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Surgical outcome of the borderline hypoplastic left ventricle: impact of the left ventricle rehabilitation strategy

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Abstract

Objective: This study aims to assess the surgical outcome of borderline hypoplastic left ventricle before and after the induction of the left ventricle rehabilitation strategy. *Methods:* A retrospective review investigated patients with borderline hypoplastic left ventricle who underwent surgical intervention between 2012 and 2022. The patient cohort was stratified into two groups based on the initiation of left ventricle rehabilitation: an early-era group (E group, 2012–2017) and a late-era group (L group, 2018–2022). Left ventricle rehabilitation was defined as palliation combined with other procedures aimed at promoting left ventricular growth such as restriction of atrial septal defect, relief of inflow/outflow obstructive lesions, and resection of endocardial fibroelastosis. *Results:* A total of 58 patients were included. Primary diagnosis included 12 hypoplastic left heart syndromes, 11 critical aortic valve stenosis, and others. A total of 9 patients underwent left ventricle rehabilitation, 8 of whom underwent restriction of atrial septal defect. As for clinical outcomes, 9 of 23 patients achieved biventricular repair in the E group, whereas in the L group, 27 of 35 patients achieved biventricular repair (39% vs. 77%, $p = 0.004$). Mortality did not differ statistically between the two groups (log-rank test $p = 0.182$). As for the changes after left ventricle rehabilitation, left ventricular growth was observed in 8 of 9 patients. The left ventricular end-diastolic volume index (from 11.4 to 30.1 ml/m^2, $p = 0.017$) and left ventricular apex-to-right ventricular apex ratio (from 86 to 106 %, $p = 0.014$) significantly increased after left ventricle rehabilitation. *Conclusions:* The introduction of the left ventricle rehabilitation strategy resulted in an increased proportion of patients achieving biventricular repair without a concomitant increase in mortality. Left ventricle rehabilitation was associated with enhanced left ventricular growth and the formation of a well-defined left ventricle apex. Our study underscores the significance of left ventricle rehabilitation strategies facilitating successful biventricular repair. The data suggest establishing restrictive atrial communication may be a key factor in promoting left ventricular growth.

Introduction

The surgical management of patients presenting with a borderline hypoplastic left ventricle remains controversial, with diverse approaches adopted across different institutions.[1–5] Traditionally, for patients with this diagnostic spectrum, a decision was made at the first admission whether initial biventricular repair is feasible or single ventricle palliation towards Fontan circulation should be performed.[6,7] The decision-making process is complicated and mainly determined by the initial left ventricular volume and aortic valve/mitral valve size.[4,8–10] In 2009, Emani et al. reported left ventricle rehabilitation as the first palliative procedure for borderline hypoplastic left ventricle.[1] In their experience, initial procedures including restriction of atrial septal defect, resection of endocardial fibroelastosis, and aortic and/or mitral valvuloplasty promoted the development of left ventricle and improved the left ventricle function. Subsequently, a subset of patients could undergo biventricular repair. Furthermore, Akintürk et al. demonstrated that Giessen hybrid approach as a left ventricle rehabilitation strategy increased the left ventricular volume and concluded that this approach may increase the chances of achieving biventricular circulation in patients with borderline hypoplastic left ventricle.[2] Although both strategies are nowadays recognised as the "left ventricle rehabilitation strategy", we conducted the strategy that attempts to increase left ventricle size by promoting flow through the left ventricle, relieving inflow and outflow tract obstructions, and resecting endocardial fibroelastosis.[1,11,12] Before 2018, we decided on the primary biventricular repair or single ventricle palliation at the time of initial admission. Since 2018, we adopted the left ventricle rehabilitation strategy to a subset of patients with borderline hypoplastic left ventricle to postpone the decision making until late infancy. In the present study, we compared the clinical course and outcomes of patients between the two eras before and since 2018. We evaluated the impact of adopting the left ventricle rehabilitation strategy on outcomes. Furthermore, we evaluated the changes in left ventricular volume and its related parameters in the patients who underwent left ventricle rehabilitation procedures.

Methods

Patients and data collection

This study was a single-center retrospective analysis of all patients who presented to the German Heart Center Munich between January 2012 and March 2022 with the diagnosis of borderline hypoplastic left ventricle. Patients who had undergone at least one surgical procedure were included in the criteria. In this study, borderline hypoplastic left ventricle was defined by using body surface area-indexed left ventricular end-diastolic volume. Echocardiography was performed at first admission, and patients with echo-measured left ventricular end-diastolic volume below 30 ml/m^2 and small aortic valve/mitral valve (z-score < -2.0) were included in the study. Patients with extremely small aortic valve and mitral valve (z-score < -5.0) were excluded as classical hypoplastic left heart syndrome. Patients with complex anatomies, such as atrioventricular discordance or straddling mitral valve, were excluded from this study (2 patients with congenitally corrected transposition of the great arteries and 1 patient with straddling mitral valve). A review of medical records including in-hospital and outpatient notes, echocardiography, and operation records was performed.

