm$ 0.023	.0004
Increasing PAP at evaluation (systolic)		
LVAD*	0.083 $\pm$ 0.023	.006
Decreasing exercise maximum MVO_2 †		
Return to class IV	-1.61 $\pm$ 0.59	.0002
Decreasing exercise maximum MVO_2 ‡		
Event-free survival	0.89 $\pm$ 0.24	.008
Increasing preoperative mean LAP§		

PAP, Pulmonary artery pressure; LVAD, left ventricular assist device; MVO_2 , oxygen consumption; LAP, left atrial pressure.

*Early-phase risk factor (all other events contain late-phase risk factors).

†Natural logarithmic transformation.

‡Inverse transformation.

§Natural logarithmic transformation.

technique of entry of variables into the multivariable model.¹⁹ The *P* value criterion for retention of variables in the final models was .1.

Durability of acute LV improvement. Serial echocardiographic measurements, hemodynamics, and clinical assessment were performed immediately preoperatively, immediately postoperatively, 3, 6, 12 months, and annually postoperatively in survivors. Intraoperative transesophageal echocardiography was obtained from all patients with HP Sonos 5.0/3.7-MHz probes with an HP Sonos 1500/2500 echocardiography machine (Hewlett-Packard Company, Palo Alto, Calif). LV dimensions and volumes were quantified using the disks from the apical 4-chamber view. The amount of mitral valve regurgitation was assessed qualitatively using a categorical grade from 0 (none) to +4 (severe).

LV ejection fraction (LVEF), LVEDD, LV end-diastolic volume index (LVEDVI), and mitral valve regurgitation grade were analyzed by longitudinal data analysis method.²⁰ A random coefficients model was fitted to the repeated measures to quantify postoperative time trends (Proc mixed in SAS; SAS Institute, Inc, Cary, NC). For the analysis of mitral regurgitation, we used longitudinal repeated-measures modeling for ordinal categorical variables (Proc GenMod in SAS), assuming a multinomial distribution with an ordinal logistic characteristic (link function). All these analyses used the exact time of assessment and all available data, although they were truncated in patients at the time of death, transplantation, or follow-up.

Presentation. Mean values are presented $\pm$ 1 SD. Confidence levels (CL) for proportions are 68%, corresponding to 1 SE. Nomograms were constructed by solving each multivariable equation for freedom from each event at 3 years.

Results

Time-related outcomes

Survival. There were 2 hospital deaths (3.2%, CL 1.0%-7.5%). Survival was 99%, 80%, and 60% at 30 days, 1 year, and 3 years (Fig 1). This included 3 patients who died after transplantation; thus, survival before transplantation was 99%, 82%, and 64% at 30 days, 1 year, and 3 years. The risk of death (hazard function) consisted of two phases, an early phase that peaked after about 4 months (with a risk of approximately 6%/month) and a constant hazard phase of 1.2%/month that merged with the early hazard phase by 12 months (Fig 1). Mode of death included heart

Fig 3. Time-related freedom from return to functional class IV heart failure after PLV. Also shown in the figure is the hazard-function analysis for risk of return to class IV heart failure, depicted enlarged for clarification (scale is 0%-25%). Numbers within *parentheses* represent patients.

Fig 4. Time-related freedom from composite events (defined as death, relisting for transplantation, implantation of LVAD, or return to class IV heart failure) after PLV. Also shown in the figure is the hazard-function analysis for risk of composite events, depicted enlarged for clarification (scale is 0%-25%). Numbers within *parentheses* represent patients.

failure/arrhythmias (11 patients), unwitnessed sudden death (4 patients), multiorgan failure (4 patients, 1 after transplantation), and stroke, witnessed cardiac arrest, and acute rejection (1 patient each).

LVAD. Eleven patients (18%, CL 13%-24%) received an LVAD as rescue therapy. Of these, 2 died of multiorgan failure, 8 received a heart transplant, and 1 was removed from LVAD support after LV recovery (this patient was in New York Heart Association class III

after 3 years). Freedom from LVAD was 85%, 83%, and 82% after surgery at 30 days, 1 year, and 3 years (Fig 2). The hazard function rapidly declined after a peak of 1.8%/month at 30 days after surgery (Fig 2).

Class IV heart failure. Thirty-two patients returned to class IV heart failure. Freedom from class IV failure was 81%, 57%, and 42% at 30 days, 1 year, and 3 years (Fig 3). The hazard function rapidly declined from a peak of 8.4%/month at 30 days postoperatively, giving

Fig 5. Nomogram depicting the risk of late (at 3 years) death in relation to increased systolic pulmonary artery (PA) pressure.

