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ORIGINAL ARTICLE

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Short-term results in infants with multiple left heart obstructive lesions

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Abstract

Objective: Deciding on a surgical pathway for neonates with ≥2 left heart obstructive lesions is complex. Predictors of the successful biventricular (2V) repair in these patients are poorly defined. The goal of our study was to identify patients who underwent the 2V repair and assess anatomic and echocardiographic predictors of success.

Design: Infants born between July 2015 and August 2017 with ≥2 left heart obstructive lesions with no prior interventions were identified (n = 19). Patients with aortic or mitral valve (MV) atresia and critical aortic stenosis were excluded. Initial echocardiograms were reviewed for aortic, MV, tricuspid valve annulus size, and left (LV) and right (RV) ventricle diastolic longitudinal dimensions. The valve morphology and presence of a ventricular septal defect (VSD) and coarctation were assessed. Clinical outcomes included successful 2V repair, complications, and repeat interventions or surgeries. Failed 2V repair was defined as a takedown to single ventricle (1V) physiology, cardiac transplantation, or death.

Results: For 2V repair, 14/19 patients were selected and for 1V, 5/19 patients were selected. Initial surgical procedures of the 2V group were simple coarctation repair (5), complex coarctation/arch reconstruction +/− septal defect closure (6), hybrid stage 1 (2), and none (1). Three of the 2V patients required reintervention in the first 90 days. The LV to RV diastolic longitudinal ratio >0.75 and mitral/tricuspid ratio of <0.8 were observed in 13/14 of the 2V patients. The LV:RV ratio and the aortic valve z score were significantly larger in the 2V group compared to the 1V group. All patients in the 1V group had a nonapex forming LV. There was no mortality with follow-up to three years of age.

Conclusions: This study showed excellent short-term and midterm surgical results in the 2V population. The LV:RV diastolic longitudinal ratio may be a useful tool in the risk stratification of a successful 2V repair even in cases with a small MV.

KEYWORDS

congenital heart disease, echocardiography, left heart obstruction, Shone's complex, surgical outcomes

1 | INTRODUCTION

Management of infants with multiple left heart obstructive lesions remains challenging and individualized thoughtful decision-making process is required in each case due to the wide anatomic and physiologic spectrum.[1] The management options range includes no intervention to complex, staged, and single-ventricle (1V) palliation. In most cases, the surgical planning must be determined in the newborn period, particularly in the decision to pursue 1V vs a biventricular (2V) strategy.[1] In patients where a 2V repair is initiated, recurrent, or new obstructions, as well as pulmonary hypertension can complicate the success.[2-4] There is a considerable risk of death in patients who fail 2V repair and require conversion to a 1V.[5,6]

Predictors of successful 2V repair in this patient population are not well defined. It has been previously determined that factors described in the evaluation of critical aortic stenosis are not applicable to this patient population.[7] At present, there are no accepted guidelines for determining whether a patient with ≥2 left side obstructions is more suitable for a 2V or 1V palliation. The goal of this study was to identify patients who had a 2V repair and assess anatomic and echocardiographic predictors of success compared to patients selected for 1V palliation.

2 | METHODS

This is a single-center retrospective cohort study. Demographic and clinical information was collected from 19 patients with ≥2 left heart obstructive lesions who were born or transferred to the Cleveland Clinic Children's Hospital from July 2015 to August 2017 (Table 1). Patients were followed from birth up to 36 months. Patients who were transferred from an outside institution were less than two months of age without having undergone prior surgical or catheter intervention. Patients with aortic or mitral valve (MV) atresia and critical aortic stenosis were excluded. Initial echocardiograms were reviewed for aortic, mitral, tricuspid valve annulus size as well as for left (LV) and right (RV) ventricle diastolic longitudinal dimensions. If the initial echocardiogram did not have these measurements, they were made by a single pediatric cardiologist. A second pediatric cardiologist assigned random patients to confirm measurements and evaluate for discrepancies. Mitral and aortic valve morphology, stenosis, presence of a ventricular septal defect (VSD), and aortic coarctation were assessed (Table 2). The clinical outcome with regard to success as a 2V repair, complications/morbidities, and repeat interventions or surgeries was determined. Major morbidities included the need for reoperation within 30 days, stroke, or the need for ECMO. A failed 2V repair was defined as a takedown to 1V physiology, cardiac transplantation, or death. The decision to pursue the 2V repair or 1V palliation was made on a case-by-case basis after the team discussion. An approval for this study was received from the Cleveland Clinic Institutional Review Board.