As we changed our surgical strategy and the first left ventricle rehabilitation procedure was performed in 2018, patients were divided into 2 groups: patients who were operated between 2012 and 2017 (early (E) group) and patients who were operated between 2018 and 2022 (late (L) group). The surgical outcomes were compared between the groups.

Echocardiography and measurement of left ventricle structures

The left ventricle structures were measured regularly by echocardiography. Two-dimensional echocardiographic measurements were performed during each admission for assessment. Aortic diameter, mitral valve diameter, left ventricular end-diastolic diameter, end-systolic diameter, and left ventricular ejection fraction were assessed in the parasternal long-axis view. The z-score, indicating the standard deviation from the mean diameter for a normal population indexed to body surface area, was calculated using the z-scores of cardiac structures, as outlined by Pettersen et al.[13] Body surface area was determined using the Haycock method based on body weight and height.[14] Left ventricular volume and the left ventricular apex-to-right ventricular apex ratio were measured from the apical 4-chamber view, with left ventricular apex-to-right ventricular apex ratio (%) measurements depicted in Supplementary Figure S1. Left ventricular volumes were computed using monoplane Simpson's method indexed to body surface area.[15] Scores for borderline left ventricle which Rhodes et al. (Rhodes score) and Hickey et al. (CHSS-2 score) reported were calculated using two-dimensional echocardiographic data from the first admission.[8,9]

Left ventricle rehabilitation procedure and surgical technique

Left ventricle rehabilitation was defined as palliation combined with other procedures aimed at promoting left ventricular growth. To promote left ventricular growth, restriction of atrial septal defect, relief of inflow/outflow obstructive lesions (surgical aortic and mitral valvuloplasty), and endocardial fibroelastosis resection were performed. Arch reconstruction combined with pulmonary artery banding had been performed prior to the introduction of the left ventricle rehabilitation strategy, and this procedure was not included in the left ventricle rehabilitation. Patients who underwent transcatheter balloon aortic valvuloplasty combined with bilateral pulmonary artery banding were included in the definition of left ventricle rehabilitation, and these patients underwent ductal stenting at the same time as balloon aortic valvuloplasty. Restriction of atrial septal defect was performed in a subset of patients. The surgical procedure was performed through a median sternotomy with cardiopulmonary bypass, and under cardiac arrest or ventricle fibrillation, the atrial septal defect was restricted using a fenestrated patch closure (2–4 mm fenestration). Some patients who underwent atrial septal defect restriction had concomitant procedures such as arch reconstruction, endocardial fibroelastosis resection, and mitral valvuloplasty. Transcatheter ductal stenting was performed to maintain ductal-dependent circulation after left ventricle rehabilitation. For endocardial fibroelastosis resection, removal of this noncompliant endocardial material by sharp dissection with a surgical scalpel or tenotomy scissors, was performed through the mitral valve orifice or the left ventricle outflow tract.

Indication of biventricular repair and left ventricle rehabilitation

Indication of biventricular repair was not determined by a fixed protocol, but was done under consideration of various parameters. In the E group, the general indication of biventricular repair was that the left ventricular end-diastolic volume before biventricular repair exceeded 20 ml/m^2. On the other hand, single ventricle palliation was indicated in cases of patients with left ventricular end-diastolic volume < 20 ml/m^2, aortic valve z-score < -2.0, and mitral valve z-score < -2.0. In the L group, the strategy has changed. Left ventricle rehabilitation was mainly indicated for patients whose left ventricular end-diastolic volume was below 15 ml/m^2 and who had inflow/outflow obstruction, endocardial fibroelastosis, or non-restrictive atrial septal defect. In patients with left ventricular end-diastolic volume >15 ml/m^2, primary or staged biventricular repair was selected depending on the valve size and the preoperative status. Single ventricle palliation was indicated for extremely small left ventricular end-diastolic volume below 10ml/m^2.

Follow-up and clinical outcome

Patients were under the care of paediatric cardiologists in an outpatient setting, with follow-up times defined as the duration from the date of birth to the last follow-up. For patients who died, follow-up ended at the time of death. The primary endpoints of the study were the survival rate and total number of patients who achieved biventricular repair. Biventricular repair was defined as intracardiac repair to a biventricular circulation, one ventricle serving the pulmonary and the other the systemic circulation, and recovery from ductal-dependent circulation. When intracardiac biventricular repair was performed, all intracardiac and great vessel shunts were closed, except for a small interatrial communication which was left as intended.

Statistical analysis

Categorical variables were presented as absolute numbers and percentages. The chi-square test was employed for categorical data, while continuous variables were expressed as medians with interquartile ranges. An independent sample *t*-test was used for normally distributed variables, and Mann–Whitney *U* test was applied for variables not conforming to normal distribution. A univariable Cox proportional hazard regression model was used to assess mortality and outcomes. Time-related survival was modelled with nonparametric Kaplan–Meier estimates and analysed by the log-rank test. Comparison of pre- and postoperative left ventricle dimensions was analysed by a paired *t*-test. Associated factors for achieving biventricular repair were identified using logistic regression analysis. Variables with a significance level below 0.05 in the univariate model were included in the multivariate model for selected analysis. *P*-values below 0.05 were considered significant. Data analysis was performed using SPSS version 28.0 for Windows (IBM, Ehningen, Germany) and R-statistical software (R Foundation for statistical computing, Vienna, Austria).

