Growth of left heart structures following the hybrid procedure for borderline hypoplastic left heart

George Ballard, Shane Tibby, Owen Miller, Thomas Krasemann, Eric Rosenthal, David Anderson, Conal Austin, Shakeel Qureshi, and John Simpson*

Department of Congenital Heart Disease, Evelina Children’s Hospital, Guy’s and St Thomas Hospital Foundation Trust, 6th Floor, Westminster Bridge Road, London SE1 7EH, UK

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Aims

The ‘hybrid’ procedure is an alternative to the Norwood operation in classical hypoplastic left heart syndrome to support the systemic circulation until subsequent palliation. This approach has been extended to infants with the borderline development of left heart structures. We investigated whether or not a hybrid procedure for ‘borderline’ cases of underdevelopment of the left heart would lead to any improvement in the growth of those structures relative to body size or would impact on eventual repair.

Methods and results

Serial echocardiograms were reviewed in cases in whom left heart development was judged borderline for adequacy to support the systemic circulation. z-scores of left heart structures and aortic discriminant scores were plotted sequentially following the hybrid procedure and random-coefficient linear-mixed models were applied to quantify growth rates. Seven infants met the inclusion criteria. At birth, the median (range) of aortic discriminant scores was 2.67 (2.36 to 2.12), suggesting that a biventricular repair would not be feasible. Following a hybrid procedure, aortic discriminant scores increased with time and three infants were managed with a biventricular repair. The rate of change was significantly higher in infants who achieved a biventricular repair compared with those who did not ($P = 0.01$).

Conclusion

The hybrid procedure allows time for growth of left heart structures in selected infants, and serial echocardiography may assist in identifying those children who may ultimately achieve a biventricular circulation.

Keywords

Echocardiography • Heart defects • Congenital • Paediatrics • Imaging

Background

Classical hypoplastic left heart syndrome (HLHS) is characterized by aortic atresia with or without mitral atresia with severe underdevelopment of the left ventricle.1 Variants of this condition include aortic stenosis with underdevelopment of the left ventricle, severe coarctation of the aorta, and severely unbalanced atrioventricular septal defects. Such cases are most commonly managed with a Norwood procedure as the initial surgical palliation.2–4

In some neonates with underdevelopment of left heart structures, there may be difficulty at the outset in deciding whether the left heart is adequate to support the systemic circulation and whether a single-ventricle or biventricular repair should be undertaken. There have been reports of an increase in the rate of growth of the left heart documented with z-scores following intervention for critical aortic stenosis.5,6 Scoring systems such as the aortic discriminant score have been devised to assist in early decision-making in neonates with critical aortic stenosis.7,8 In severe coarctation of the aorta, case series have also described the dilemma with regard to the optimal approach. In that context, a single measurement of the aortic discriminant score was not helpful in predicting outcome.9,10

The hybrid procedure11 (consisting of interventional ductal stenting and surgical bilateral pulmonary artery banding) in the management of hypoplastic left heart has permitted effective palliation of small neonates and others in whom it is desirable to avoid
cardiopulmonary bypass. Previous reports have described the use of the hybrid procedure as a bridge to biventricular repair but have provided no measurements of growth to assist with the selection of the optimal approach.

We report a series of neonates who underwent a hybrid procedure because of the borderline development of left heart structures. Serial echocardiographic measurements were performed, including the aortic discriminant score, to gauge whether growth of left heart structures improved with time. This has the potential advantage that decision-making with regard to the eventual type of repaired could be reviewed over time, permitting optimization of the eventual type of repair.

Methods

Approval for this retrospective analysis was obtained according to the institutional policy. The departmental database (Heartsuite, Systeria, Glasgow, UK) was interrogated to identify all infants who underwent hybrid procedures between December 2005 (first procedure performed at our centre) and June 2008, during which a total of 18 hybrid procedures were performed. Sixty-six infants had Norwood operations for classical HLHS during the same time period. Of the 18 infants who underwent hybrid procedures, 11 had classical HLHS and were excluded. Seven had ‘borderline’ left heart structures, of which the dominant lesion was aortic stenosis in three patients, coarctation of the aorta in three patients, and aortic atresia with ventricular septal defect in one patient (Table 1).