TABLE 1 Demographic overview of the study patient population

Variable	Biventricular repair (n = 14)	Single ventricle repair (n = 5)	P value
Gender	5 Male (36%)	5 Male (100%)	.033[a]
Birth weight (kg)	3.07 (1.85, 3.72)	3.63 (2.88, 4.7)	.67[b]
Gestational age at birth	38 (35,40)	38 (35,39)	.89[b]
Weight at first surgery (kg)	3.2 (1.9, 4.6)	3.7 (2.9, 4.7)	.11[b]
Prenatal diagnosis	14 (100%)	5 (100%)	*
Genetic syndrome	5 (36%)	0 (0%)	.51[a]
Age at 1st procedure (days)	6 (2, 66)	4 (1, 8)	.17[b]

Notes: Statistics presented as median (min and max). Genetic syndromes: CHARGE, PKU, 22q11 deletion, VACTERL, and 15q11.2 deletion.
[a]Fisher's exact test.
[b]Kruskal-Wallis test.
*indicates the p-value could not be accurately calculated.

3 | STATISTICAL ANALYSIS

Data were described using medians and ranges for continuous variables and counts and percentages for categorical variables. The two groups (2V and 1V) were compared with regards to demographic and clinical characteristics using Wilcoxon rank-sum tests for continuous and ordinal characteristics and Chi-square or Fisher's exact test for categorical characteristics.

Sample sizes for individual variables reflect the missing data. All analyses were performed on a complete-case basis. All tests were 2-tailed and performed at a significance level of 0.05. The SAS 9.4 software (SAS Institute, Cary, NC) was used for all analyses.

4 | RESULTS

Demographic and clinical characteristics of the patient cohort are presented in Tables 1 and 2. Patients were followed for up to 36 months from diagnosis. There was no mortality in this population. For 2V repair, 14/19 (74%) patients were selected and thus there were zero failed 2V repairs. Initial surgical procedures of the 2V group were simple coarctation repair (5), complex coarctation/arch reconstruction +/− VSD closure (6), hybrid stage 1 (2), and none (1) (Table 2). The patient requiring no intervention had a hypoplastic MV with normal morphology, hypoplastic aortic valve, and a VSD with no coarctation. The decision was made to allow her to grow and she has done well. This patient was considered a part of the biventricular group since her LV is tolerating a full cardiac output. Three (23%) of the 2V patients required reintervention in the first 90 days, two for recoarctation and the other required a Ross procedure. One of the patients who required reintervention for coarctation also required a

TABLE 2 Clinical characteristic differences and *P* values between the biventricular and single ventricle groups

Clinical characteristic	Biventricular repair (*n* = 14)	Single ventricle repair (*n* = 5)	*P* value
VSD	6 (43%)	0 (0%)	.60[b]
Mitral/tricuspid valve ratio	0.58 (0.35-0.83)	0.37 (0.34-0.47)	.026[a]
Mitral valve annulus (mm)	6.6 (4.5-8.8)	6 (4-7.1)	.19[a]
Mitral valve *z* score	−3.0 (−4.8 to −1.63)	−4.1 (−5.5 to −2.2)	.16[a]
Aortic valve annulus (mm)	5.05 (3.9-6.3)	4.1 (2.2-4.5)	.026[a]
Aortic valve *z* score	−2.5 (−3.97 to −0.96)	−4.3 (−4.75 to −3.29)	.005[a]
LV/RV longitudinal dimension	0.89 (0.75-1)	0.67 (0.46-0.85)	.006[a]
Apex forming left ventricle	10 (71%)	0 (0%)	.011[b]
Ascending aorta (mm)	6.3 (4.5-7.6)	5.3 (4.7-8.6)	.31[a]
Distal transverse arch (mm)	3.4 (2.1-4.5)	3.6 (2.1-4.9)	.71[a]
Coarctation	13 (93%)	5 (100%)	.99[b]

Notes: Data are not available for all subjects. Statistics presented as median (min, max) or *N* (column %).
[a]Kruskal-Wallis test;
[b]Fisher's exact test;

Ross procedure at seven months of age. No patients required reintervention on the MV, despite 5/14 patients having parachute MV. There were no major morbidities (defined as the need for reoperation within 30 days, stroke, or the need for ECMO). All 1V patients had successful Glenn procedures. No patient was taken from 2V to 1V pathway.

