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Staged Left Ventricular Recruitment After Single-Ventricle Palliation in Patients With Borderline Left Heart Hypoplasia

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Objectives The goal of this study was to review results of a novel management strategy intended to rehabilitate the left heart (LH) in patients with LH hypoplasia who have undergone single-ventricle palliation (SVP).

Background Management of patients with hypoplastic LH syndrome and borderline left ventricle (LV) involves 2 options: SVP or biventricular repair. We hypothesized that staged LV recruitment and biventricular conversion may be achieved after SVP by using a strategy consisting of relief of inflow and outflow tract obstructions, resection of endocardial fibroelastosis, and promotion of flow through the LV.

Methods Patients with hypoplastic LH and borderline LV who underwent traditional SVP ($n = 34$) or staged LV recruitment ($n = 34$) between 1995 and 2010 were retrospectively analyzed and compared with a control SVP group.

Results Mean initial *z*-scores for LH structures before stage 1 SVP were not significantly different between groups. Mortality occurred in 4 of 34 patients after LV recruitment and in 7 of 34 after traditional SVP. LH dimension *z*-scores increased significantly over time after LV recruitment, whereas they declined after traditional SVP, with significant interaction between stage of palliation and treatment group. Restriction of the atrial septum (conducted in 19 of 34 patients) was the only predictor of increase in left ventricular end-diastolic volume ($p < 0.001$). Native biventricular circulation was achieved in 12 patients after staged LV recruitment; all of these patients had restriction at the atrial septum.

Conclusions In these patients with borderline LH disease who underwent SVP, it is possible to increase LH dimensions by using an LV recruitment strategy. In a subset of patients, this strategy allowed establishment of biventricular circulation. (J Am Coll Cardiol 2012;60:1966–74) © 2012 by the American College of Cardiology Foundation

Neonates with hypoplastic left heart (LH) disease present a unique challenge. At the extremes of mild LH hypoplasia associated with aortic stenosis or coarctation on one end, and hypoplastic left heart syndrome with aortic and mitral atresia on the other, the appropriate management is typically obvious. Patients who have mild LH hypoplasia may require relief of valvular or aortic arch obstruction to preserve biventricular physiology, whereas single-ventricle palliation (SVP) with staged procedures, starting with the Norwood operation, are performed in patients who have severe hypoplasia (1).

At the center of the spectrum, accounting for about 65% of patients, are many variants of borderline LH hypoplasia for which management is not so clear, although SVP is the most commonly applied approach (2,3). In this group, all levels of the LH complex are often affected; this includes valvular stenosis, ventricular hypoplasia, and endocardial fibroelastosis (EFE), which prevent independent function of the left ventricle (LV) as the systemic ventricle. Some patients who have a borderline LH may be well suited for eventual biventricular management but are at higher risk if such a strategy is pursued definitively, particularly in the newborn period (4–7). To pursue the possibility of eventual biventricular circulation in patients who are at high risk for initial biventricular repair, we have applied a strategy in which the circulation is initially supported with SVP while staged procedures are used to relieve inflow and outflow tract obstructions, resect EFE, and promote blood flow

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through the LV. We have termed this approach "staged LV recruitment."

We hypothesized that staged LV recruitment results in growth of LH structures, and eventual biventricular conversion, in patients with borderline LH who are at high risk or are deemed not candidates for definitive early biventricular repair. The primary goal of the current study was to examine the effects of this strategy on LH dimensions and compare these results with the natural history of LH dimensions in a similar group of patients undergoing traditional SVP. We also sought to determine the effects of staged LV recruitment on the clinical outcomes at mid-term follow-up and establish the predictors of increases in LH dimensions among patients undergoing staged LV recruitment.

Methods

Study design. This study was a retrospective review of all patients who presented to Children's Hospital Boston between 2001 and 2010 with a postnatal echocardiographic diagnosis of hypoplastic LH disease and borderline LV who underwent staged LV recruitment. Borderline LH was defined according to a combination of clinical and anatomic criteria. LH hypoplasia, with aortic, mitral, and left ventricular end-diastolic volume (LVEDV) *z*-scores between −5 and −0.5 and presence of LV EFE were pertinent anatomic features. Candidates were deemed to be dependent on prostaglandin infusion or have failed initial attempts at biventricular repair (e.g., balloon dilation of aortic valve, coarctation repair). Patients were excluded if they had aortic or mitral atresia, ventricular septal defect, heterotaxy syndrome, or atrioventricular or ventriculoarterial discordance. Patients undergoing staged LV recruitment were compared with a control group of patients meeting anatomic criteria for borderline LH disease (i.e., LH structure *z*-scores between −5 and −0.5 who underwent traditional SVP between 1995 and 2010). This atypical case-control group included historic as well as contemporary controls. The study was approved by the institutional review board of Children's Hospital Boston.

The primary outcome measures included change in size of LH structures indexed to body surface area over time, as measured by using echocardiography and magnetic resonance imaging, and clinical outcomes (mortality, biventricular conversion). In addition, clinical or treatment variables affecting the size of LH structures were recorded to determine predictors of increased LH size over time. Interventions performed before stage 1 SVP (fetal or postnatal balloon dilation of the aortic valve, attempted biventricular repair), details of staged operative procedures, postoperative course, and reinterventions after biventricular conversion were documented.

Staged LV recruitment strategy. The staged LV recruitment strategy used a combination of methods applied as adjuncts to the initial Norwood procedure, bidirectional Glenn procedure (BDG), or Fontan procedure, or as separate methods when necessary. The following techniques were applied.