Results

Patient characteristics and echocardiogram data

A total of 58 patients were included in the study, with 23 in the E group and 35 in the L group. Patient characteristics are detailed in Table 1. The most common diagnosis was borderline HLHS ($n = 12$, 21%). Critical aortic valve stenosis and unbalanced atrioventricular septal defect accounted for 11 patients each (19%). As for intracardiac and extracardiac obstructions, a single obstructive lesion in the left ventricle was observed in 16 patients (28%), multiple obstructive lesions in 16 patients (28%), and arch obstruction in 32 patients (55%). Regarding concomitant diagnoses, restrictive foramen ovale and endocardial fibroelastosis were observed in 4 patients (7%) and 7 patients (12%), respectively. There was no statistical difference in birth conditions, primary diagnosis, associated anomalies, or initial physiology between the groups.

Initial measurements of left ventricle structures are detailed in Table 1. The initial echocardiographic left ventricle measurements showed left ventricular end-diastolic diameter of 11 (9–13) mm, left ventricular end-systolic diameter of 6 (5–9) mm, left ventricular end-diastolic volume of 12.1 (7–21.4) ml/m^2, and left ventricular end-systolic volume index of 3.2 (1.5–7.2) ml/m^2. These measurements of the left ventricle were similar between the two groups. The median diameters of aortic valve and mitral valve were 5 (4–6) mm and 8 (7–10) mm, respectively. Similarly, there were no significant differences between the two groups in these measurements.

Initial operation data and clinical course

The details of the initial operation are presented in Table 2. Median age and weight at initial operation were 10 (7–18) days and 3.2 (2.9–3.7) kg, respectively. As for the procedure, the number of primary biventricular repair was 6 (25%) in the E group and 13 (37%) in the L group ($p = 0.380$). On the other hand, 11 patients underwent the Norwood procedure in the E group compared to only 2 patients in the L group (43%, vs. 6%, $p < 0.001$). Other palliations without a procedure to promote left ventricular growth were performed in 7 patients in the E group, and in 11 patients in the L group. For details, the procedures in the E group included 4 cases of aortic arch repair with pulmonary artery banding, 2 cases of central pulmonary artery banding, and 1 case of bilateral pulmonary artery banding. The procedures in the L group included 4 cases of aortic arch repair with pulmonary artery banding, 4 cases of central pulmonary artery banding, and 3 cases of bilateral pulmonary artery banding. In the L group, a total of 9 patients (26%) underwent left ventricle rehabilitation as the first palliation. Operative deaths and postoperative extracorporeal membrane oxygenation support occurred in 4 patients each (7%) with no significant difference between the two groups.

The following clinical course of each group is depicted in Figure 1. The median follow-up duration was 4.6 years (2.0–7.4). In patients who underwent primary biventricular repair, only one patient in the L group died 20 days after biventricular repair, who had concomitant anomalous origin of the left coronary artery from the pulmonary artery. In patients who underwent Norwood procedure as the first procedure in the E group, 2 patients died following the Norwood procedure, and 7 patients subsequently underwent bidirectional cavopulmonary shunt. Only 1 patient underwent biventricular conversion 2 years after Norwood procedure. This patient was diagnosed with aortic atresia, hypoplastic aortic arch and ventricular septal defect, and underwent Rastelli-type biventricular repair at the age of 2 years (tunnel patch through left ventricle to neo-aorta, and right ventricle to pulmonary artery conduit). The patient survived the procedure and is doing well. On the other hand, in the L group, both patients who underwent Norwood procedure subsequently underwent bidirectional cavopulmonary shunt. As for the patients who underwent other palliations without a procedure to promote left ventricular growth, subsequent biventricular repair was performed in 2 patients (E group) and 6 patients (L group). In patients who underwent left ventricle rehabilitation, 8 patients subsequently underwent biventricular repair and only 1 patient underwent bidirectional cavopulmonary shunt. However, there were two early postoperative deaths, occurring 2 and 15 days after biventricular repair, respectively, both attributed to heart failure.

The total number of patients who achieved biventricular repair was 27 (77%) in the L group. The number of patients who achieved biventricular repair significantly increased in the L group compared to the E group (39% versus 77%, $p = 0.004$). The total number of deaths was 6 (26%) in the E group and 5 (14%) in the L group. The Kaplan–Meier curve representing survival after birth also showed no significant difference between the groups (Figure 2, $p = 0.182$).