Statistically significant differences were noted between the 1V and 2V group. 1V patients had significantly smaller mitral/tricuspid valve ratios (*P* = .026), aortic valve annuli, and *z* scores (*P* = .026 and .005, respectively) and LV/RV diastolic longitudinal ratios (*P* = .006) (Table 2). There was no difference between the two groups with regard to the aortic valve morphology or the presence and size of a VSD (Table 2 and Figures 1 and 2). A mitral/tricuspid valve ratio of <0.8 was observed in 13/14 of the 2V patients, but >0.4 and a LV to RV diastolic longitudinal ratio of >0.75 (Table 2 and Figure 3). Of note, all patients with aortic valve annulus ≥5 mm (*n* = 8) and MV annulus ≥7.5 mm (*n* = 4) had successful 2V repair. No patients had endocardial fibroelastosis. There was also a significant difference whether the LV was apex forming, with 5/5 of the 1V patients having nonapex forming LV compared to 4/14 of the 2V group (*P* = .011).

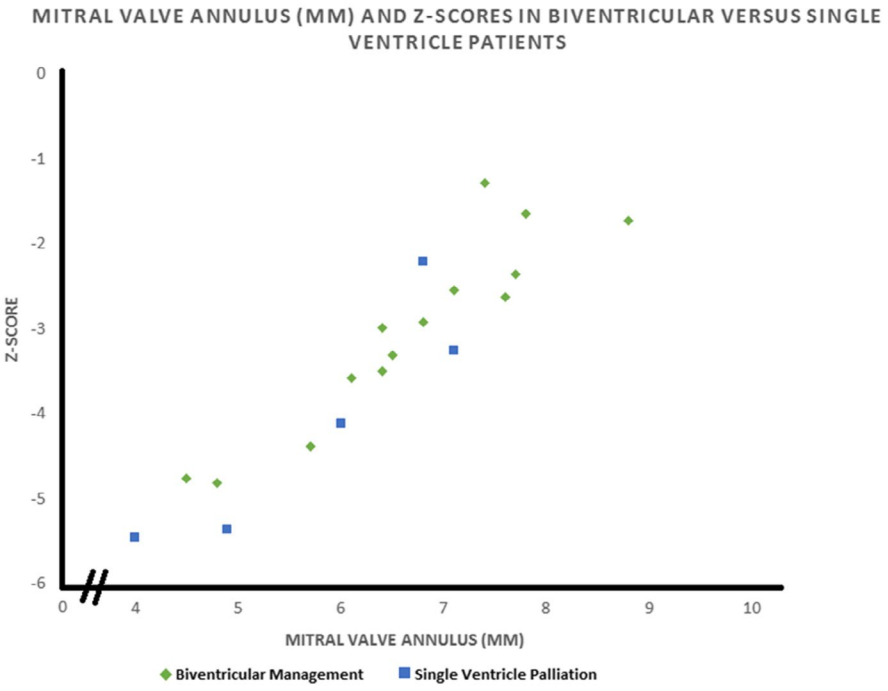

FIGURE 1 Comparison of mitral valve annulus (mm) and *z* scores in neonates with multiple left heart obstructions who underwent successful biventricular management compared to neonates in the same time period who underwent single ventricle palliation