Fig 6. Nomogram depicting the risk of late (at 3 years) return to class IV heart failure in relation to decreased maximum exercise oxygen consumption.

way to a slightly increasing hazard of 1% to 1.9%/month between 12 and 36 months (Fig 3).

Event-free survival. Event-free survival was 80%, 49%, and 26% at 30 days, 1 year, and 3 years (Fig 4). The hazard function revealed a rapidly declining early phase with a risk of 8.6%/month at 30 days, which merged with a slightly declining late phase between 3.3% and 2.2%/month at 12 to 36 months of follow-up (Fig 4).

Predictors. For each time-related outcome, a single predictor was identified (Table II). Increased pulmonary artery systolic pressure (beyond 40 mm Hg) at evaluation was a powerful predictor of poor survival (Fig 5). Reduced maximum exercise oxygen consump-

tion at baseline was associated with a rapid return to class IV heart failure (Fig 6). The higher the left atrial pressure, the lower the event-free survival (Fig 7). Preoperative mitral valve regurgitation was not a risk factor for any post-PLV outcome (Figs 8 and 9). When follow-up time-related echocardiographic assessment of postoperative mitral valve regurgitation was considered, it was found unlikely to be related to death (coefficient 0.39 ± 0.35 ; $P = .3$), return of class IV heart failure (coefficient -0.017 ± 0.27 ; $P = .5$), or event-free survival (coefficient 0.24 ± 0.22 ; $P = .3$). Furthermore, no significant risk with respect to survival, return to class IV heart failure, or the composite late event was

Fig 7. Nomogram depicting the risk of late (at 3 years) composite events in relation to increased mean left atrial pressure (P_{LA}).

Fig 8. Influence of preoperative mitral regurgitation on survival after PLV. The patients were divided into 2 groups; 1 group with mitral regurgitation grade 0, 1+, or 2, and 1 group of patients with mitral regurgitation grade 3+ or 4+. Note the lack of significance between the groups ($P = .7$).

associated with the resection and reimplantation of anterior, posterior, or both papillary muscles.

Durability of acute LV improvement. PLV reduced the LVEDD immediately preoperatively compared with immediately postoperatively (from 8.4 ± 1.1 cm to 5.92 ± 0.8 cm; $P = .01$) and the LVEDVI (from 133 ± 48.6 mL to 64.1 ± 26 mL; $P < .0001$) while it increased the LVEF (16 ± 7.6 to 31.5 ± 10.9 ; $P < .0001$). Late changes in the LVEDD, LVEDVI, and function were also examined to determine the degree of redilatation

and subsequent impact, if any, on LVEF. Analysis of both LVEDD and LVEDVI postoperatively demonstrated a small but steady trend toward redilatation and increase in volumes (Figs 10 and 11), and late LVEF showed a small but steady decline (Fig 12, Table III).

The proportion of patients with no mitral valve regurgitation declined between operation and the 3-month assessment, giving rise to an increased number of patients with 1+ regurgitation and, to a lesser extent, an increased number with 2+ regurgitation (Tables IV and

Fig 9. Influence of preoperative mitral regurgitation on event-free survival after PLV. The patients were divided into 2 groups: 1 group with mitral regurgitation grade 0, 1+, or 2, and 1 group of patients with mitral regurgitation grade 3+ or 4+. There was a tendency, although nonsignificant, for a difference between the 2 groups of patients ($P = .1$).

Fig 10. Change in end-diastolic diameter across time. Each gray line represents values for a single patient. *Pre* equals the immediate pre-PLV value and *time 0* is the immediate post-PLV value. The dotted line connects the median value pre-PLV with the mean predicted value immediately after PLV. One heavy line is the average time trend representing the so-called fixed-effects portion of the longitudinal data model.

V and Fig 13). However, 3+ mitral regurgitation developed in only 1 patient, and this was the patient with valvular cardiomyopathy. He also had worsening LV function and a high pulmonary vascular resistance. He received a transplant but died of right ventricular dys-

function. None of the patients had MR that was judged to be related to papillary muscle reimplantation.