Abbreviations and Acronyms

ASD = atrial septal defect
BDG = bidirectional Glenn procedure
EF = ejection fraction
EFE = endocardial fibroelastosis
LA = left atrial
LH = left heart
LV = left ventricle
LVEDV = left ventricular end-diastolic volume
SVP = single-ventricle palliation

RESECTION OF EFE. EFE resection involved removal of the noncompliant fibroelastic endocardial material by sharp dissection. At stage 1 SVP, this was performed through the mitral valve orifice; at subsequent stages, visualization was attained either through the mitral valve or the LV outflow tract. EFE resection was initiated on the posterior LV wall, inferior to the mitral apparatus, and continued down to the apical and septal surface of the LV.

MITRAL VALVULOPLASTY. The mitral valve was approached transeptally, and commonly used techniques to reduce inflow obstruction included division of tethering secondary or accessory chordae, separation of fused papillary muscles, chordal elongation, commissurotomy, augmentation of deficient leaflets, and removal of the fibroelastic tissue that thickened the leaflet.

AORTIC VALVULOPLASTY. Techniques used for left ventricular outflow tract obstruction included commissurotomy, primary repair for leaflet tear when present, debridement of thickened aortic valve leaflets, augmentation of deficient leaflets with pericardium, and subvalvular resection of membrane, muscle, or accessory mitral chordal attachments.

ATRIAL SEPTAL DEFECT RESTRICTION. Restriction of the interatrial communication was performed in some patients, either by partial primary reapproximation of the rim of the atrial septal defect (ASD) or by fenestrated pericardial patch closure (4-mm fenestration), as a means of promoting blood flow through the LV. Early in the experience (2001 to 2004), all patients undergoing rehabilitation procedures underwent restriction of the ASD; subsequent decisions to restrict were based on the subjective impression of adequacy of LH structures, successful EFE resection, and growth potential. In patients undergoing restriction of the ASD, the duration of restriction and transseptal gradient was recorded. Significant restriction was defined as follows: 1) restriction of the atrial septum at any surgical stage; 2) presence of a transseptal gradient of >5 mm Hg by echocardiographic measurement; and 3) maintenance of this gradient for >30 days after surgical restriction.

TRANSCATHETER INTERVENTIONS. Transcatheter balloon dilation of the aortic and mitral valves was performed for recurrent stenosis after surgical valvotomy in selected patients. Balloon atrial septostomy or stent placement was

applied in patients who developed significant left atrial (LA) hypertension after surgical ASD restriction.

ADDITION OF ACCESSORY PULMONARY BLOOD FLOW. In the subset of patients who underwent a stage 2 BDG, a right ventricle-to-pulmonary artery shunt or systemic-to-pulmonary artery shunt was provided to increase pulmonary venous return in an attempt to augment LV preload, either at the time of the BDG or as a separate procedure. The decision to augment pulmonary blood flow was based on the surgeon's subjective impression of the potential for LV recruitment.

Biventricular conversion. Candidates were considered favorable for conversion once near-normalization of LH structures size and function was demonstrated by using noninvasive and invasive imaging. The biventricular conversion procedure included takedown of the aortopulmonary anastomosis and re-establishment of separate LV and right ventricle outflow tract continuity either by direct reanastomosis or by translocation of the pulmonary artery root into the LV outflow tract with conduit reconstruction of the right ventricular outflow tract. In patients who had undergone a BDG, the superior vena cava was disconnected from the pulmonary artery and reconnected to the right atrium, usually at the appendage. In patients with a completed Fontan circulation, the inferior cavopulmonary baffle was also taken down. After biventricular conversion, the need for reintervention was documented, and the most recent echocardiogram was reviewed to determine the LV outflow gradient, dimensions of the left-sided structures, and tricuspid valve regurgitation jet velocity to estimate right ventricle pressures.

Echocardiographic measurements. All initial postnatal echocardiograms were reviewed to determine the initial LV, mitral valve, and aortic valve dimensions before stage 1 SVP. All measurements were indexed to body surface area and expressed as *z*-scores. The presence of mitral or aortic regurgitation was recorded, and the atrial septum was examined to determine the size of the defect. The gradient across the atrial septum was determined by using color wave Doppler analysis.

To determine the progression of LH dimensions over time, serial echocardiographic measurements of LH size were obtained from patients who survived beyond the BDG. In these patients, the echocardiograms before each subsequent stage of palliation as well as the most recent follow-up were examined. For the patients in the staged LV recruitment group who underwent biventricular conversion, the echocardiogram before biventricular repair was used to measure "most recent" LH dimensions. Likewise, for patients in the traditional SVP group who underwent cardiac transplantation, the echocardiogram before transplantation was evaluated as the "most recent" study.

Valvular regurgitation score. The cumulative duration of significant valvular regurgitation (moderate or greater) for both aortic and mitral valves was calculated by reviewing each subject's echocardiogram and summing the durations of the intermittent periods of significant valvular regurgitation.

Statistical analysis. Data regarding sex and percentage of patients undergoing fetal or postnatal balloon aortic valvuloplasty in the traditional SVP and the staged LV recruitment groups were compared by using the Fisher exact test. LH dimensions (LVEDV, long-axis dimension, and aortic and mitral valve diameters) were compared over time between patients undergoing staged LV recruitment and traditional SVP. A 2-way, mixed model, repeated-measures analysis of variance (ANOVA) approach was used to compare differences in *z*-scores for LH dimensions at different stages of repair (baseline = before stage 1, before BDG, before Fontan) between patients in each group. A compound symmetry correlation structure was used to handle the longitudinal data from the same patients over time with the Akaike information criterion to assess model fit to the longitudinal data (8). All *z*-scores are reported in terms of the mean ± SE, and 2-tailed p values were Bonferroni adjusted to correct for multiple comparisons (9). A subgroup analysis was conducted to evaluate the effect of significant restriction of atrial septum on each of the 4 *z*-scores in the staged LV recruitment group by using the same ANOVA strategy. Longitudinal analysis of ejection fraction (EF) for the LV rehabilitation group was performed by using repeated-measures ANOVA. Statistical analysis was conducted with SPSS version 18.0 (SPSS, Inc., Chicago, Illinois).