Left ventricular growth after left ventricle rehabilitation

Table 3 provides details on the patients who underwent left ventricle rehabilitation. The median Rhodes score and CHSS-2 score were -1.82 (from -2.49 to -1.42) and -23.7 (from -33.6 to -15.5), respectively. Eight patients (89%) underwent left ventricle rehabilitation in the neonatal period. The most frequent procedure for promoting left ventricular growth was atrial septal defect restriction ($n = 7$, 78%). Other procedures included 2 transcatheter

Table 1. Baseline cohort characteristics

Variables: *N* (%) or median (IQR)	Total cases (*N* = 58)	E group (*N* = 23)	L group (*N* = 35)	*p*-value
Male sex	37 (64)	15 (65)	22 (63)	0.855
Premature	6 (10)	3 (13)	3 (8.6)	0.584
Genetic anomaly	8 (14)	3 (13)	5 (14)	0.893
Fetal intervention	4 (7)	0 (0)	4 (11)	0.093
Primary diagnosis				
Borderline HLHS	12 (21)	6 (26)	6 (17)	0.411
Shone complex	3 (5)	0 (0)	3 (9)	0.149
Critical AS with hypo LV	11 (19)	3 (13)	8 (23)	0.351
Congenital MS	2 (3)	1 (4)	1 (3)	0.761
Conotruncal heart malformations	3 (5)	0 (0)	3 (9)	0.149
Unbalanced AVSD	11 (19)	7 (30)	4 (11)	0.071
Aortic coarctation with VSD	8 (14)	1 (4)	7 (20)	0.091
Others	8 (14)	5 (22)	3 (6)	0.155
Concomitant diagnosis				
Restrictive foramen ovale	4 (7)	2 (9)	2 (6)	0.661
Endocardial fibroelastosis	7 (12)	2 (9)	5 (14)	0.523
Ductal-dependent circulation	47 (81)	19 (82)	28 (80)	0.804
With retrograde aortic blood flow	5 (9)	2 (9)	3 (9)	0.987
Without retrograde aortic blood flow	42 (72)	17 (74)	25 (71)	0.836
Obstructive lesions				
Single obstructive lesion	16 (28)	5 (22)	11 (31)	0.419
Multiple obstructive lesions	16 (28)	6 (26)	9 (26)	0.975
Arch obstruction	32 (55)	13 (57)	19 (54)	0.867
TTE data at birth				
IVSd z-score	4.3 (2.8–5.4)	4.5 (3.3–5.9)	3.8 (2.8–5.4)	0.502
LVDd z-score	−5.2 (-6.3–−3.0)	−4.6 (-6.3–−2.4)	−5.4 (-6.3–−3.7)	0.223
LVDs z-score	−2.7 (−3.7–−1.4)	−2.7 (−3.4–−1.2)	−2.7 (−3.8–−1.4)	0.457
LVEDVI	12.1 (7.0–21.4)	12.1 (5.9–25.3)	12.1 (7.4–18.0)	0.303
LVESVI	3.2 (1.5–7.2)	3.0 (1.7–8.4)	3.7 (1.2–7.0)	0.313
LVEF	73.8 (53.0–88.7)	73.1 (47.3–88.7)	77.0 (54.0–88.7)	0.618
Aortic valve z-score	−2.1 (−2.8–−1.2)	−2.4 (−2.8–−2.0)	−1.6 (−2.6–−1.2)	0.641
Mitral valve z-score	−1.8 (−3.1–−0.2)	−1.4 (−3.2–−0.8)	−1.8 (−3.1–−0.2)	0.641
LVa/RVa	87 (71–100)	82 (64–91)	88 (76–100)	0.275
Rhodes score	−1.27 (−1.94–−0.82)	−1.29 (−2.25–−0.80)	−1.26 (−1.93–−0.88)	0.344
CHSS-2 score	−52.1 (−79.5–−29.6)	−55.8 (−81.6–−34.8)	−45.7 (−78.3–−26.6)	0.419

AVSD = atrioventricular septal defect; HLHS = hypoplastic left heart syndrome; IVS = interventricular septum; LVa/RVa = left ventricular apex-to-right ventricular apex ratio; LVDd = left ventricular end-diastolic diameter; LVDs = left ventricular end-systolic diameter; LVEDVI = left ventricular end-diastolic volume index; LVEF = left ventricular ejection fraction; LVESVI = left ventricular end-systolic volume index; TTE = transthoracic echocardiogram; VSD = ventricular septal defect.

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Table 2. Initial operation

Variables	Total	E group	L group	*p*-value
Number	58	23	35	
Initial operative data				
Age at first operation (days)	10 (7–18)	13 (8–22)	8 (6–15)	0.040
Weight at first operation	3.2 (2.9–3.7)	3.1 (2.7–3.6)	3.3 (2.9–3.8)	0.257
Procedure				
Norwood	13 (22)	11 (48)	2 (6)	<0.001
LV rehabilitation	9 (16)	0 (0)	9 (26)	0.008
Other palliation	17 (29)	7 (29)	10 (29)	0.879
Primary biventricular repair	19 (33)	6 (25)	13 (37)	0.380
Mortality and morbidity				
Operative death	4 (7)	2 (9)	2 (6)	0.661
ECMO	4 (7)	3 (13)	1 (3)	0.134

ECMO = extracorporeal membrane oxygenation; LV = left ventricle.