Automatic implantable cardioverter/defibrillators. Of the 62 patients, 28 had implantable cardioverter/defibrillators, including 7 who had the device preop-

Fig 11. Change in end-diastolic volume index across time. Each *gray line* represents values for a single patient. *Pre* equals the immediate pre-PLV value and *time 0* is the immediate post-PLV value. The *dotted line* connects the median value before PLV with the mean predicted value immediately after PLV. One *heavy line* is the average time trend representing the so-called fixed effects portion of the longitudinal data model.

Fig 12. Change in ejection fraction across time. Each *gray line* represents values for a single patient. *Pre* equals the immediate pre-PLV value and *time 0* is the immediate post-PLV value. The *dotted line* connects the median value before PLV with the mean predicted value immediately after PLV. One *heavy line* is the average time trend representing the so-called fixed-effects portion of the longitudinal data model.

eratively. During follow-up, 10 patients had ventricular arrhythmias treated by the implantable cardioverter/defibrillator: 2 of the 7 (29%) with preoperative devices and 8 of 21 (38%) with postoperative devices.

Discussion

Principal findings. In the present study we have demonstrated that PLV for dilated cardiomyopathy is associated with a significant early failure rate and event-free survival at 3 years of only 26%. Furthermore,

Table III. Factors associated with increasing LV measures

Factors*	Coefficient $\pm$ SD	P value
LVEF		
Higher LVEF evaluation	0.51 $\pm$ 0.17	.006
Decrease across time†	-1.57 $\pm$ 0.28	<.0001
Indexed LVEDV		
Increase across time‡	0.029 $\pm$ 0.005	<.0001
LVEDD		
Increase across time§	0.009 $\pm$ 0.002	.0003

LV, Left ventricular; SD, standard deviation; LVEF, left ventricular ejection fraction; LVEDV, left ventricular end-diastolic volume; LVEDD, left ventricular end-diastolic dimension.

*In all cases, the larger the value immediately preceding PLV, the larger the change across time of follow-up.

†Natural logarithmic transformation of time.

‡Interaction term between indexed end-diastolic volume at evaluation and natural logarithmic transformation of time (months).

§Interaction term between end-diastolic dimension at evaluation and natural logarithmic transformation of time (months).

some risk factors for failure have been determined, and the lack of correlation between preoperative mitral regurgitation and clinical outcome has been established. With rare exceptions, late failure was not associated with redilation, drop in LVEF, or return of mitral regurgitation even for patients with papillary muscle resection.

We observed 80% survival at 1 year, which compares favorably with survival reported from other centers.^{6,9-11,21} However, since the freedom from composite events at the same time was only 49%, this indicates that the aggressive use of LVADs and transplantation accounts for this seemingly high survival at 1 year. This is corroborated by the fact that 3-year overall survival was only 60%. It should also be emphasized that varying patient selection and surgical techniques make comparison between centers difficult. Other centers have combined the outcomes for idiopathic dilated cardiomyopathy with patients who underwent PLV for ischemic cardiomyopathy. We excluded our patients with ischemic cardiomyopathy, because reconstruction for ischemic disease has a long history and a much more predictable beneficial effect than does PLV for idiopathic disease.^{22,23} Also, unlike others, we did not think it was adequate to simply report survival and, therefore, sought to determine whether patients were significantly improved by creating the composite event for failure, but not necessarily fatal events.

Although the failure rate was high after PLV, a number of event-free survivors had improvement in subjective clinical status and objective measurements (maximum exercise oxygen consumption) even though

Table IV. Parameter estimates for longitudinal model of mitral valve regurgitation progression across time

Parameter	Estimate $\pm$ SD	P
Months after PLV*	-0.43 $\pm$ 0.090	<.0001
Intercepts†		
1 (Grades 0 vs > 0)	1.03 $\pm$ 0.25	<.0001
2 (Grades $\leq$ 1 vs > 1)	2.6 $\pm$ 0.38	<.0001
3 (Grades $\leq$ 2 vs 3)	5.2 $\pm$ 1.02	<.0001

SD, Standard deviation; PLV, partial left ventriculectomy.

*In [months] natural logarithmic transformation.