Results

Patient characteristics. From January 1995 to December 2010, 34 patients with borderline LH disease underwent staged LV recruitment and 34 patients underwent traditional SVP. Attempts at staged LV recruitment were initiated in 2001. The traditional SVP group consisted of 11 patients who underwent stage 1 palliation before 2001, and 23 patients who were contemporary with the staged LV recruitment patients. LH dimensions on the initial postnatal echocardiogram as well as other demographic and patient characteristics are shown in Table 1. There were no significant differences in LH dimensions between the 2 groups at the time of initial postnatal evaluation. In the traditional SVP group, 5 of 34 patients underwent attempts at biventricular management by postnatal balloon aortic valvuloplasty before undergoing stage 1 palliation. Significantly more patients in the staged LV recruitment group underwent fetal and postnatal aortic balloon valvuloplasty, and 2 patients had surgical procedures for biventricular repair before the stage 1 procedure.

Clinical outcomes. A flowchart depicting the clinical progression of patients in each group at most recent follow-up is shown in Figure 1. At a median post–stage 1 follow-up of 9.0 years (1 to 16 years), 7 of 34 patients in the traditional SVP group died, 25 patients had Fontan physiology, and 1

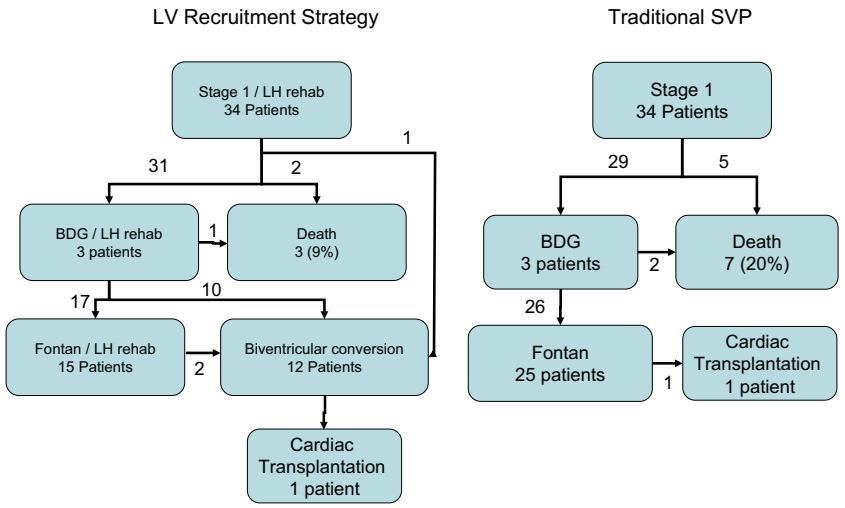

Figure 1 **Current Status of Patients With Borderline LH Undergoing Stage 1 Procedure**

The flowchart depicts the clinical course of patients with borderline left heart (LH) hypoplasia who underwent traditional single-ventricle palliation (SVP) or staged left ventricle (LV) recruitment. The number of patients at each particular stage of palliation at most recent follow-up is shown in **shaded boxes**. Patients in the staged LV recruitment group were most likely to undergo biventricular conversion after a bidirectional Glenn procedure (BDG). rehab = rehabilitation.

underwent cardiac transplantation. At a median follow-up of 5.2 years (1 to 9 years), 4 of 34 patients in the staged LV recruitment group died, 2 after a stage 1 procedure and 2 after stage 2 SVP. Of these patients, 1 was diagnosed with centrotubular myopathy after the stage 1 procedure, and medical care was redirected. The other 3 patients died, likely of cardiac causes: 1 died approximately 1 month after stage 1 palliation, 1 after BDG due to severe biventricular dysfunction, and 1 after BDG due to tricuspid regurgitation and right ventricle dysfunction. Thirteen patients underwent biventricular conversion, but 1 subsequently underwent cardiac transplantation because of ventricular dysfunction. Thus, at most recent follow-up, of the 30 survivors, 3 patients (10%) had BDG physiology, 15 patients (50%) had Fontan physiology, and 12 patients (40%) had native biventricular circulation.

Table 1 **Pre-Operative Patient Characteristics and Size of Left Heart Structures**

Characteristic	Staged LV Recruitment (n = 34)	Traditional SVP (n = 34)	p Value
Male	25 (74%)	27 (79%)	0.78
LVEDV *z*-score	−2.5 ± 1.2	−2.9 ± 0.2	0.07
LV long *z*-score	−2.9 ± 1.8	−3.2 ± 1.9	0.51
Aortic annulus *z*-score	−3.1 ± 1.0	−2.9 ± 1.0	0.42
Mitral valve *z*-score	−2.0 ± 1.3	−2.2 ± 1.6	0.57
Fetal balloon aortic valvuloplasty	14 (41%)	2 (6%)	<0.001
Postnatal balloon aortic valvuloplasty	19 (56%)	5 (15%)	<0.001

Values are n (%) or mean ± SD.

LV = left ventricle; LVEDV = left ventricular end-diastolic volume; SVP = single -ventricle palliation.

