Cardiology in the Young (2015), **25**, 1482–1488
doi:10.1017/S1047951115002267

Original Article

Characterising adequacy or inadequacy of the borderline left ventricle: what tools can we use?*

Michelle Kaplinski, Meryl S. Cohen

Division of Cardiology, The Children's Hospital of Philadelphia, University of Pennsylvania, Perelman School of Medicine, Philadelphia, Pennsylvania, United States of America

Abstract Borderline left ventricle refers to a spectrum of left ventricular underdevelopment, typically associated with other cardiac anomalies. The left ventricle may be mildly hypoplastic, as is sometimes seen accompanying aortic coarctation, or it can be severely hypoplastic, as is seen in hypoplastic left heart syndrome. For patients with a borderline left ventricle that is at either extreme, the treatment decision is relatively straightforward. Those with the most severe form of left ventricle hypoplasia will require single ventricle palliation or cardiac transplantation, whereas those with the mildest form may not need any intervention. It is the management strategy of children that fall within the grey zone of the spectrum, which continues to be controversial and remains variable within and among different institutions. Cardiac diseases with associated left ventricle hypoplasia include critical aortic stenosis, mitral stenosis, coarctation of the aorta, arch hypoplasia, cor triatriatum, unbalanced common atrioventricular canal, Shone's complex, total anomalous pulmonary venous return, and complex conotruncal abnormalities. In this review, we will discuss the assessment and management of infants with borderline left ventricle with critical aortic stenosis or arch obstruction and associated mitral anomalies.

Keywords: Left ventricular hypoplasia; critical aortic stenosis; aortic arch hypoplasia; endocardial fibroelastosis; mitral stenosis

Received: 6 September 2015; Accepted: 18 September 2015

Introduction

Borderline left ventricle refers to a spectrum of left ventricular underdevelopment, typically associated with other cardiac anomalies.[1,2] The left ventricle may be mildly hypoplastic, as is sometimes seen accompanying aortic coarctation, or it can be severely hypoplastic, as is seen in hypoplastic left heart syndrome.[3–5] For patients with a borderline left ventricle that is at either extreme, the treatment decision is relatively straightforward. Those with the most severe form of left ventricle hypoplasia will require single ventricle palliation or cardiac transplantation, whereas those with the mildest form may not need any intervention. It is the management strategy of children that fall within the grey zone of the spectrum, which continues to be controversial and remains variable within and among different institutions. Cardiac diseases with associated left ventricle hypoplasia include critical aortic stenosis, mitral stenosis, coarctation of the aorta, arch hypoplasia, cor triatriatum, unbalanced common atrioventricular canal, Shone's complex, total anomalous pulmonary venous return, and complex conotruncal abnormalities. For the purposes of this review, we will limit our discussion to borderline left ventricles with critical aortic stenosis or arch obstruction and associated mitral anomalies.

*Presented at the Children's Hospital of Philadelphia Cardiology 2015: 18th Annual Update on Pediatric and Congenital Cardiovascular Disease: "Challenges and Dilemmas", Scottsdale, Arizona, United States of America, Wednesday February 11, 2015–Sunday, February 15, 2015.

Correspondence to: Meryl S. Cohen, MD, Professor of Pediatrics, Division of Cardiology, The Children's Hospital of Philadelphia, 34th Street and Civic Center Blvd. Philadelphia, PA 19104, United States of America. Tel: +2155903354; Fax: +2155903788; E-mail: cohenm@email.chop.edu

Aetiology of left ventricle hypoplasia

There are many hypotheses regarding the aetiology of left ventricle hypoplasia. The "flow theory" suggests that decreased flow through the left ventricle in fetal life impedes growth of the left-sided structures.