†Intercepts for each grade change.

overall ventricular function was not restored to normal and cardiac output changes were modest.^{7,8} These patients did benefit from PLV, and multivariate analysis to assess risk factors has given some insight into the predictors of poor outcome. Earlier analysis based on our smaller patient population with shorter follow-up could only reveal young age and preoperative diastolic function to be risk factors for failure.^{13,24} It was further recognized that these younger patients represented a more severely diseased patient population with higher pulmonary artery pressure and a higher requirement for inotropic support.¹³ On the basis of the present group of patients and follow-up, we were able to identify further preoperative risk factors including increased systolic pulmonary artery pressure, decreased maximum exercise oxygen consumption, and increased left atrial pressure. Presumably, PLV in patients without these risk factors will increase the 26% subgroup of patients who were alive and well in late follow-up. Emergency surgery,²¹ preoperative poor ventricular compliance (ie, diastolic dysfunction),²⁴ increased myocardial cell diameter,^{14,25} and a left dominant coronary artery system²⁶ are other suggested risk factors for failure. We did not have the tissue analyzed for myocardial cell diameter and, therefore, cannot comment.

The reduction in LV wall stress quantified by echocardiography and magnetic resonance imaging scans and the improvement in LV systolic function may be offset by a reduction in compliance.^{24,27-29} Computer modeling and finite element analysis indicate that the reduction in LV diastolic function will blunt the improvement in myocardial efficiency.^{29,30} We have clues that suggest that reduced compliance at baseline may contribute to poorer late outcomes, that is, higher pulmonary artery and left atrial pressures in this study, higher pulmonary artery pressures in young patients in the prior study,¹³ and compliance function derived from pressure-area loops.²⁴ Also, late exercise hemodynamics after PLV showed a significant increase in cardiac index with exer-

Fig 13. Change in mitral valve regurgitation across time. Each *symbol* represents a grade of mitral regurgitation for various grades as time progresses, using the actual trend of regurgitation within each patient, only crudely illustrated by the aggregate proportions at each time point (see Table IV). The number of observations of grade was 56, 38, 18, and 14 immediately postoperatively, and at 3, 12, and 24 months, respectively.

Table V. Progression of mitral valve regurgitation

Regurgitation grade	Time									
	Baseline		1 wk		3 mo		12 mo		24 mo	
	No	%	No	%	No	%	No	%	No	%
0	1	2	34	81	20	53	11	61	6	43
1+	3	5	6	14	11	29	5	28	6	43
2+	12	20	2	5	6	16	2	11	2	14
3+	24	40	0	0	1	3	0	0	0	0
4+	20	33	0	0	0	0	0	0	0	0
Total	60	100	42	100	38	100	18	100	14	100

cise (2.2 ± 0.5 to 3.8 ± 1.6 ; $P = .0077$), but a marked increase in pulmonary artery pressures (pulmonary artery systolic 52 ± 20 mm Hg to 79 ± 17 mm Hg; $P = .0001$; pulmonary artery mean 36 ± 12 mm Hg to 52 ± 10 mm Hg; $P = .0003$), also suggesting abnormal compliance.³¹ We postulate, but cannot absolutely confirm with this small group of patients, that stiff fibrotic hearts are very prone to failure with this operation. To treat these patients without transplantation will require a procedure that decreases wall stress and improves systolic function and myocardial efficiency without impairing diastolic function. Devices in development may bring us much closer to this goal.³²⁻³⁵

The influence of mitral valve repair per se in PLV is of interest. Indeed, it has been shown that mitral valve

repair can reverse LV remodeling and dysfunction in patients with dilated or ischemic cardiomyopathy combined with severe (4+) mitral regurgitation.³⁶⁻³⁸ It should be emphasized, though, that in the present patient population (as with most cardiomyopathy patients), the mitral regurgitation was generally less severe. Furthermore, multivariate analysis of risk factors could not distinguish any favorable effects of PLV and mitral valve repair in patients with preoperative moderately severe (3+) or severe (4+) mitral regurgitation in relation to patients with mild (1+) to moderate (2+) mitral regurgitation. If anything, there was a tendency toward a worse outcome for patients with preoperative mitral regurgitation grades 3 to 4 ($P = .1$). This is also supported by reports on the isolated positive

effect of PLV, without mitral valve reconstruction, in patients with dilated cardiomyopathy lacking mitral regurgitation.^{39,40} However, to maintain the beneficial effects of PLV, we thought it was important to prevent the return of mitral regurgitation and redilatation of the left ventricle.^{8,12} Therefore, we were very aggressive with valve repair to avoid chronic volume overload that we thought might lead to late redilatation and failure. There was a slight increase in the mitral regurgitation during follow-up, but 4+ regurgitation did not develop in any patient and 3+ regurgitation developed in only 1 patient. Mitral regurgitation after surgery was not associated with clinical failure. Whether the repair held up due to the small annuloplasty ring, the Alfieri repair, or the reconstruction of the left ventricle that reduced apical displacement of the papillary muscles cannot be determined from this study.