Operative details. Technical details of each staged procedure, including specific LH rehabilitation techniques used, are outlined in Table 2. Accessory pulmonary blood flow was provided only in patients with BDG physiology and was

Table 2 **Operative Details of Staged Palliative Procedures**

Stage	LH Rehabilitation	Traditional SVP
Stage 1	(n = 34)	(n = 34)
Median age (days)	18.2 (0–190)	9.1 (0–146)
BTS (%)	18 (53%)	24 (71%)
EFE resection	21 (62%)	—
Mitral valvuloplasty	19 (56%)	—
Aortic valvuloplasty	13 (38%)	—
ASD restriction	13 (38%)	—
Post-operative ECMO	6 (18%)	4 (12%)
Stage 2	(n = 31)	(n = 29)
Median age (months)	6.4 (3–14)	5.9 (2–12)
EFE resection	18 (58%)	—
Mitral valvuloplasty	15 (48%)	—
Aortic valvuloplasty	12 (39%)	—
ASD restriction	10 (32%)	—
Accessory pulmonary blood flow	15 (48%)	—
Post-operative ECMO	2 (6%)	1 (3%)
Stage 3	(n = 17)	(n = 25)
Median age (yrs)	2.6 (1.6–5.1)	2.7 (1.6–4.8)
EFE resection	7 (41%)	—
Mitral valvuloplasty	6 (35%)	—
Aortic valvuloplasty	7 (41%)	—
ASD restriction	3 (18%)	—

Values are median (range) or n (%).

ASD = atrial septal defect; BTS = Blalock-Taussig shunt; ECMO = extracorporeal membrane oxygenation; EFE = endocardial fibroelastosis; LH = left heart; SVP = single-ventricle palliation.

achieved via polytetrafluoroethylene conduit to the pulmonary artery from the innominate artery in 5 patients, right ventricle in 8, and ascending aorta in 2. In addition to LH rehabilitation performed at the time of stage 1 SVP, BDG, or Fontan, 11 additional procedures solely for LH rehabilitation were performed in 9 patients. Thus, the median total number of surgical procedures required between stage 1 SVP and the most recent follow-up was 3 for traditional SVP patients and 4 for staged LV recruitment patients ($p < 0.05$).

LA hypertension after restriction of ASD. Twelve of the 19 patients with significant ASD restriction underwent catheter-based septal balloon dilation and/or stenting due to development of LA hypertension. The indications for ASD balloon dilatation/stenting were respiratory insufficiency requiring reintubation in 3 patients, persistent inotropic support in 2, and asymptomatic LA hypertension demonstrated at elective catheterization in 7. Among these 19 patients with ASD restriction, 6 required an unplanned catheterization and catheter-based intervention. The mean LA pressure in these patients at the time of ASD enlargement was 19 ± 2.6 mm Hg. Four patients underwent repeat restriction of the communication at a subsequent staged operation. The 19 patients who had ASD restriction had a mean ventilatory time after ASD restriction of 9.4 ± 8.0 days (median 6.0 days; range 1 to 28 days) and a mean intensive care unit stay of 17.5 ± 22.5 days (median 7.0 days; range 1 to 96 days).

LH dimensions as a function of time. Longitudinal echocardiographic measurements of LH dimensions were obtained from the 30 patients in the staged LV recruitment group and the 28 patients in the traditional SVP group who survived beyond the BDG (Fig. 2). With respect to LVEDV and LV long-axis *z*-scores, ANOVA displayed a significant interaction between stage of palliation and group ($F = 13.76$, $p < 0.001$) and $F = 34.04$, $p < 0.001$, respectively), which indicated no differences in *z*-scores before stage 1 SVP but significant differences between groups before BDG ($p < 0.005$) and before Fontan or biventricular repair ($p < 0.001$), with more positive *z*-scores among patients who underwent staged LV recruitment. With respect to mitral and aortic valve *z*-scores, ANOVA showed a significant interaction between stage of palliation and group ($F = 5.30$, $p = 0.007$ and $F = 28.98$, $p < 0.0001$, respectively), indicating no differences in *z*-scores before stage 1 SVP or before BDG, but highly significant differences between the 2 groups before the Fontan or biventricular repair ($p < 0.001$).

Impact of valvular regurgitation on biventricular conversion. In patients undergoing staged LV recruitment, significant mitral valvular regurgitation was seen in 17 of 34 patients. The median cumulative duration of mitral regurgitation in these patients was 115 days (range 2 to 564 days). Significant aortic regurgitation was seen in 14 of 34 patients, with a median duration of 232 days (range 5 to 1,790 days). There was no correlation between duration or presence of valvular regurgitation and successful biventricular conversion by univariate analysis.

Relation between ASD restriction and LH dimensions. Patients undergoing staged LV recruitment were analyzed separately to determine the predictors of increase in LH dimensions. By univariate analysis, the only variable found to be predictive of an increase in LVEDV over time was significant restriction of the ASD at any stage. Repeated-measures ANOVA revealed significant differences in LVEDV, LV long-axis, and aortic valve *z*-scores between patients with and without ASD restriction before the Fontan procedure ($p < 0.05$ for each dimension) with no significant differences detected before stage 1 SVP or BDG (Fig. 3). Mitral valve *z*-scores were not significantly different at baseline between patients who had an ASD restriction and those who did not ($p = 0.45$), although *z*-scores were significantly more positive in the ASD-restricted subgroup before BDG ($p = 0.04$) and before the Fontan procedure ($p = 0.004$). All patients who eventually underwent biventricular conversion had significant restriction of the ASD during staged LV recruitment.

Ejection fraction. Longitudinal analysis of echocardiograms from patients who underwent staged LV recruitment indicated significant increases in EF from initial postnatal echocardiogram to that obtained just before BDG or Fontan/biventricular conversion (overall change across the whole period, $p = 0.004$), suggesting a benefit of the surgical approach with respect to function (Fig. 4).