Echocardiography

Echocardiographic studies were performed using Philips 7500, IE33 (Philips, Andover, MA, USA), and General Electric Vivid 7 ultrasound systems (General Electric Corporation, Milwaukee, WI, USA). Serial echocardiograms were reviewed by a single cardiologist (G.B.) to avoid interobserver error. Measurements were obtained from archived images following the same protocol described by Rhodes et al.48 The data analysis was retrospective and did not have an impact on patient management.

Statistical analysis

The temporal profiles for the left heart structures (defined in the Methods section) were compared using random coefficient linear-mixed models. Estimation was via full maximum likelihood. A comparison was made between the two groups: those who subsequently underwent biventricular vs. univentricular repair. P-values were calculated for each left heart variable using type III tests for the following null hypotheses (H0): (i) intercept H0: the intercepts (value at birth) of the left heart structures for the total cohort are equal to zero; (ii) group H0: the intercepts of the univentricular and biventricular groups do not differ, (iii) time H0: the temporal profile (the rate of change of the structural variable) for the entire cohort is equal to zero, and (iv) group–time interaction H0: the rate of change for a particular structural variable does not differ between the univentricular and biventricular groups. Model checking involved the inspection of residual and normal plots. All statistical analyses were performed with SPSS version 15 (SPSS, Chicago, IL, USA).

### Table 1 Initial demographics of the borderline left ventricle population

<table>
<thead>
<tr>
<th>Patient</th>
<th>Diagnosis</th>
<th>Birth weight (kg)</th>
<th>Age at hybrid (days)</th>
<th>Initial aortic discriminant score</th>
<th>Outcome</th>
<th>Follow-up to definitive procedure (days)</th>
<th>Final aortic discriminant score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>AA/AVSD</td>
<td>2.33</td>
<td>19</td>
<td>−3.26</td>
<td>Univentricular</td>
<td>165</td>
<td>−4.16</td>
</tr>
<tr>
<td>2</td>
<td>CoA</td>
<td>2.36</td>
<td>9</td>
<td>−1.62</td>
<td>Univentricular</td>
<td>296</td>
<td>−1.4</td>
</tr>
<tr>
<td>3</td>
<td>AS</td>
<td>4.65</td>
<td>14</td>
<td>−1.26</td>
<td>Biventricular</td>
<td>333</td>
<td>−1.58</td>
</tr>
<tr>
<td>4</td>
<td>AS</td>
<td>3.8</td>
<td>16</td>
<td>−1.62</td>
<td>Biventricular</td>
<td>333</td>
<td>−1.4</td>
</tr>
<tr>
<td>5</td>
<td>CoA/AS</td>
<td>3</td>
<td>3</td>
<td>−2.37</td>
<td>Univentricular</td>
<td>333</td>
<td>−1.58</td>
</tr>
<tr>
<td>6</td>
<td>AS</td>
<td>3.52</td>
<td>6</td>
<td>−2.63</td>
<td>Biventricular</td>
<td>333</td>
<td>−2.37</td>
</tr>
<tr>
<td>7</td>
<td>CoAVSD</td>
<td>1.96</td>
<td>8</td>
<td>−2.87</td>
<td>Biventricular</td>
<td>333</td>
<td>−1.4</td>
</tr>
</tbody>
</table>

AA, aortic atresia; CoA, coarctation; AS, aortic stenosis; VSD, ventricular septal defect.
Results

Seven patients were identified as having borderline left heart structures (Table 1). The median birth weight was 3.0 kg (range, 2.33–4.65 kg) and median age at hybrid procedure was 9 days (range, 3–19 days). Four patients eventually proceeded to a single-ventricle circulation and three underwent a biventricular repair. The median echocardiographic follow-up to the definitive procedure was 296 days (range, 50–496 days).