This study answered several other questions about the late effects of PLV.⁴¹ Late redilatation was unusual and, therefore, was not the cause of failure. The modest improvement in LVEF decreased very slowly but was not associated with failure. The incidence of sudden death was relatively low ($n = 4$) and can be avoided after this operation, in large part by the liberal use of implantable cardioverter/defibrillators and amiodarone. A previous study failed to show that the ventricular tachycardia morphology was related to the surgical scar.⁴²

Initially there was a discussion that this operation should be evaluated in a randomized trial versus medical therapy or cardiac transplantation.^{7,16,39,41,43,44} We resisted this strategy for several reasons. First, comparing the earliest "learning curve" results of this complex operation to established therapies without some preliminary experience with patient selection, operative technique, and perioperative care seemed premature. We pursued our strategy of a carefully monitored prospective study to accrue information to determine whether such a study would be warranted, and in which patients. Second, the practical aspects of a large multicenter clinical surgical trial were daunting. These aspects included funding, careful patient selection, uniform surgical technique and postoperative care, as well as management of the medical control population or transplant arm of the study. We did not think this study could be contemplated until clinical follow-up indicated that such a trial warranted the time and expense required. Finally, as events unfolded, we became aware of devices that may be applied to the same patient population, but with the expectation of a lower morbidity and with Food and Drug Administration oversight

of clinical trials.³²⁻³⁵ In this regard we think the Batista operation may be a step along the way (like the Vineberg operation before coronary artery bypass) and that a prospective study is no longer warranted.

Limitations of the study. This is a prospective but not randomized study; therefore, no direct comparison to other surgical procedures or medical therapy alone can be made. Although this study was aimed at investigating the impact of the surgical procedure, it was considered important to maximize pharmacological treatment postoperatively. Therefore, postoperative adjustment of drugs may have contributed to some observed positive effects. Malignant arrhythmias, which were the cause of death in some early patients, may have been avoided by implantation of defibrillators in all patients; this was only routinely done in later patients. Serial comparisons are naturally biased in that only patients reaching follow-up are included in the analysis performed. We attempted to account for this by our statistical analysis of results. Nevertheless, patients whose treatment failed early could not have values obtained later, and some patients lived far from Cleveland and could not return for follow-up. However, follow-up was complete for clinical events.

Clinical inferences. In conclusion, in this pilot study of PLV with mitral valve surgery for dilated cardiomyopathy, we observed a 60% 3-year survival and 26% freedom from failure. Failures were largely unpredictable from preoperative clinical studies, but risk factors included increased left atrial and systolic pulmonary artery pressures and decreased maximum exercise oxygen consumption. Modest improvement in LV systolic function was sustained and late ventricular dilatation was rare. Correction of preoperative mitral regurgitation did not account for the clinical benefit, and some evidence indicates that worsening diastolic function may have contributed to failures. We infer from these observations that the Batista procedure is not a predictable reliable alternative to transplantation. In other cultures and socioeconomic settings this procedure may be further investigated, or in a nontransplant population, or as an alternative to LVADs as a "biologic" bridge-to-transplantation. In our opinion, the experience was not a dead end, however, and may have spawned devices that can be applied with a low morbidity to change LV shape and improve LV function.

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Discussion

Dr Gianni Angelini (*Bristol, England*). I congratulate Dr Franco-Cereceda and his colleagues for this excellent presentation, which undoubtedly will shed further light on what is still a very controversial surgical procedure. We in Bristol had a similar experience in terms of early outcome and late follow-up, the only difference being that we only operated on patients who were not suitable for transplantation. In your series, Dr Franco-Cereceda, it is my feeling that you made a deliberate attempt to preserve the mitral valve. We recently reported 2 cases in which an interpapillary resection and a successful repair of the mitral valve required further revision because we were unable to discontinue cardiopulmonary bypass. After an enlarged resection and mitral valve replacement, the patient did well.

Do you think your approach may have limited in some of your cases the extension of your resection and therefore undermined the full potential of the surgical procedure?

My second question relates to papillary reimplantation. I am slightly uncomfortable about this technique. Do you think this may have affected the long-term ventricular function and perhaps even mitral valve competence? Since you have 2 fairly large groups of patients in whom the mitral valve was repaired, with or without implantation of the papillary muscle, can you describe how these 2 groups did at late follow-up and whether there was any difference?