Length of hospitalization. The cumulative duration of hospitalization for surgery, catheterization, or medical treatment from stage 1 SVP to most recent follow-up was a median of 94 days in the LV recruitment group (range 37 to 518 days), compared with 54.5 days in the traditional SVP group (range 8 to 348 days) ($p = 0.006$).

Biventricular conversion. Thirteen of 34 patients in the staged LV recruitment group underwent biventricular conversion procedure. Ten of the 13 patients underwent conversion from BDG circulation, 1 after stage 1 procedure, and 2 patients underwent takedown of the Fontan. A median of 4 surgical procedures (range 3 to 6) had been performed in these patients before conversion. Echocardiographic measurements obtained before biventricular conversion revealed a mean LVEDV *z*-score of 0.21 ± 0.78, aortic valve *z*-score of −0.57 ± 0.60, and mitral valve annular diameter *z*-score of −0.77 ± 0.37. Figure 5 presents echocardiograms from a patient who underwent LV rehabilitation and demonstrates increased LV size over time. On the magnetic resonance imaging obtained before biventricular conversion, the average indexed LVEDV was 67 ± 5.5 ml/m^2, and the average mitral/tricuspid valve inflow ratio was 1.3 ± 0.2. At catheterization before biventricular conversion, the mean LA pressure measured during balloon occlusion of the ASD was 14 ± 4.7 mm Hg.

At the median follow-up of 2.9 years (range 1 to 6 years) after biventricular conversion, there was no mor-

tality. Reoperation after biventricular conversion was performed in 4 patients: mitral valve repair in 1, mitral replacement in 1, an aortic valve repair in 1, and ventricular assist device followed by cardiac transplantation due to progressive LV dysfunction caused by coronary insufficiency in 1. The mean aortic valve gradient by echocardiography at the most recent follow-up in the 12 patients with native biventricular circulation was 13 ± 5 mmHg. The estimated right ventricle pressure (by tricuspid regurgitation jet velocity) was less than or equal to one-half the systemic pressure in 6 patients and more than one-half the systemic pressure in 4 patients (right ventricle pressure could not be estimated due to the lack of tricuspid regurgitation in 2 patients).

Discussion

This study documents the natural history of LH dimensions in patients with borderline LH hypoplasia who underwent SVP and demonstrates how a surgical strategy of staged LV recruitment may alter the natural history of LH diminution. In the cohort of patients who underwent LH rehabilitation, cumulative restriction of the ASD for at least 30 days was associated with higher likelihood of increased LH dimensions over time. Patients undergoing staged LV recruitment demonstrated gradual improvement in LV ejection fraction. Finally, this study demonstrates that staged LV recruitment can result in LV salvage and eventual conversion to a biventricular circulation in a significant subset of patients.