Causes of decreased flow include intrinsic left ventricle disease such as endocardial fibroelastosis, intracardiac obstruction, or extrinsic compression of the left side of the heart. Endocardial fibroelastosis is a poorly understood entity that causes diffuse fibrosis of the left ventricle endocardium. It is associated with severe diastolic dysfunction and cessation of left ventricle growth in utero.[5,6] Intracardiac obstruction includes premature closure or restriction of the foramen ovale, mitral stenosis and/or aortic stenosis, and coarctation of the aorta.[7] Finally, extrinsic compression may occur in patients with a left-sided mass, including congenital diaphragmatic hernia or congenital cystic adenomatoid malformation.[8] There have been several genetic syndromes and genes that have been implicated in the aetiology of left ventricle hypoplasia as well; Jacobsen syndrome, HAND-1, HAND-2, and NOTCH are the most notable and have mainly been implicated in aortic stenosis.[9,10]

Even with advancements in survival for both cardiac transplantation and single ventricle palliation, the potentially severe morbidity associated with these surgical options makes biventricular repair more appealing; however, accomplishing a biventricular circulation in the setting of borderline left ventricle carries short-term and long-term risks. The major morbidities associated with biventricular repair include multiple re-interventions and pulmonary hypertension.[11–14] Re-interventions include arch re-operation, left ventricle outflow repair, and mitral valve replacement.[13–16] Moreover, conversion to a single ventricle strategy for "failed" biventricular repair is associated with significant morbidity and mortality.[14]

Congenital heart defects associated with left ventricular hypoplasia

Critical aortic valve stenosis

With critical aortic stenosis, there is duct-dependent systemic circulation. It is, thus, often difficult to predict whether relief of the outflow obstruction will result in a viable biventricular circulation or whether the left ventricle itself is too small to support the systemic output. To complicate issues further, the mitral valve is often stenotic or becomes stenotic over time. Left ventricular hypoplasia is associated with critical aortic stenosis likely related to cessation of growth.[17,18] Over the past three decades, many investigators have reported the potential risk factors for poor outcome after biventricular repair in patients with critical aortic stenosis. Smaller left ventricle size has been consistently associated with higher mortality in this cohort in multiple studies.[17–21] A left ventricular end-diastolic volume $<20\ ml/m^2$ has been considered too small for systemic viability.[22] Other researchers have focused on specific characteristics of the left ventricle such as endocardial fibroelastosis.[17,18] In earlier studies, endocardial fibroelastosis was diagnosed only during autopsy. More recent studies have suggested that endocardial fibroelastosis is difficult to diagnose by echocardiography and can be more accurately diagnosed by cardiac magnetic resonance.[23] Nevertheless, even in prospective analyses, endocardial fibroelastosis can be difficult to diagnose using echocardiography or cardiac magnetic resonance.[24] Endocardial fibroelastosis portends left ventricle diastolic dysfunction and poor filling even when the aortic stenosis is relieved by surgical or transcatheter valvotomy. In the presence of endocardial fibroelastosis, the consequence of biventricular repair may be left atrial hypertension and eventual pulmonary hypertension.[24] In the long term, restrictive cardiomyopathy may develop.[25,26]

In 1991, Rhodes et al designed one of the first studies that analysed multiple variables and their impact on surgical outcomes for critical aortic stenosis.[27] A multivariate equation using echocardiographic measurements was developed to help predict patients who would be more suitable for a biventricular repair (Fig 1). A score of less than −0.35 correctly predicted death (retrospectively) after biventricular repair in 88% of patients in whom it was applied. Risk factors were also identified for death after biventricular repair, including left ventricle length, aortic root size, mitral valve area, and left ventricle mass. The mortality rate was 100% in patients who had two or more of these risk factors and only 8% in those with one or zero. As these criteria are from an earlier surgical era, the Ross and Konno procedure were not taken into account. Thus, the small aortic root size may not be as relevant today. Despite this limitation, the "Rhodes" score is ubiquitous and is often used to help paediatric cardiologists and surgeons determine the best surgical approach for patients with congenital aortic stenosis and left ventricle hypoplasia.

The Congenital Heart Surgeons Society also sought to determine patients with aortic stenosis and

14.0 (body surface area) + 0.943 (indexed aortic root dimension) + 4.78 (long-axis dimension of the heart) + 0.157 (indexed mitral valve area) – 12.03.

Figure 1.
Multivariate equation used as Rhodes score for successful biventricular repair.[27]

https://doi.org/10.1017/S1047951115002267 Published online by Cambridge University Press

Survival benefit = Intercept + b1 (age at entry) + b2 (z-score of aortic valve at the sinuses) + b3 (grade of EFE) + b4 (ascending aorta diameter) + b 5 (presence of moderate or severe tricuspid regurgitation) + b6 (z-score of the left ventricular length)

Figure 2.
Congenital Heart Surgeons Society's multiple linear regression equation for survival benefit after biventricular repair.[28]

10.98 (body surface area) + 0.56 (aortic annulus z-score) + 5.89 (left ventricular to heart long-axis ratio) – 0.79 (grade 2 or 3 endocardial fibroelastosis) – 6.78.