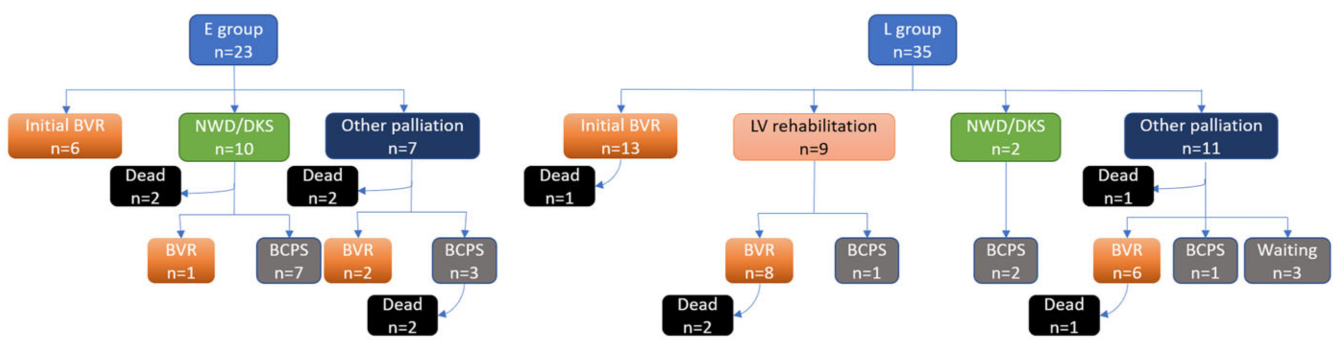

Figure 1. Subsequent procedures and mortality for patients in each group. BCPS = bidirectional cavopulmonary shunt; BVR = biventricular repair; NWD/DKS = Norwood procedure or Damus-Kaye-stansel procedure; TCPC = total cavopulmonary connection; numbers are patients at this stage at the end of the study.

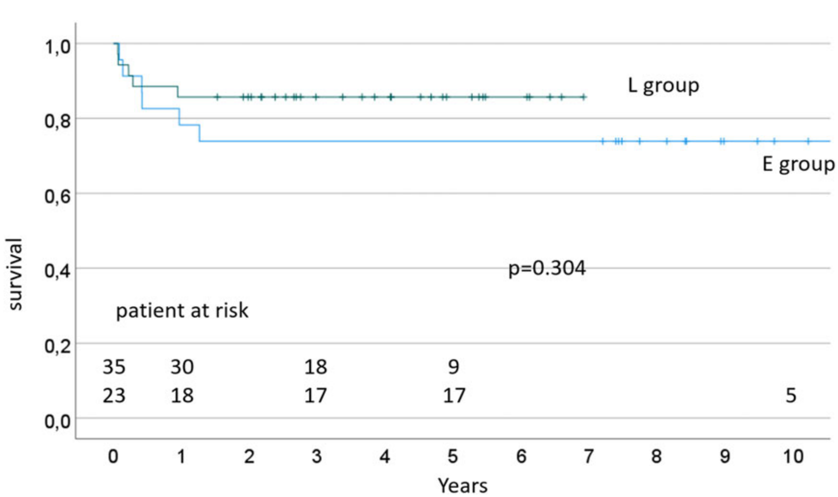

Figure 2. Survival after birth in each group. The blue line represents patients in the E group. The green line represents patients in the L group.

Table 3. Detail of rehabilitation procedure

Patients	Diagnosis	Age (days) at op	Procedure	Cardio pulmonary bypass time (min)	Aortic cross clamp time (min)
1	TAC, MS, PS, PFO	340	palliative RV-PA, MS release, PFO closure	306	182
2	AS, hypoplastic arch, EFE	17	bilPAB, AVP, fenestrated ASD closure, EFE resection	123	58
3	HLHS (MS, AS)	6	bilPAB, fenestrated ASD closure	43	0
4	shone complex, ASD, VSD	8	PAB, fenestrated ASD closure	47	20
5	AS, CoA, ASD, mVSD	7	bilPAB, fenestrated ASD closure	58	0
6	HLHS (MS, AS)	6	bilPAB, fenestrated ASD closure	55	0
7	AS, MS, CoA, EFE	6	bil PAB, BVP	0	0
8	AS, MS, CoA, VSD	6	PAB, fenestrated ASD closure, arch reconstruction	143	53
9	AS, VSD, EFE	5	bil PAB, BVP	0	0
	Major complication	**Clinical course**	**Rehabilitation duration (days)**	**Outcome**	
	ECMO	Rastelli (fenestrated IAS)	1806	BVR	Alive
		Norwood→PCPC	83	SVP	Alive
	AKI	arch repair (fenestrated IAS)→Ross–Konno	241	BVR	Alive
	AKI, SIRS	ICR (fenestrated IAS)	57	BVR	Alive
	Arrythmia	AVP, ICR (fenestrated IAS)	389	BVR	Alive
		AVP, arch repair (fenestrated IAS)	235	BVR	Alive
		Ross–Konno	56	BVR	Dead (15 days)
		Spontaneous VSD closure, debanding	118	BVR	Alive
		Ross–Konno	64	BVR	Dead (2 days)