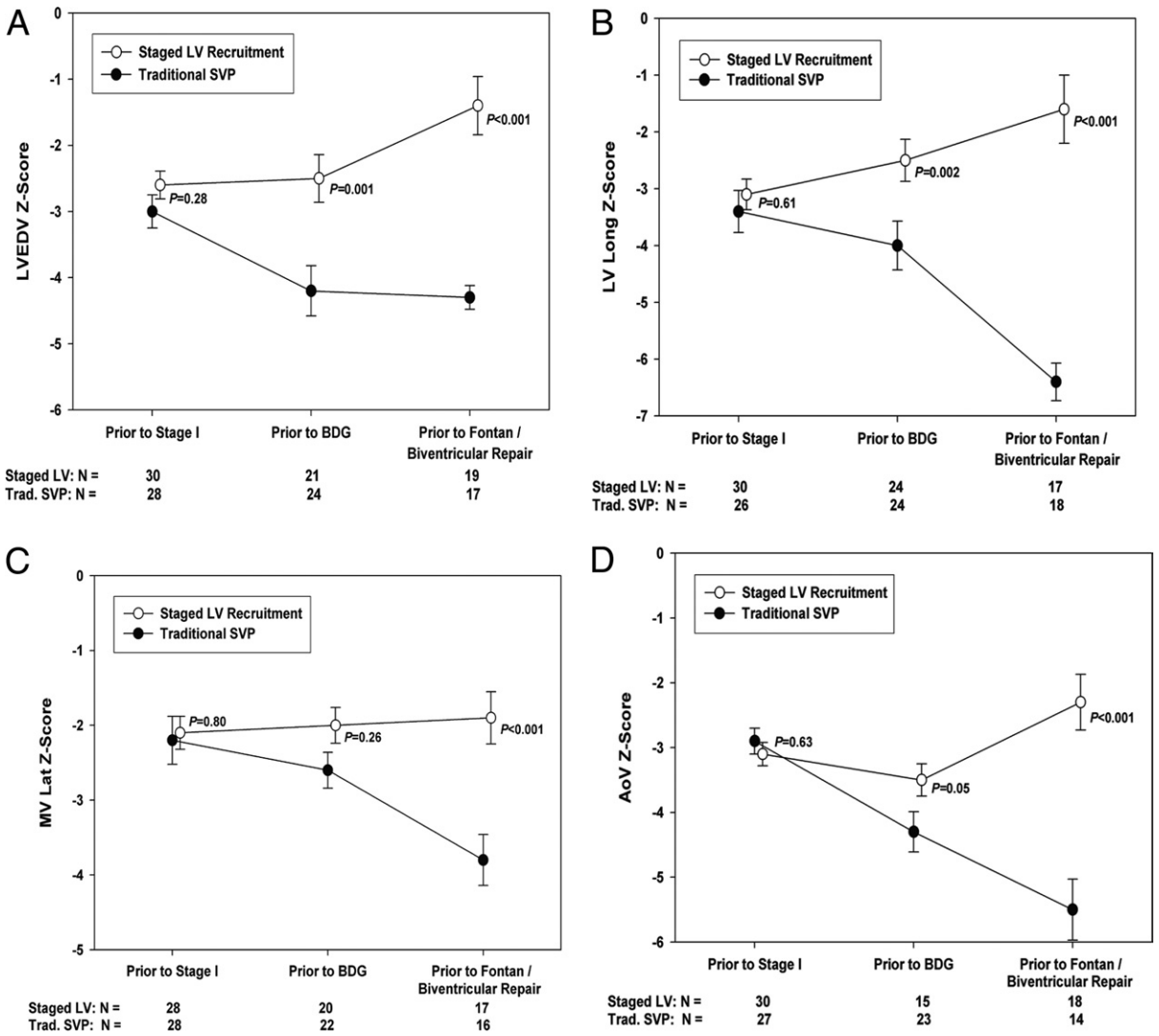

Figure 2 LH Dimensions at Various Palliative Stages in Patients Undergoing Staged LV Recruitment or Traditional SVP

Significant interaction between stage and treatment group was identified for each LH dimension ($p < 0.01$ by analysis of variance). **Open circles** = staged LV recruitment; **solid circles** = traditional SVP. Error bars are SEs. AoV = aortic valve; LAT = lateral dimension; LVEDV = left ventricular end-diastolic volume; MV = mitral valve; other abbreviations as in Figure 1.

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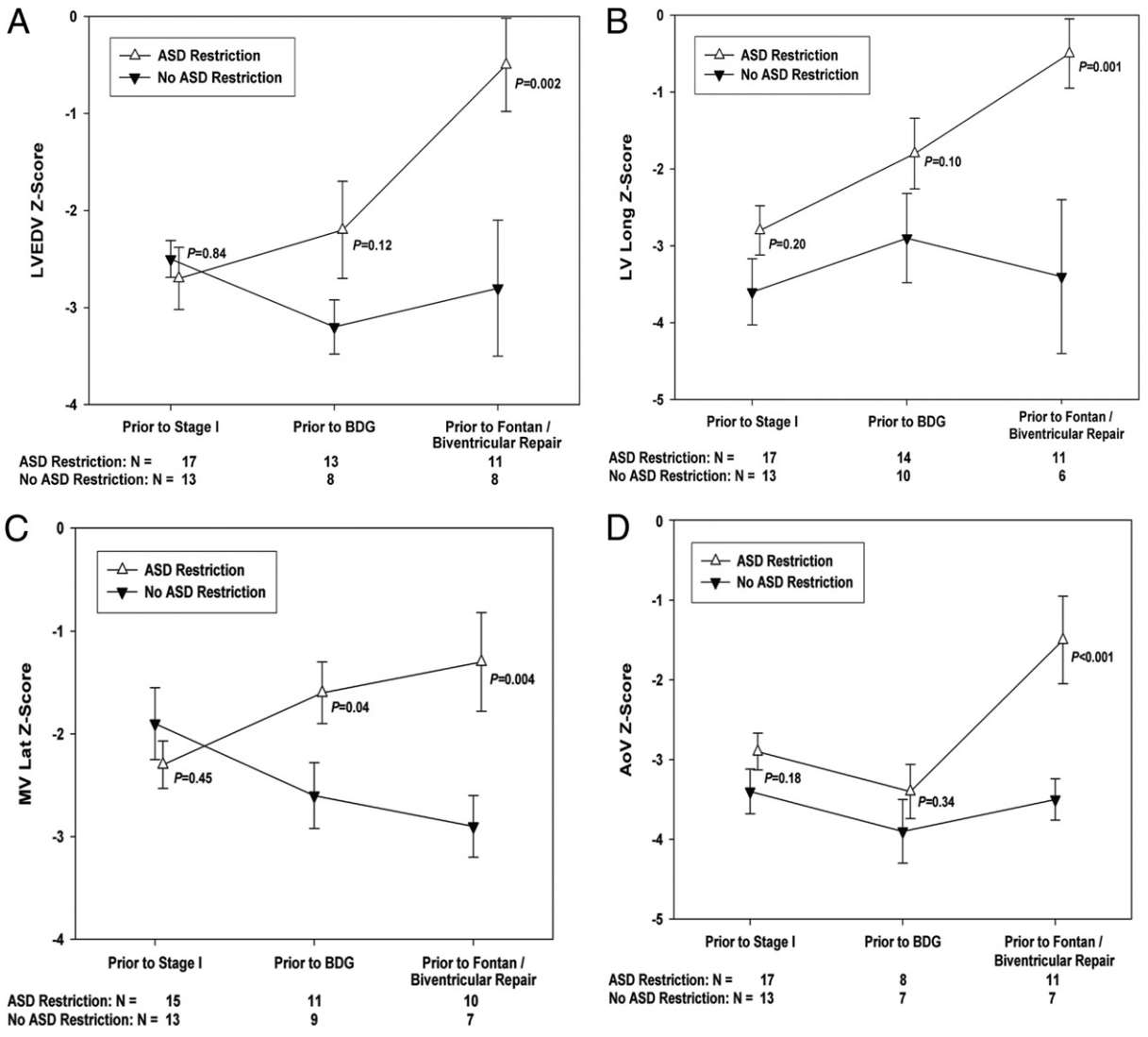

Figure 3 **Comparison of LH Dimensions Between ASD and No ASD Restricted Subgroups**

Patients with restriction of the atrial septal defect (ASD) had significantly higher *z*-scores for each LH dimension before the Fontan procedure or biventricular repair (all $p < 0.01$). Error bars are SEs. Abbreviation as in Figures 1 and 2.