Figure 3.
New scoring system for aortic stenosis and left ventricular hypoplasia.[29]

small left ventricles who would do well with a biventricular repair.[28] This study was unique in that it also considered risk factors for single ventricle palliation. A multivariable analysis of factors associated with outcomes was used to predict the magnitude and the direction of the survival benefit for the optimal pathway – biventricular repair or single ventricle palliation (Fig 2). Unlike the Rhodes score, the Congenital Heart Surgeons Society incorporated endocardial fibroelastosis into the scoring system, as well as tricuspid regurgitation – a risk factor in single ventricle palliation. Of note, it did not include a measure of mitral valve size, which many consider critical to help determine left ventricle viability.

More recently, Colan et al further refined the Rhodes criteria, yielding a model (Fig 3) that was similar to it, but with a reported 90% accuracy at predicting survival with biventricular circulation among neonates with critical aortic stenosis and a mitral valve area z-score of less than −2.[29] This equation assumes that any patient with a mitral valve z-score worse than −2 does not require biventricular repair. It should be noted that all these scoring systems have not been validated for other types of left ventricle hypoplasia. In fact, many patients who have "failed" these criteria have had successful biventricular repair procedures.[30,31] This is especially true for patients with arch hypoplasia. Therefore, the Congenital Heart Surgeons Society and modified Rhodes criteria should be used exclusively for patients with critical aortic stenosis.

Once a child is born with critical aortic stenosis, the evaluation of left ventricle size becomes critical in order to determine whether biventricular repair is possible; however, much has been learnt about this disease by how it evolves before birth. Many fetuses with aortic stenosis progress to develop hypoplastic left heart syndrome in utero.[32,33] This observation, first noted in the 1980s, has been the impetus for the field of fetal cardiac intervention. In mid-gestation, some fetuses with critical aortic stenosis will present with a left ventricle that is dilated, poorly functioning, and evident of endocardial fibroelastosis.[33] Over the course of the pregnancy, this type of left ventricle often has cessation of growth such that it is markedly hypoplastic at birth. In a fetal study assessing critical aortic stenosis, fetuses that developed hypoplastic left heart syndrome were more likely to exhibit reversal of flow in the transverse aortic arch and foramen ovale, monophasic flow across the mitral valve, and left ventricle dysfunction compared with fetuses with viable left ventricles at birth.[34] Others have suggested that patients who develop aortic stenosis postnatally have little or no growth of the left ventricle, aortic valve, or mitral valve during fetal life; thus, following the trajectory of growth of these structures is helpful to predict severity of disease.[35,36] Mid-gestation risk factors for cessation of left ventricle growth are used to justify fetal aortic balloon valvuloplasty to potentially promote forward flow through the left ventricle, and thus growth of the left-sided structures.[37]

Aortic arch hypoplasia

Aortic arch hypoplasia has been associated with left ventricle hypoplasia as well. The aortic valve may be small but is typically not stenotic. Often, the mitral valve is normal in structure but hypoplastic. In some cases, the mitral valve is structurally abnormal, present either as a parachute or an arcade valve. Similar to critical aortic stenosis, the decision-making process regarding aortic arch hypoplasia and a small left ventricle is also challenging.

There are several issues that make aortic arch hypoplasia different from critical aortic stenosis. In critical aortic stenosis, the left ventricle is often small but distended because of endocardial fibroelastosis (Fig 4a). Thus, it is not as amenable to alterations in filling to promote growth. In contrast, the left ventricle in aortic arch hypoplasia is typically slim and not apex-forming (Fig 4b). Thus, increased flow into the left ventricle may potentially increase the left ventricle size.