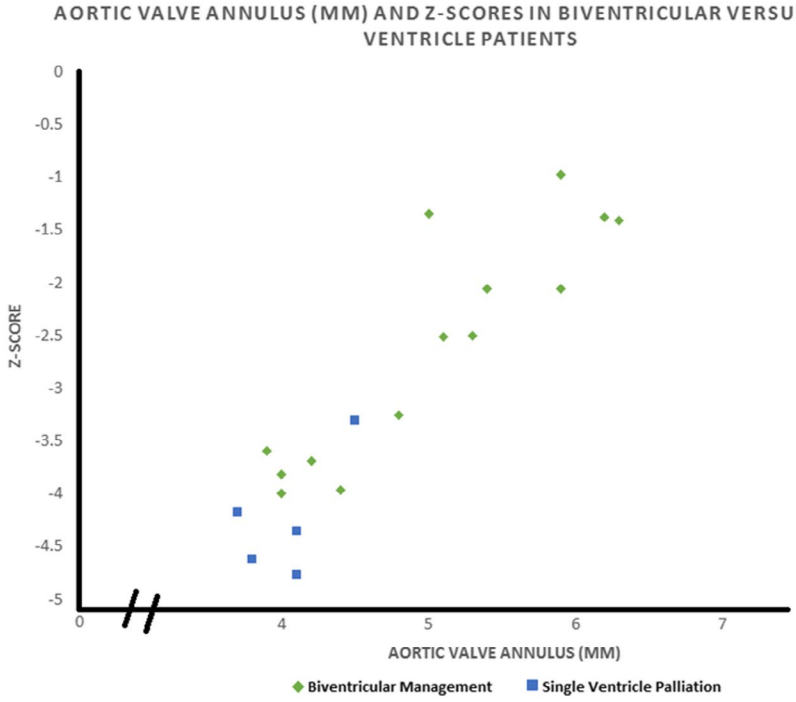

FIGURE 2 Comparison of aortic valve annulus (mm) and *z* scores in neonates with multiple left heart obstructions who underwent successful biventricular management compared to neonates in the same time period who underwent single ventricle palliation

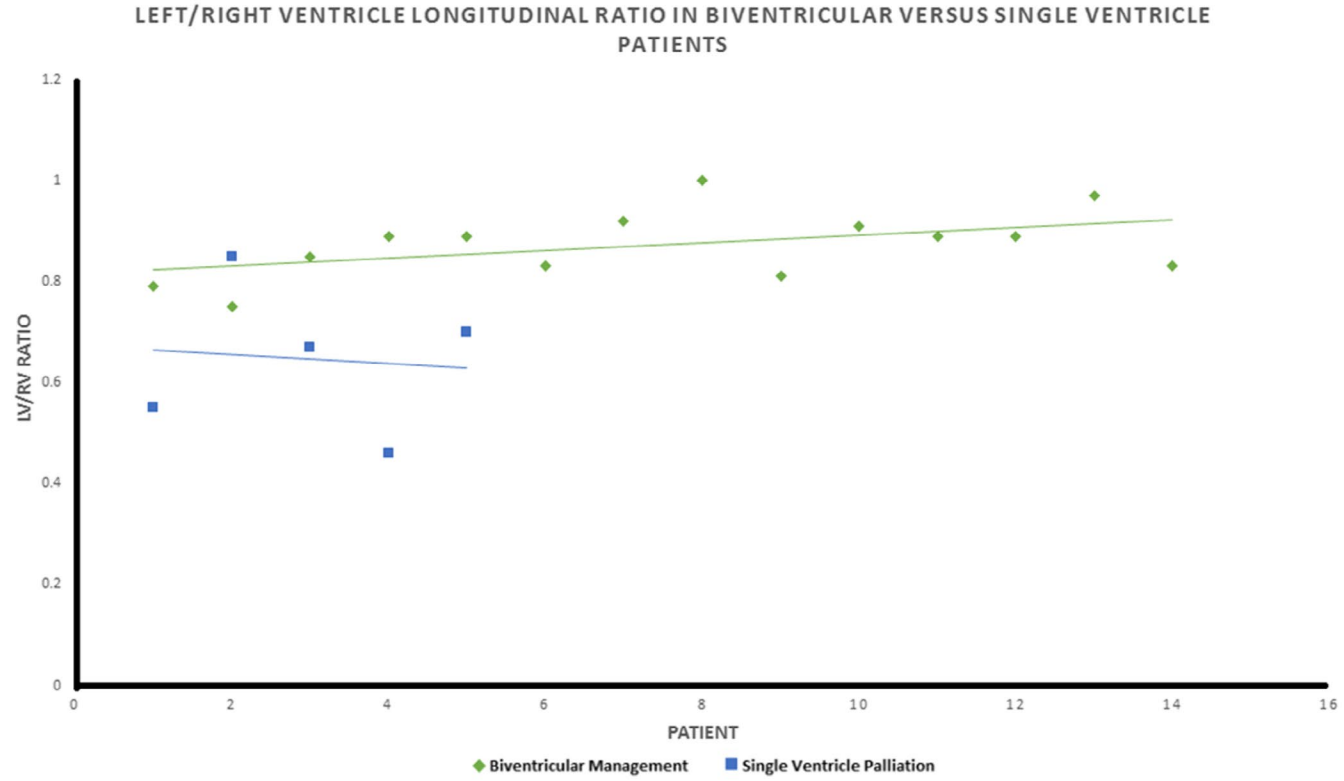

FIGURE 3 Comparison of the left ventricle to right ventricle longitudinal ratio in patients with multiple left heart obstructions who underwent successful biventricular management compared to neonates in the same time period who underwent single ventricle palliation

5 | DISCUSSION

This study presents an analysis of short-term results of infants with multiple left heart obstructions. We compared the 2V patients in this cohort with the 1V palliation in order to identify anatomic and echocardiographic differences between them. Within our dataset, there were excellent short-term results in patients selected for 2V repair; however, the rate of reintervention remains high in this patient

population. As expected, several of our patients required reintervention.[6,8,9] Importantly, none of our patients required intervention on the MV, despite 36% of patients having a parachute MV, a factor which has previously been shown to be detrimental for successful 2V repair.[6] It is worth mentioning that no patient required a takedown to 1V.