However, compared with traditional SVP, this approach is associated with increased duration of hospitalization and need for additional surgical procedures.

Rationale for LH recruitment. The staged LV recruitment strategy is designed to facilitate flow through and loading of the LH in an effort to stimulate flow- and load-mediated growth. The growth potential of the LV has been demonstrated in patients with borderline LH structures who undergo initial biventricular repair by balloon dilation of the aortic valve, with adjunctive surgical repair of coarctation, aortic stenosis, and mitral stenosis when necessary (10,11). However, the potential to achieve ongoing enlargement of LH structures in patients after SVP has not been previously demonstrated. This study extends the findings of previous studies by demonstrating the potential to increase LH dimensions after SVP if adjunctive LH rehabilitation procedures are used.

ASD restriction as a predictor of LH growth. This study found that restriction of the ASD had the greatest impact on increase in LH dimensions over time, and our current practice is to perform ASD restriction in all patients who have been judged to have adequate resection of EFE and relief of aortic and mitral stenosis. Although ASD restriction was found to be the single most important predictor of increased LH structures, a definitive causative relation could not be established. ASD restriction may simply serve as a surrogate for adequacy of EFE resection and valvuloplasty because it is used at the discretion of the surgeon. Because all patients undergoing staged LV recruitment underwent EFE resection, it is difficult to distinguish the impact of this

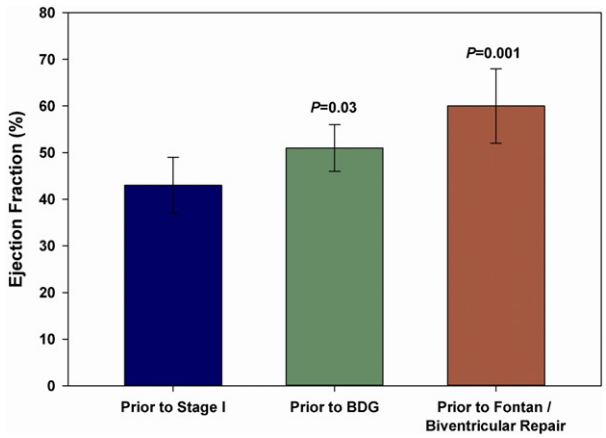

Figure 4 **Mean EF at Each Stage in Patients Undergoing Staged LV Recruitment**

Mean ejection fraction (EF) at BDG and Fontan procedure or biventricular repair is compared with value before stage 1 procedure. EF increased over time in this cohort. Abbreviations as in Figure 1.

component on the overall outcome. Although ASD restriction was associated with LH growth, it cannot be inferred that ASD restriction alone without other LH rehabilitation maneuvers will be equally effective at increasing LH dimensions.

The effects of ASD restriction on LVEDV may be due to the increase in LA pressure, which contributes to both a rightward shift of the LV end-diastolic pressure-to-volume relation and to true growth due to chronic increased loading of, and blood flow through, the LV. The stimulus for ventricular growth is LV blood flow, and all components of LH rehabilitation are designed to optimize LV blood flow (12).

Optimal degree of ASD restriction. Although patients who underwent ASD restriction demonstrated significant enlargement in LH dimensions, subsequent balloon dilation of the ASD was required in a significant number of patients because of elevated LA pressure. Further investigation is required to determine the degree of ASD restriction that promotes LH enlargement without deleterious elevation of LA pressures. Our current practice is to maintain a 4-mm fenestration within the ASD patch, which typically results in a transeptal gradient of 5 to 7 mm Hg.

Timing of LV recruitment. Most patients undergoing LH rehabilitation demonstrated the greatest increase in LH dimensions after the BDG. Because preload- and flow-mediated increase in LH dimensions is a time-dependent process, the short duration (4 months) between the stage 1 SVP and BDG may partly explain the relatively minor changes within that time period. Furthermore, LH rehabilitation maneuvers (particularly EFE resection, mitral and aortic valvuloplasty) are technically challenging to perform in neonates as part of the stage 1 SVP. The result is suboptimal EFE resection and relief of valvular stenosis. The more extensive EFE resection and valvuloplasty that are possible at the time of the BDG may explain the subsequent increase in LH dimensions.

LV growth versus dilation. From this clinical experience, it is not possible to state definitively whether the observed increase in ventricular dimension represents true LV "growth" or merely dilation. It is important to note, however, that the changes in chamber volume occurred gradually over weeks and months even in the presence of a significantly higher LA and LV end diastolic pressures, compared with right atrial and right ventricle pressures, respectively.

LV growth implies increased LV mass by cardiomyocyte hyperplasia and hypertrophy concomitant with LV dilation. Conversely, LV dilation without an increase in myocardial mass implies remodeling that may be detrimental long-term. Furthermore, intrinsic myocardial abnormalities have been described in patients who have hypoplastic LH dis-