Early postnatal studies have demonstrated that neonates with coarctation of the aorta and a hypoplastic, but morphologically normal, left ventricle can have successful secondary growth of the left-sided

https://doi.org/10.1017/S1047951115002267 Published online by Cambridge University Press

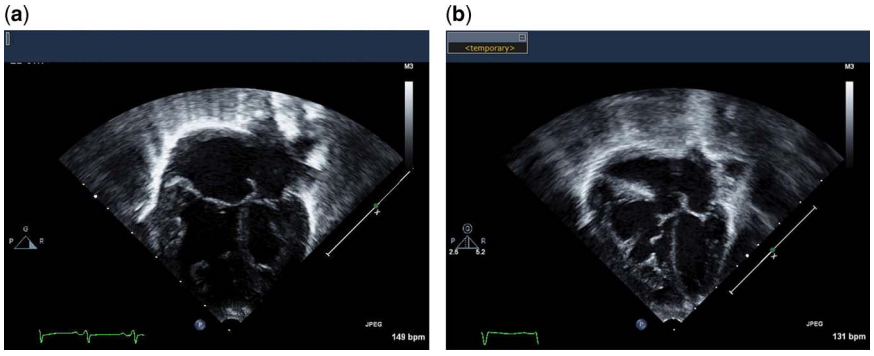

Figure 4.
*(**a**) In critical aortic stenosis, the left ventricle (LV) is often small but distended because of endocardial fibroelastosis (EFE). Thus, it may not be amenable to alterations in filling to promote growth. (**b**) In contrast, the LV in aortic arch hypoplasia is typically slim and not apex-forming. Increased flow into the LV may potentially increase the LV size.*

$$\left(\frac{\left(\frac{(MV_{4C}/AV_{PSLA})}{(LVL_{4C}/RVL_{4C})}\right)+MPA}{BSA}\right)$$

Figure 5.
Echocardiographic scoring system for borderline left ventricle.[41] AVPSLA, aortic valve annulus measured in cm in the parasternal long-axis view in mid systole; BSA, patient's body surface area, in m^2; LVL4C, left ventricular length measured in cm in the 4-chamber view at end diastole; MPA, main pulmonary artery diameter measured in cm either in the parasternal long-axis or short-axis view in mid systole; MV4C, mitral valve annulus measured in cm in the apical four-chamber view at end diastole; RVL4C, right ventricular length measured in cm in the 4-chamber view at end diastole.

structures after repair.[31,38] Pulchalski et al reported that the mitral and aortic valve z-scores increased significantly after repair of coarctation of the aorta even in patients who start with mitral and aortic valve z-scores of as low as −4.[39] In their cohort, all the patients survived, but 20% of them required re-intervention, which was primarily to address the left ventricular outflow tract. A follow-up study of the same population demonstrated that the overall freedom from re-intervention was 76% at 15 years after the original arch repair.[40]

Recently, a scoring system has been devised to help determine viability of biventricular repair in patients with borderline left ventricle, regardless of other associated lesions (Fig 5).[41] Predictors include mitral valve annulus size, aortic valve annulus size, left ventricular length, right ventricular length, main pulmonary artery diameter, and patient's body surface area. Successful biventricular repair has been associated with a score of ⩽16.2, with 100% sensitivity and specificity. This score has not yet been prospectively validated.

Arch obstruction often presents in a more subtle manner in utero than critical aortic stenosis. Often, a discrepancy between left ventricle and right ventricle size is the most notable feature.[42] Quartermain et al reported that postnatal aortic arch obstruction was common in fetuses with LV:RV size discrepancy.[43] A ratio of ⩽0.6 had good sensitivity for the prediction of need for neonatal arch intervention. Others have shown that measures of the ascending aorta, aortic isthmus, and pulmonary valve-to-aortic valve diameter ratio are good predictors of postnatal coarctation.[44,45] Slower rate of growth of the aortic valve is also quite sensitive and specific for predicting coarctation of the aorta.[45]

Mitral valve disease

The mitral valve is one of the most important factors in determining the feasibility of biventricular repair. Mitral valve abnormalities are associated with arch hypoplasia and critical aortic stenosis and are often a component of Shone's complex.[46] When mitral valve abnormality is the primary disease, survival after surgical intervention is quite poor compared with intervention on other valves.[47] Many patients with left ventricle hypoplasia have structural mitral valve disease, most typically arcade mitral valve, with shortened or no chordae tendinae, or parachute mitral valve, with the majority of chordae tendinae attached to one papillary muscle. Importantly, mitral stenosis is often not present at birth, only to progress over time after initial repair. Previous studies assessing the success of biventricular repair in patients with borderline left ventricle have reported high rates of re-intervention, particularly of the mitral valve, with mitral valvuloplasty or mitral valve replacement being common.[12–14] In a recent study of 49 infants and children who underwent the Ross/Konno procedure, mitral valve disease was highly associated

https://doi.org/10.1017/S1047951115002267 Published online by Cambridge University Press

with mortality.[16] Morbidity included multiple re-operations on the mitral valve and pulmonary hypertension. Others have used selection criteria that focus on mitral valve disease in determining whether a biventricular repair should be attempted.[48] Using these factors, biventricular repair can be successful with the mitral valve having little impact on the outcome; however, re-operation rates for other left-sided issues remain quite high.[48] Among all considerations for biventricular repair, the mitral valve must remain an important focus of the evaluation.