Dr Franco-Cereceda. Thank you very much, Dr Angelini, for those remarks. The impact of mitral valve repair or replacement in relation to the Batista procedure has attracted a great deal of attention. It is important to realize that what we say is not that the mitral valve repair is not beneficial for the heart. We see, as have others, that with a postoperative return of mitral valve regurgitation the outcome is worse.

We could not see any real differences in outcome between patients undergoing resection of the papillary muscle and those with an intact papillary muscle. The subvalvular apparatus is important for survival in general in mitral valve regurgitation, and preservation of the valve is important to obtain the best possible results, because there will always be some changes in the geometry when the papillary muscles are removed. Basically, all patients received an annuloplasty system and the Alfieri stitch.

As shown in the figures, there is no redilatation, indicating that we have no return of mitral valve regurgitation, and there are essentially no differences between the groups with and without papillary muscle resection.

Dr Hisayoshi Suma (*Kamakura, Japan*). We continue to perform ventriculoplasty for nonischemic dilated cardiomyopathy and have done 68 cases in 3 years with a 2-year survival of 71%. From this experience, we have learned that some patients with nonischemic dilated cardiomyopathy have a bad septum and a relatively intact lateral wall, which is detectable on intraoperative echocardiography. The ordinary Batista procedure could be dangerous in such cases, so we have used endoventricular anteroseptal patch plasty in 9 patients.

Have you found that the extent of myocardial damage in nonischemic dilated cardiomyopathy is not always homogeneous and some surgical modification is necessary when the weakest part is located in the septum?

Dr Franco-Cereceda. Thank you, Dr Suma, for your remarks and your question. We know of the very elegant studies performed by you and your colleagues in Japan. What we have been trying to do is resect the lateral wall and, if needed, the posterior wall, but I am sure that modifications of the procedure can be done. Such modifications would definitely include patching of the septum. We have not been doing that, and we do not anticipate any more of these operations, so I cannot comment more than that.

Dr O. Howard Frazier (*Houston, Tex*). In July of 1996, at about the same time this procedure was started in Cleveland, we did our first case. The patient was severely ill with class IV disease and remains well in class I nearly 4 years later. However, our long-term results in general reflect what was so ably presented here. A comparison of our results with those of a nontransplant center in Belgrade, Yugoslavia, though, revealed a very interesting correlation between myocyte diameter and relatively good results, which they experienced, as well as duration of heart failure. This may simply mean that the favorable outcomes may be more reflective in the less ill patients, as I think your data seemed to support—patients with better myocardial oxygen consumptions and low pulmonary pressures. Yet 26% of your patients remain out of class IV. Do you think it could be an alternative to transplantation in a properly selected group?

Dr Franco-Cereceda. Thank you, Dr Frazier, for your remarks and your question. First, let me comment on your studies on myocyte sites and fibrosis. Your suggestion of a histologic classification system regarding these procedures is a very intriguing one. We know of your excellent results, and we also know that you, in comparison with the Belgrade

group, have been looking at the different reasons for the differences in outcome.

With regard to your question, I think you are right that it is important not to delay if you are going to operate on these patients. It is probable that the more severe the disease, the more unfavorable the outcome. But, as you mentioned, 26% of our patients are event-free at 3 years' follow-up. There is definitely something to this operation.

The reason that we will not use it at The Cleveland Clinic is that we are a transplant institution. Later in this meeting, Dr Patrick McCarthy will present some other surgical options for these patients. We are definitely not condemning the operation. We are merely stating that it is unpredictable and unreliable and should be restricted to cases not amenable to transplantation or other modes of therapy.

Notice of correction

In the February 2001 issue of the *Journal*, in the article by Bellinger and associates titled "Developmental and Neurologic Effects of Alpha-Stat Versus pH-Stat Strategies for Deep Hypothermic Cardiopulmonary Bypass in Infants," (2000;121:374-83), an error was made. Fig 1 was published twice and Fig 2 was omitted. The correct version of Fig 2 is published below, and the correct version of the article is available online at www.mosby.com/jtcvs.

Fig 2. Box plots of Mental Development Index scores stratified by treatment group (alpha-stat vs pH-stat) and diagnosis group (D-TGA, TOF/other, and VSD/CAVC). Within a box, the solid bar represents the median value, the dashed line represents the mean value, the upper boundary of the closed box represents the 75th percentile, and the lower boundary of the closed box represents the 25th percentile. The vertical lines extend to the 10th and 90th percentiles, with more extreme values plotted as diamonds