Interventions

Those patients with a univentricular repair underwent an average of 2.8 cardiac interventions. Prior to their definitive operation, one patient required stenting of the aorta proximal to the ductal stent to allow retrograde flow to the aortic arch, and one patient required catheter interventions on the interatrial septum (Table 2). The definitive operation in those patients who underwent a single-ventricle palliation was a combined Stage I Norwood and Glenn operation. This entailed a take-down procedure of the removal of the ductal stent, debanding of both the branch pulmonary arteries, hemi-Fontan construction, aortic arch reconstruction, and atrial septectomy where necessary. This is referred to as a Norwood/Glenn procedure for the purpose of this paper. Those patients who achieved a biventricular repair underwent, on average, 3.7 cardiac interventions. The increased number of interventions in the biventricular group tended to be surgical optimization of the left heart structures, with aortic valve and mitral valve (MV) surgical interventions, in two cases, a Ross procedure as the definitive intervention.

One patient who underwent biventricular repair subsequently developed pulmonary hypertension and died (Patient 3). All other patients are currently alive and well (Table 2).

Growth trajectories

Calculated growth trajectories for the left heart structures are shown in Table 3. Overall, the aortic discriminant score demonstrated the most convincing increase and was able to discriminate between the univentricular and biventricular groups. The z-scores for both aortic measurements at birth (intercepts) were significantly less than zero, with the univentricular group displaying smaller values than the biventricular group (both \( P < 0.01 \)). Elsewhere, the intercept values did not differ between the two groups. The aortic discriminant score showed an increase over time (\( P < 0.001 \)), with a faster rate of growth for the biventricular group (interaction \( P = 0.01 \)). Other z-scores showed a trend towards positive growth with time, including: MV annulus (\( P = 0.06 \)), LVId (\( P = 0.07 \)), sinus of Valsalva diameter (\( P = 0.05 \)), and LAR (\( P = 0.08 \)); however, the growth rate for the univentricular vs. biventricular groups did not differ for any single measurement (interaction \( P \)-values all >0.10). Individual growth trajectories are shown for the two aortic measures in Figure 1, and the growth trajectories of the aortic discriminant score for prototypical patients in the univentricular and biventricular groups are shown in Figure 2.

Discussion

Decision-making with regard to the optimal type of repair is difficult in the management of infants with the borderline development of left heart structures. Data have been produced with the aim of assisting management of patients with critical aortic stenosis \(^7,8,17\) and coarctation of the aorta. \(^9,10\) These reports have focused on decision-making in the early neonatal period, because established procedures such as the Norwood operation are undertaken at that time. Thus, to date, the management approach is decided early in life. In recent years, the hybrid procedure has been developed, which maintains systemic blood flow by stenting of the arterial duct and limits pulmonary blood flow by the application of bilateral branch pulmonary artery bands. \(^11,18\) This provides an opportunity to relieve critical left heart obstruction, while leaving options open with regard to the final type of repair. In our centre, the decision to perform a hybrid is taken following a joint cardiology/cardiac surgical conference, where the relevant echocardiograms are reviewed. z-scores of individual cardiac structures are available and the aortic discriminant score is used within the department, although these have generally served as a guide rather than dictating management. Following the hybrid operation, magnetic resonance imaging is routinely used to assess anatomy, which complements echocardiographic imaging to reach final decisions on the management. In clinical practice, the decisions were made by consensus at these meetings following the review of imaging data.
The data we present confirm a statistically significant improvement in the aortic discriminant score with time. There was a trend to improvement of the aortic annulus score, sinus of Valsalva diameter score, MV annulus, LVIDs, and LAR with time following a hybrid approach, in a group of infants with the borderline development of left heart structures. In the early neonatal period, all of our patients had low aortic discriminant scores that would have suggested eventual management towards a single-ventricle type of repair, accepting that the use of such scoring is more accepted for critical aortic stenosis than other lesions (Figure 1).