New treatment strategies for borderline left ventricle

Fetal intervention

With the observation that fetal critical aortic stenosis can evolve into hypoplastic left heart syndrome, fetal intervention was explored as early as 25 years ago.[32,33] Transcatheter fetal aortic valve dilation has been performed successfully in over one hundred fetuses over the last decade, much to the credit of the team at Boston Children's Hospital. Although it has been technically successful, the number of patients who have had a successful and sustained biventricular repair after birth has remained limited.[37,49] Moreover, multiple re-interventions over the first few years of life are common.[49] Fetal aortic valvuloplasty can result in aortic valve and mitral valve growth.[50,51] It has also been shown to improve left ventricle function in some patients.[49,51] Importantly, these cohorts have been studied without a control group. Thus, it is difficult to know whether fetuses without fetal intervention would have had a different outcome. Moreover, fetal intervention poses a procedural risk to the mother and a 10% mortality rate for the fetus. Nonetheless, fetal intervention has moved the field of paediatric cardiology forward and will likely continue to have a place in treatment of the borderline left ventricle.

Left ventricle rehabilitation strategy

For left ventricle hypoplasia with arch obstruction, arch repair is often the only surgical procedure necessary because the mitral and aortic valves are unobstructed and endocardial fibroelastosis is not present. On the other hand, for patients with aortic valve disease, mitral valve disease, and endocardial fibroelastosis, surgical strategy may be more complicated. Several new treatment strategies have been proposed over the last decade to augment forward flow into the left ventricle, and thus promote growth of the left-sided structures; one such method, now termed left ventricle rehabilitation, includes a combination of techniques to relieve inflow and outflow tract obstruction coupled with endocardial fibroelastosis resection. Endocardial fibroelastosis resection during a Ross/Konno procedure was first reported in 1997 and resulted in improved diastolic function and improved left ventricular stroke volume.[52] Emani et al recently evaluated nine patients who underwent left ventricular rehabilitation surgery; there was no operative mortality and no deaths from cardiac causes after a median of 25 months of follow-up,[53] but two patients did require re-operation. There was a decrease in left atrial pressure and left ventricular end-diastolic pressure with improved ejection fraction post-operatively; however, pulmonary artery pressure and pulmonary vascular resistance were not reported. These patients require close follow-up over a more extended period of time, with follow-up haemodynamic measurements to determine what happens to the pulmonary vascular resistance and pulmonary artery pressures over time.

The same group has also proposed another newer surgical strategy – that is, performing left ventricle recruitment in a staged manner. An initial Norwood procedure is performed, but the atrial septum is left restrictive on purpose to promote forward flow through the mitral valve. After a variable period of time of growth, the left ventricle is "rehabilitated" with endocardial fibroelastosis resection, mitral valve chordal elongation, and repair of the left ventricular outflow tract. Of the 34 patients in the staged recruitment group, 13 of them underwent biventricular conversion.[54] At the median follow-up of 2.9 years (range 1–6 years), there has been no mortality. Re-operation after biventricular conversion has been performed in four patients. In about half of the patients, the right ventricle pressure has been reported as half the systemic arterial pressure. In the other half, the right ventricle pressure has not been measured or is more than half of the systemic pressure. Of note, pulmonary vascular resistance, left atrial pressures, and pulmonary artery pressures have not been reported in this cohort. It also remains to be seen whether the left ventricle growth that is seen is actual growth or pathologic dilation. Further follow-up studies need to be performed to validate these findings. Hammel et al published a report of four patients who had critical aortic stenosis and severe left ventricular dilation and dysfunction.[55] They also proposed a two-stage surgical approach. The first stage consisted of surgical aortic valvotomy, bilateral pulmonary artery banding, and atrial septectomy. The second stage included patch closure of the atrial septal defect, ligation of the ductus arteriosus, and removal of the pulmonary artery bands. Prostaglandin infusion continued between the stages to maintain right ventricle contribution to systemic perfusion. The results were mixed, with two patients dying before the second stage and two patients surviving with a normal left ventricle ejection fraction. These reports demonstrate

the extreme variability of outcomes in patients with borderline left ventricles, regardless of treatment.