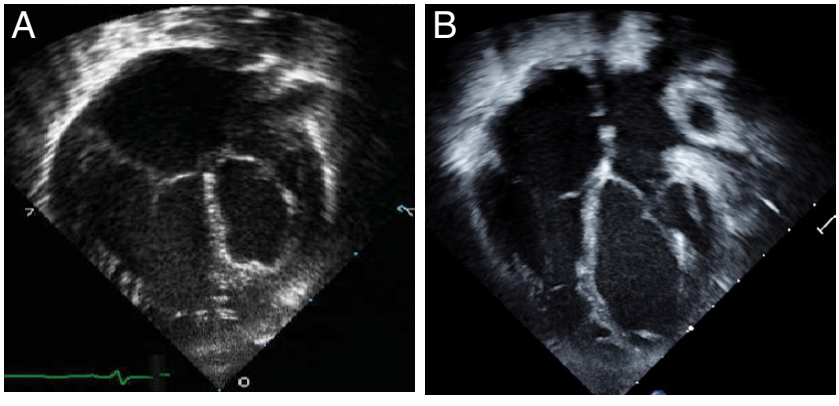

Figure 5 **Echocardiogram of Representative Patient Who Underwent Staged LV Recruitment**

The LV is endocardial fibroelastosis–bound and nonapex forming **(A)** before stage 1 but apex forming and normal in size **(B)** before biventricular conversion.

ease, and the effects of staged LV recruitment on these intrinsic abnormalities warrant further investigation (13).

Improvement in EF. Although EFE is generally believed to impede diastolic myocardial performance by preventing relaxation, this study demonstrated that ventricular function can significantly improve with LV rehabilitation procedures, specifically EFE resection. Given the cartilaginous consistency and thickness of the EFE material, it is likely that this material can restrict both diastolic and systolic function.

Study limitations. Attempts at biventricular conversion in this patient population were guided by the assumption that a biventricular circulation will result in improved maximal oxygen delivery relative to traditional SVP and will avoid the long-term complications of leaving the right ventricle as the systemic ventricle, as well as the impact of chronic elevation of systemic venous pressures on end-organ function. However, this hypothesis has not been proven previously, nor was it addressed by this study.

An attempt was made to compare serial LH dimensions in patients undergoing staged LV recruitment with those taken from a set of closely matched patients who underwent traditional SVP. However, because this was a retrospective study, and because a large proportion of traditional SVP patients were from an earlier era (before 2001), some degree of inherent selection bias is likely present. Similarly, although ASD restriction was associated with LH enlargement, it is possible that this therapy was applied in the most favorable candidates because the decision to perform restriction was based on the surgeon's judgment rather than objective criteria.

Impact on current institutional approach. After the experience outlined here, our institutional approach has been to attempt staged LV recruitment in all patients who have borderline LH hypoplasia. LH rehabilitation procedures, particularly EFE resection and ASD restriction, are rarely performed at the stage 1 procedure but are applied at the BDG stage and beyond. All patients undergo ASD restriction to 4 mm at the BDG. Asymptomatic LA hypertension is tolerated, and ASD enlargement is limited to patients who demonstrate clinical sequelae.

Conclusions

Staged LV recruitment results in growth of LH structures over time and facilitates conversion to biventricular circulation in a subset of patients. ASD restriction is predictive of increases in LH dimensions, although a causative relation cannot be definitively established. Excessive restriction can result in LA hypertension and require subsequent enlargement; further investigation is required to determine the optimal size of ASD restriction that balances LV throughput with LA hypertension. Long-term follow-up and hemodynamic comparison of patients after staged LV recruitment and traditional SVP are necessary to establish the long-term benefits of this novel strategy.

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REFERENCES

1. Ohye RG, Sleeper LA, Mahony L, et al. Comparison of shunt types in the Norwood procedure for single-ventricle lesions. N Engl J Med 2010;362:1980–92.
2. Corno AF. Borderline left ventricle. Eur J Cardiothorac Surg 2005; 27:67–73.
3. Schwartz ML, Gauvreau K, Geva T. Predictors of outcome of biventricular repair in infants with multiple left heart obstructive lesions. Circulation 2001;104:682–7.
4. Lofland GK, McCrindle BW, Williams WG, et al. Critical aortic stenosis in the neonate: a multi-institutional study of management, outcomes, and risk factors. Congenital Heart Surgeons Society. J Thorac Cardiovasc Surg 2001;121:10–27.
5. Hickey EJ, Caldarone CA, Blackstone EH, et al. Critical left ventricular outflow tract obstruction: the disproportionate impact of biventricular repair in borderline cases. J Thorac Cardiovasc Surg 2007;134: 1429–36; discussion 1436–7.
6. Serraf A, Piot JD, Bonnet N, et al. Biventricular repair approach in ducto-dependent neonates with hypoplastic but morphologically normal left ventricle. J Am Coll Cardiol 1999;33:827–34.
7. Tchervenkov CI, Tahta SA, Jutras LC, Beland MJ. Biventricular repair in neonates with hypoplastic left heart complex. Ann Thorac Surg 1998;66:1350–7.
8. Vittinghoff E, Glidden D, Shiboski S, McCulloch C. Regression Methods in Biostatistics: Linear, Logistic, Survival, and Repeated Measures Models. New York, NY: Springer, 2005.
9. Cabral HJ. Multiple comparisons procedures. Circulation 2008;117: 698–701.
10. Han RK, Gurofsky RC, Lee KJ, et al. Outcome and growth potential of left heart structures after neonatal intervention for aortic valve stenosis. J Am Coll Cardiol 2007;50:2406–14.
11. McElhinney DB, Lock JE, Keane JF, Moran AM, Colan SD. Left heart growth, function, and reintervention after balloon aortic valvuloplasty for neonatal aortic stenosis. Circulation 2005;111:451–8.
12. Taber LA. Biomechanical growth laws for muscle tissue. J Theor Biol 1998;193:201–13.
13. Mahmut N, Thompson M, Kinnear C, et al. Cellular senescence in hypoplastic left heart syndrome: young patients with old hearts. Circulation 2008;118:S907–8.

Key Words: borderline left ventricle ■ endocardial fibroelastosis ■ left ventricular recruitment.