AKI = acute kidney injury; AS = aortic stenosis; ASD = atrial septal defect; AVP = aortic valvuloplasty plasty; bilPAB = bilateral pulmonary artery banding; BVP = balloon valvuloplasty; BVR = biventricular repair; CoA = aortic coarctation; ECMO = extracorporeal membrane oxygenation; EFE = endocardial fibroelastosis; HLHS = hypoplastic left heart syndrome; ICR = intracardiac repair; MS = mitral stenosis; PAB = pulmonary artery banding; PS = pulmonary stenosis; RV-PA = right ventricle to pulmonary artery shunt; SIRS = systemic inflammatory response syndrome; SVP = single ventricle palliation; TAC = truncus arteriosus communis; VSD = ventricular septal defect.

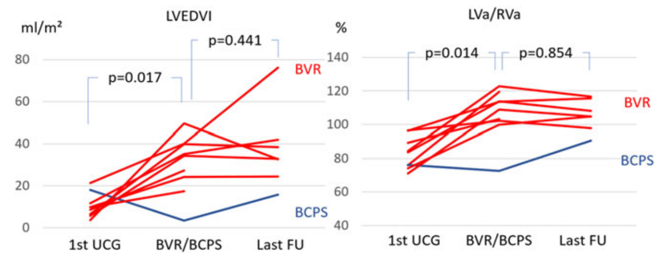

Figure 3. The changes of LVEDVI and LVa/RVa ratio after LV rehabilitation. The red line represents the patients who reached biventricular repair. The blue line represents the patients who underwent single ventricle palliation after LV rehabilitation. BCPS = bidirectional cavopulmonary shunt; BVR = biventricular repair; LV = left ventricle; LVa/RVa = left ventricular apex-to-right ventricular apex ratio; LVEDVI = left ventricular end-diastolic volume.

balloon aortic valvuloplasty, relief of mitral valve stenosis, aortic valvuloplasty, and endocardial fibroelastosis resection. The median rehabilitation duration was 118 days (61–315). A total of 8 patients reached biventricular repair, while only 1 patient underwent single ventricle palliation after left ventricle rehabilitation. Endocardial fibroelastosis resection was performed in only one patient, and this patient underwent single ventricle palliation because the left ventricle did not grow after left ventricle rehabilitation.

The results of left ventricle measurements before and after left ventricle rehabilitation are presented in Figure 3. The mean left ventricular end-diastolic volume increased from 10.6 ± 5.8 ml/m^2 to 30.1 ± 13.8 ml/m^2 (p = 0.017) after rehabilitation. The mean left ventricular apex-to-right ventricular apex ratio increased from 86 ± 14% to 106 ± 15% after rehabilitation (p = 0.014). In detail, in 8 patients both left ventricular end-diastolic volume and left ventricular apex-to-right ventricular apex ratio increased after left ventricle rehabilitation, and they underwent biventricular repair. Conversely, left ventricular end-diastolic volume and left ventricular apex-to-right ventricular apex ratio decreased in one patient despite left ventricle rehabilitation. This patient underwent bidirectional cavopulmonary shunt. The changes of other left ventricle measurements are shown in Supplementary Table 2. As for the left ventricle measurement of follow-up, from biventricular repair/BCPS to the last follow-up, mean left ventricular end-diastolic volume and left ventricular apex-to-right ventricular apex ratio increased slightly (left ventricular end-diastolic volume: from 32.4 ml/m^2 to 37.5 ml/m^2, left ventricular apex-to-right ventricular apex ratio: from 104% to 105%), but there was no significant difference (left ventricular end-diastolic volume: $p = 0.441$, left ventricular apex-to-right ventricular apex ratio: $p = 0.854$). Echo cardiograms (apical 4-chamber view) of two representative cases are shown in Supplementary Figure 2.

Associated factors affecting the achievement of biventricular repair

To evaluate factors affecting the achievement of biventricular repair, we performed a linear regression analysis (Table 4). The results indicated a significant association between the left ventricular apex-to-right ventricular apex ratio and biventricular repair achievement ($p = 0.004$, odds ratio: 1.076). Similarly, affiliation to group L was identified as an associated factor of achieving biventricular repair ($p = 0.006$, odds ratio: 4.815). Multiple obstructive lesions and interventricular septum diameter were negatively associated with biventricular repair ($p = 0.042$, odds ratio: 0.290, $p = 0.036$, odds ratio: 0.630). In the multiple linear regression analysis, the affiliation to group L ($p = 0.016$: odds ratio 8.507) and left ventricular apex-to-right ventricular apex ratio ($p = 0.038$ odds ratio: 1.059) were identified as independent factors for the achievement of biventricular repair.