Conclusions

Left ventricle hypoplasia is not a homogeneous diagnosis, and thus should not be treated as one. Complicating matters is the fact that there are morphological and physiological changes that occur during fetal, neonatal, and post-operative life; determining the severity of disease at all levels of obstruction remains extraordinarily challenging. Using a scoring system may incorrectly lead a clinician down the wrong surgical pathway. More confounding is the fact that biventricular failure cannot be recognised until it is attempted, whereas single ventricle palliation failure has nothing to do with the risk factors of borderline left ventricle. The different scoring systems available are labour-intensive and vulnerable to error. Newer strategies such as the Ross operation with or without a Konno procedure are very effective treatments for aortic stenosis. Endocardial fibroelastosis resection may have benefit but long-term results remain to be seen. If a biventricular repair is attempted, a thorough evaluation of the mitral valve and its apparatus and a consistent method to evaluate the presence and severity of endocardial fibroelastosis are essential. Multiple re-interventions are common in this population and should be expected. Pulmonary hypertension and restrictive cardiomyopathy may be the long-term consequences of aggressive left ventricle rehabilitation. As a community, we have yet to determine whether this pathway is "better" than a good single ventricle palliation.

References

1. Morell VO, Quintessenza JA, Jacobs JP. Biventricular repair in the management of hypoplastic left heart syndrome. Cardiol Young 2004; 14: 101–104.
2. Tchervenkov CI, Tahta SA, Jutras LC, et al. Biventricular repair in neonates with hypoplastic left heart complex. Ann Thorac Surg 1998; 66: 1350–1357.
3. Schwartz ML, Gauvreau K, Geva T. Predictors of outcome of biventricular repair in infants with multiple left heart obstructive lesions. Circulation 2001; 104: 682–687.
4. 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: 1429–1436.
5. Cohen MS, Rychik J. The small left ventricle: how small is too small for biventricular repair? Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu 1999; 2: 189–202.
6. Lurie PR. Changing concepts of endocardial fibroelastosis. Cardiol Young 2010; 20: 115–123.
7. Feit LR, Copel JA, Kleinman CS. Foramen ovale size in the normal and abnormal human fetal heart: an indicator of transatrial flow physiology. Ultrasound Obstet Gynecol 1991; 1: 313–319.
8. Siebert JR, Haas JE, Beckwith JB. Left ventricular hypoplasia in congenital diaphragmatic hernia. J Pediatr Surg 1984; 19: 567–571.
9. Garg V, Muth A, Ransom J, et al. Mutations in NOTCH1 cause aortic valve disease. Nature 2005; 437: 270–274.
10. Ye M, Coldren C, Lai X, et al. Deletion of ETS-1, a gene in the Jacobsen syndrome critical region, causes ventricular septal defects and abnormal ventricular morphology in mice. Hum Mol Genet 2010; 19: 648–656.
11. Hickey EJ, Caldarone Ca, McCrindle BW. Left ventricular hypoplasia: a spectrum of disease involving the left ventricular outflow tract, aortic valve, and aorta. J Am Coll Cardiol 2012; 59 (Suppl 1): S43–S54.