The statistical analysis noted some differences between the 1V and 2V groups. Significant differences in mitral/tricuspid valve ratios, aortic valve annuli, and *z* scores, and LV/RV diastolic longitudinal dimensions were found between the 1V and 2V groups; however, there is an overlap between the groups. Several of these markers have been studied previously and were not found to be significant in the success of a 2V repair and due to the overlap in these markers in our study, we caution that using any single measurement for decision-making may be inaccurate.[6] All the patients with an MV ≥7.5 mm and an aortic valve ≥5 mm achieved the 2V repair.[10] Regarding the role in apex forming LV, we found that those with an apex forming LV, even with small MV dimensions (tall and thin LV) had a successful 2V repair. The 1V group had one patient with an LV/RV ratio >0.75, the decision was made to pursue 1V palliation for this patient due to the LV being nonapex forming, and a moderately hypoplastic aortic and MV annuli. All patients in the 1V group had nonapex forming LVs. It is important to note that 4/10 of the 2V patients had nonapex forming LV. Interestingly, anatomic factors which had previously been identified as risk factors for a failed 2V were not found to be significant in our study, including the presence of a moderate to large VSD (3), unicuspid aortic valve (2) and MV annulus, and *z* score.[2,6,12] We recognize that some institutions may rely heavily on the MV annulus and *z* score; however, solely relying on one variable is not supported by our data and previous literature.[6,9,12] However, our study is a small single-center experience and a larger study with more power would better evaluate this.

Several studies have highlighted improved outcomes and reduced morbidity in patients with congenital heart disease who were prenatally diagnosed.[11] In our study, all patients were prenatally diagnosed and the prevention of cardiogenic shock and unrecognized heart failure due to the prenatal diagnosis, and controlled delivery conditions may have helped to minimize our postsurgical complications.

Our study and previous findings show that there are no proven anatomic factors that definitively guide a patient down a definitive surgical pathway. The decision-making process is a multifactorial complex process that may require shared decision-making between different parts of the cardiac team and often with the families. Prior studies have listed mathematical formulas that were developed retrospectively as a means of determining in which patients are suitable for a 2V repair.[12] However, though it is a great first step, using these formulae is often troublesome and prone to error.[12] Additionally, they have not been prospectively validated and the use of these formulas was mainly for the cases of isolated aortic stenosis and do not encompass the multitude of variable left heart obstructive lesions that can occur.[5]

6 | LIMITATIONS

The retrospective nature of this study results in several important limitations. The most obvious limitation is that it is not possible to know whether patients who were selected for 1V palliation would have successful 2V repairs. In addition, this is a study assessing only short-term outcomes, representing patients followed for 3 years or less; it is unknown what future surgical or interventional procedure will be required. It is possible that they could require prosthetic valves, pacemakers, or develop pulmonary hypertension as a consequence of having proceeded with a 2V repair. Our study has now transitioned from retrospective to prospective as we continue to follow this group of patients for further longitudinal data.

7 | CONCLUSIONS

Decision-making in patients with two left heart obstructive lesions remains challenging. We propose the use of mitral/tricuspid valve ratio, the aortic annulus size, and *z* score and the LV/RV diastolic longitudinal dimension as factors to help predict whether a patient will have successful 2V repair though there is a significant overlap and there is no one factor that predicts 2V circulation in all cases. Validation of these findings at a multiinstitutional level is the next step in patient management.

CONFLICTS OF INTEREST

The authors report no conflicts of interest for this study.

AUTHOR CONTRIBUTIONS

Jeremy Steele, Rukmini Komarlu and Francine Erenberg were the designers of the study. Jeremy Steele collected all of the data. Collectively all three were responsible for composing the manuscript.

Sarah Worley provided the in depth statistical analysis and also helped with study design.

Tarek Alsaied and Christopher Statile provided critical revisions and assistance in writing of the manuscript.

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