When we analysed the factors affecting successful biventricular repair (death after biventricular repair and patients who developed pulmonary hypertension after biventricular repair were excluded), the results were nearly the same as the analysis above, except for multiple obstructive lesions (Supplementary Table 1).

Discussion

Diagnosis of borderline left ventricle

Although Corno et al. reported several parameters that should be taken into consideration, the definition of the borderline left ventricle remained unclear.[16] In this study, we defined the borderline hypoplastic left ventricle by LVEDVI less than 30 ml/m^2. The surgical management of patients with borderline hypoplastic left ventricle necessitates careful patient selection. While extreme cases are straightforwardly directed towards either staged single ventricle palliation or biventricular physiology, the decision becomes intricate in cases with borderline hypoplasia of the left ventricle. Traditionally, left ventricle hypoplasia unsuitable for biventricular repair is defined by left ventricular end-diastolic volume of less than 20 ml/m^2.[3] However, recent studies on left ventricle rehabilitation have broadened the understanding of borderline hypoplastic left ventricle. In this study, patients diagnosed with borderline hypoplastic left ventricle exhibited left ventricular end-diastolic volume of 12.1 ml/m^2 and left ventricular end-systolic volume index of 3.2 ml/m^2. These results might suggest that patients with smaller left ventricle were considered for a strategy aimed at biventricular repair than before.

Surgical strategy for borderline left ventricle

In this study, we compared the patients before 2018 (early era) and since 2018 (late era). Birth conditions, primary diagnosis, initial physiology, and echocardiographic demonstrations were similar between the groups. Before 2018, we initially decided to perform single ventricle palliation or biventricular repair at the first admission. The hybrid procedure can delay the decision and highly invasive procedures; however, it also has certain complications such as ductal stent-related complications, retrograde coarctation of the aorta, and pulmonary stenosis after pulmonary artery banding. Besides, our primary Norwood showed good results so far. Therefore, we previously preferred primary Norwood for the patients who were thought to be better suitable for single ventricle palliation. In 2018, we adopted the left ventricle rehabilitation strategy, and this procedure was performed in selected 9 patients. As a result, fewer patients opted for primary Norwood and more patients opted for staged strategy. That is because older age often presents more options and fewer acute and late outcome risks compared to advanced neonatal surgeries.

Clinical course (surgical strategy for managing borderline left ventricle)

The management of patients with borderline hypoplastic left ventricle is often complex due to various diagnoses or left ventricle inflow/outflow obstructions. Moreover, multiple obstructions have been associated with poor survival.[17] In the E group, the Norwood

Table 4. Variables reaching to biventricular repair

Variables	*p*-value	OR	95% CI	*p*-value	OR	95% CI
(Linear regression model)						
Era	0.006	4.815	1.569–14.78	0.016	8.507	1.497–48.38
Rehabilitation	0.094	6.286	0.730–54.09			
Male sex	0.764	1.182	0.397–3.519			
Premature	0.190	0.303	0.151–1.808			
Genetic anomaly	0.844	1.167	0.251–5.421			
Cardiac diagnosis						
Single obstructive lesion	0.371	1.742	0.516–5.878			
Multiple obstructive lesions	0.042	0.290	0.088–0.958	0.451	0.466	0.064–3.404
Restrictive foramen ovale	0.696	0.667	0.087–5.091			
Endocardial fibroelastosis	0.901	0.903	0.183–4.457			
Ductal-dependent circulation						
With retrograde aortic blood flow	0.402	2.625	0.274–25.14			
Without retrograde aortic blood flow	0.967	0.975	0.297–3.200			
First UCG data						
IVS	0.036	0.630	0.409–0.971	0.098	0.670	0.417–1.077
LVDd	0.214	1.147	0.924–1.423			
LVDs	0.929	0.991	0.814–1.206			
LVEDVI	0.504	1.022	0.959–1.089			
LVESVI	0.338	0.953	0.863–1.052			
LVEF	0.214	1.018	0.990–1.047			
Aortic valve diameter	0.327	1.332	0.750–2.366			
Mitral valve diameter	0.291	1.176	0.870–1.588			
aAo diameter	0.627	0.904	0.600–1.360			
LVa/RVa	0.004	1.076	1.024–1.130	0.038	1.059	1.003–1.118

CI = confidence interval; IVS = interventricular septum; LVa/RVa = left ventricular apex-to-right ventricular apex ratio; LVDd = left ventricular end-diastolic diameter; LVDs = left ventricular end-systolic diameter; LVEDVI = left ventricular end-diastolic volume index; LVEF = left ventricle ejection fraction; LVESVI = left ventricular end-systolic volume index; OR = odds ratio; TTE = transthoracic echocardiogram.

procedure was more frequently selected for patients unable to undergo primary biventricular repair. Conversely, in the L group, other procedures, including left ventricle rehabilitation, were more frequently selected, even when an immediate biventricular repair was not feasible, in order to postpone the decision-making process regarding biventricular repair or single ventricle palliation. This approach might not only prevent extensive interventions in the neonate period but also contribute to a more accurate evaluation of the left ventricle.