12. Alboliras E, Mavroudis C, Pahl E, et al. Left ventricular growth in selected hypoplastic left ventricles: outcome after repair of coarctation of aorta. Ann Thorac Surg 1999; 68: 549–555.
13. Serraf A, Piot JD, Bonnet N, Galletti L, Planche C. Biventricular repair approach in ducto-dependent neonates with hypoplastic but morphologically normal left ventricle. J Am Coll Cardiol 1999; 33: 827–834.
14. Tchervenkov CI, Tahta SA, Jutras LC, Béland MJ. Biventricular repair in infants with hypoplastic left heart complex. Ann Thorac Surg 1998; 66: 1350–1357.
15. Cavigelli-Brunner A, Bauersfeld U, Prêtre R, et al. Outcome of biventricular repair in infants with multiple left heart obstructive lesions. Pediatr Cardiol 2012; 33: 506–512.
16. Vergnat M, Roubertie F, Lambert V, et al. Mitral disease: the real burden for the Ross-Konno procedure in children. Ann Thorac Surg 2014; 98: 2165–2172.
17. Mocellin R, Sauer U, Simon B, et al. Reduced left ventricular size and endocardial fibroelastosis as correlates of mortality in newborns and you infants with severe aortic valve stenosis. Pediatr Cardiol 1986; 4: 265–272.
18. Gundry SR, Behrendt DM. Prognostic factors in valvotomy for critical aortic stenosis in infancy. J Thorac Cardiovasc Surg 1986; 92: 747–754.
19. Latson LA, Cheatham JP, Gutgesell HP. Relation of the echocardiographic estimate of left ventricular size to mortality in infants with severe left ventricular outflow obstruction. Am J Cardiol 1981; 48: 887–891.
20. Parsons MK, Moreau GA, Graham TP, et al. Echocardiographic estimation of critical left ventricular size in infants with isolated aortic valve stenosis. J Am Coll Cardiol 1991; 18: 1049–1055.
21. Leung MP, McKay R, Smith A, et al. Critical aortic stenosis in early infancy: anatomic and echocardiographic substrates of successful open valvotomy. J Thorac Cardiovasc Surg 1991; 101: 526–535.
22. Hammon JW, Lupinetti FM, Maples MD, et al. Predictors of operative mortality in critical valvular aortic stenosis presenting in infancy. Ann Thorac Surg 1988; 45: 537–540.
23. Stranzinger E, Ensing GJ, Hernandez RJ. MR findings of endocardial fibroelastosis in children. Pediatr Radiol 2008; 38: 292–296.
24. Tuo G, Khambadkone S, Tann O, et al. Obstructive left heart disease in neonates with a "borderline" left ventricle: diagnostic challenges to choosing the best outcome. Pediatr Cardiol 2013; 34: 1567–1576.
25. Schwienbacher M, Schweigmann U, Neu N, et al. Heart transplantation in a 14-year-old boy in the presence of severe out-of-proportion pulmonary hypertension due to restrictive left heart disease: a case report. Case Rep Cardiol 2013; Epub ahead of print.
26. Friedman KG, Margossian R, Grahan DA. Postnatal left ventricular diastolic function after fetal aortic valvuloplasty. Am J Cardiol 2011; 108: 556–560.
27. Rhodes LA, Colan SD, Perry SB, et al. Predictors of survival in neonates with critical aortic stenosis. Circulation 1991; 84: 2325–2335.
28. 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.

29. Colan SD, McElhinney DB, Crawford EC, et al. Validation and re-evaluation of a discriminant model predicting anatomic suitability for biventricular repair in neonates with aortic stenosis. J Am Coll Cardiol 2006; 47: 1858–1865.
30. Blaufox AD, Wyman WL, Lopez L, et al. Survival in neonatal biventricular repair of left-sided cardiac obstructive lesions associated with hypoplastic left ventricle. Am J Cardiol 1998; 82: 1138–1140.
31. Tani LY, Minich LL, Pagotto LT, et al. Left heart hypoplasia and neonatal aortic arch obstruction: Is the Rhodes left ventricular adequacy score applicable? J Thorac Cardiovasc Surg 1999; 118: 81–86.
32. Allan LD, Sharland GK, Tynan MJ. The natural history of the hypoplastic left heart syndrome. Int J Cardiol 1989; 25: 341–343.
33. Sharland GK, Chita SK, Fagg NLK, et al. Left ventricular dysfunction in the fetus. Relation to aortic valve anomalies and endocardial fibroelastosis. Br Heart J 1991; 66: 419–424.
34. Mäkikallio K, McElhinney DB, Levine JC, et al. Fetal aortic valve stenosis and the evolution of hypoplastic left heart syndrome, patient selection for fetal intervention. Circulation 2006; 113: 1401–1405.
35. Hornberger LK, Sanders SP, Rein AJJT, et al. Left heart obstructive lesion and left ventricular growth in the midtrimester fetus. Circulation 1995; 92: 1521–1538.
36. McCaffrey FM, Sherman FS. Prenatal diagnosis of severe aortic stenosis. Pediatr Cardiol 1997; 18: 276–281.
37. Tworetzky W, Wilkins-Haug L, Jennings RW, et al. Balloon dilation of severe aortic stenosis in the fetus: potential for prevention of hypoplastic left heart syndrome: candidate selection, technique and results of successful intervention. Circulation 2004; 110: 2125–2131.
38. Minich LL, Tani LY, Hawkins JA, et al. Possibility of postnatal left ventricular growth in selected infants with non-apex-forming left ventricles. Am Heart J 1997; 133: 570–574.
39. Puchalski MD, Williams RV, Hawkins JA, et al. Follow-up of aortic coarctation repair in neonates. J Am Coll Cardiol 2004; 44: 188–191.
40. Gray RG, Tani LY, Weng HY, et al. Long-term follow-up of neonatal coarctation and left-sided cardiac hypoplasia. Am J Cardiol 2013; 111: 1351–1354.
41. Mart CR, Eckhauser AW. Development of an echocardiographic scoring system to predict biventricular repair in neonatal hypoplastic left heart complex. Pediatr Cardiol 2014; 35: 1456–1466.
42. Brown DL, Durfee SM, Hornberger LK. Ventricular size discrepancy as a sonographic sign of coarctation of the fetal aorta: how reliable is it? J Ultrasound Med 1997; 16: 95–99.
43. Quartermain MD, Cohen MS, Dominguez TE, et al. Left ventricle to right ventricle size discrepancy in the fetus: the presence of critical congenital heart disease can be reliably predicted. J Am Soc Echocardiogr 2009; 22: 1296–1301.
44. Jantzen DW, Gelehrter SK, Yu S, et al. Echocardiographic factors discriminating biventricular versus univentricular approach in the foetus with borderline left ventricle. Cardiol Young 2015; 25: 941–950.
45. Gómez-Montes E, Herraiz I, Gómez-Arriaga PI, et al. Gestational age-specific scoring systems for the prediction of coarctation of the aorta. Prenat Diagn 2014; 34: 1198–1206.
46. Shone JD, Sellers RD, Anderson RC, et al. The developmental complex of "parachute mitral valve", supravalvar ring of the left atrium, subaortic stenosis and coarctation of the aorta. Amer J Cardiol 1963; 11: 714–725.
47. McElhinney DB, Sherwood MC, Keane JF, et al. Current management of severe congenital mitral stenosis: outcomes of transcatheter and surgical therapy in 108 infants and children. Circulation 2005; 112: 707–714.
48. Avitabile C, Mercer-Rosa L, Ravishankar C, et al. Experience with biventricular intervention for neonates with mitral valve abnormalities in the setting of critical left-side heart obstruction. Ann Thorac Surg 2015; 99: 877–883.
49. Freund LR, McElhinney DB, Marshall AC, et al. Fetal aortic valvuloplasty for evolving hypoplastic left heart syndrome: postnatal outcomes of the first 100 patients. Circulation 2014; 130: 638–645.
50. Maxwell D, Allan L, Tynan MJ. Balloon dilatation of the aortic valve in the fetus: a report of two cases. Br Heart J 1991; 65: 256–258.
51. McElhinney DB, Marshall AC, Wilkins-Haug LE, et al. Predictors of technical success and postnatal biventricular outcome after in utero aortic valvuloplasty for aortic stenosis with evolving hypoplastic left heart syndrome. Circulation 2009; 120: 1482–1490.
52. Van Son JA, Falk V, Mohr FW. Ross-Konno operation with resection of endocardial fibroelastosis for critical aortic stenosis with borderline-sized left ventricle in neonates. Annal Thorac Surg 1997; 63: 112–116.
53. Emani SM, Bacha EA, McElhinney DB, et al. Primary left ventricular rehabilitation is effective in maintaining two-ventricle physiology in the borderline left heart. J Thorac Cardiovasc Surg 2009; 138: 1276–1282.
54. Emani SM, McElhinney DB, Tworetzky W, et al. Staged left ventricular recruitment after single-ventricle palliation in patients with borderline left heart hypoplasia. J Am Coll Cardiol 2012; 60: 1966–1974.
55. Hammel JM, Duncan KF, Danford DA, et al. Two-stage biventricular rehabilitation for critical aortic stenosis with severe left ventricular dysfunction. Eur J Cardiothorac Surg 2013; 43: 143–148.