Left ventricular growth after left ventricle rehabilitation

Several reports demonstrated growth of left ventricle structures after catheter intervention for aortic valve stenosis.[18,19] Additionally, not only outflow obstructions but also other factors such as inflow obstructions, volume load of the left ventricle, and endocardial fibroelastosis are considered important for left ventricular growth. Left ventricle rehabilitation focused on these factors has been reported. Emani et al. demonstrated that it is possible to increase left ventricle dimensions including left ventricular end-diastolic volume, mitral valve diameter, aortic valve diameter, and left ventricle long axis length, by using left ventricle rehabilitation.[1,11] On the other hand, Akintürk et al. demonstrated that a hybrid approach as a left ventricle rehabilitation strategy increased left ventricular volume without a highly invasive procedure.[2] However, we believe that aggressive additional procedures contribute to further left ventricular growth. We adopted a rehabilitation strategy for the high-risk patients for biventricular repair. Our results revealed that left ventricle rehabilitation with aggressive additional procedures significantly increased left ventricular end-diastolic volume and left ventricular apex-to-right ventricular apex ratio. As a result, we achieved biventricular repair in 8 of 9 patients (89%) after the left ventricle rehabilitation and more patients could achieve biventricular repair in the L group. This result was satisfying, however, it must be noted that 2 of the patients after rehabilitation died relatively early after

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biventricular repair operation. In detail, both of them underwent catheter valvuloplasty and had endocardial fibroelastosis. Lofland et al. demonstrated that the degree of endocardial fibroelastosis was a risk factor for mortality after biventricular repair in the multivariate analysis.[20] Tuo et al. reported that the presence of endocardial fibroelastosis with consequent diastolic dysfunction is more important than left ventricular volume in determining the outcome.[21] Therefore, the patients with endocardial fibroelastosis should be considered more carefully for biventricular repair indication.

Associated factors affecting the achievement of biventricular repair

Traditionally, patients with borderline hypoplastic left ventricle were commonly directed towards single ventricle palliation, and most of them were candidates for the Fontan procedure.[22] While the Fontan procedure stands as an alternative procedure for patients ineligible for biventricular repair, its long-term complications present certain disadvantages.[23] Consequently, strategies aimed at biventricular repair are commonly considered preferable, if possible. However, biventricular repair for such patients especially during the neonate period may be challenging and of high risk because of complex procedures and limited left ventricular capacity. Moreover, the conversion of a failed biventricular repair to a single ventricle physiology is associated with high mortality.[3] Therefore, it is important to determine accurately whether biventricular repair or single ventricle palliation is appropriate. Several prediction models for biventricular repair in borderline left ventricle were reported.[4] Their equation includes critical left ventricle outflow obstruction occurring at any level, each valve size, and left ventricle long axis ratio.[8–10,20] Some of them also include endocardial fibroelastosis grades.[8,20] Our result demonstrated left ventricular apex-to-right ventricular apex ratio and multiple obstructive lesions, which was consistent with these equations. Moreover, our result revealed that interventricular septum thickness was negatively associated with biventricular repair. This result might suggest that interventricular septum was an important factor in the decision-making process of biventricular repair. Affiliation with the L group was also associated with biventricular repair, which we interpreted as a positive effect of the rehabilitation strategy to achieve biventricular repair.

Limitations

This study was limited by its retrospective, non-randomised, and single-center design. This is an observational study spread over major strategy changes, but other changes in personnel and improvements in medical management were included during the study period. Although measurements of echocardiograms were taken several times, a little discrepancy can make a large difference, especially in infants. Besides, left ventricular volume measured by monoplane Simpson's method may be inferior in terms of accuracy to the biplane method. Because of the small number of patients, results should be interpreted cautiously. Additionally, the definition of borderline hypoplastic left ventricle and rehabilitation was different in each previous report and might not be consistent with our study. This study included various diagnoses such as unbalanced atrioventricular septal defect and conotruncal heart malformations. In such patients, an echo measurement of left ventricle structures may have different meanings due to the difference in anatomical structure. This is a limitation. Furthermore, assignment to the therapy was not regulated by a fixed protocol. It was the result of an individual discussion on a board consisting of paediatric cardiovascular surgeons and paediatric cardiologists.

Conclusions

After the introduction of the left ventricle rehabilitation strategy in 2018, the prevalence of biventricular repair increased in patients with borderline hypoplastic left ventricle without an increase in mortality rate. In patients who underwent left ventricle rehabilitation, a significant increase in left ventricular volume was observed in most of the patients, and successful biventricular repair was possible. Further studies are needed to clarify the indication, effectiveness, and long-term outcomes of the left ventricle rehabilitation strategy.

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