In three cases, the growth of left heart structures was sufficient for a biventricular repair to be undertaken. The rate of improvement in the aortic discriminant score was higher for infants who underwent a biventricular repair than those who underwent a single-ventricle repair. Thus, although we have applied the aortic discriminant score beyond the reported time frame and in different cardiac lesions, our data suggests that the use of such an approach may be helpful to discriminate between infants, who should be managed by a single ventricle vs. a biventricular approach following a hybrid procedure.

This study has a potentially important impact on the early management of neonates with borderline left heart structures by allowing time to gauge cardiac development over a more prolonged period of time than has been the case previously. An initial deferment of the definitive procedure allows time for consideration of a biventricular repair, which, although involving more procedures, may in the long term improve outcome when compared with a univentricular repair.

There are some disadvantages to the approach we have described. The aortic discriminant score is only an indirect measurement of growth, utilizing z-scores and constants derived from the Colan population. We have also used it in patients

### Table 3  Random coefficient models for the left heart scores

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Intercept coefficient Univent.</th>
<th>Intercept coefficient Bivent.</th>
<th>P intercept</th>
<th>P group</th>
<th>Slope coefficienta Unvent.</th>
<th>Slope coefficienta Bivent.</th>
<th>P time</th>
<th>P interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ao discriminant score</td>
<td>−3.05 (0.01)</td>
<td>−2.03 (0.01)</td>
<td>&lt;0.001</td>
<td>0.01</td>
<td>0.84 (0.01)</td>
<td>1.38 (0.01)</td>
<td>&lt;0.001</td>
<td>0.01</td>
</tr>
<tr>
<td>Ao annulus z-score</td>
<td>−5.26 (0.01)</td>
<td>−4.31 (0.01)</td>
<td>&lt;0.001</td>
<td>0.01</td>
<td>0.12 (0.01)</td>
<td>0.68 (0.01)</td>
<td>0.17</td>
<td>0.24</td>
</tr>
<tr>
<td>MV annulus z-score</td>
<td>−1.57 (0.01)</td>
<td>−0.53 (0.01)</td>
<td>0.16</td>
<td>0.43</td>
<td>0.34 (0.01)</td>
<td>0.80 (0.01)</td>
<td>0.06</td>
<td>0.26</td>
</tr>
<tr>
<td>LVIDd z-score</td>
<td>−2.35 (0.01)</td>
<td>−0.14 (0.01)</td>
<td>0.10</td>
<td>0.13</td>
<td>−0.20 (0.01)</td>
<td>−0.85 (0.01)</td>
<td>0.38</td>
<td>0.56</td>
</tr>
<tr>
<td>LVIDs z-score</td>
<td>−0.42 (0.01)</td>
<td>0.84 (0.01)</td>
<td>0.78</td>
<td>0.41</td>
<td>−0.53 (0.01)</td>
<td>−0.39 (0.01)</td>
<td>0.07</td>
<td>0.76</td>
</tr>
<tr>
<td>Sinus of Valsalva z-score</td>
<td>−4.48 (0.01)</td>
<td>−1.73 (0.01)</td>
<td>0.18</td>
<td>0.29</td>
<td>0.82 (0.01)</td>
<td>0.45 (0.01)</td>
<td>0.05</td>
<td>0.38</td>
</tr>
<tr>
<td>Left atrial z-score</td>
<td>−0.49 (0.01)</td>
<td>0.94 (0.01)</td>
<td>0.86</td>
<td>0.79</td>
<td>0.57 (0.01)</td>
<td>0.71 (0.01)</td>
<td>0.35</td>
<td>0.86</td>
</tr>
<tr>
<td>LAR</td>
<td>0.86 (0.01)</td>
<td>0.82 (0.01)</td>
<td>0.00</td>
<td>0.54</td>
<td>0.01 (0.01)</td>
<td>0.08 (0.01)</td>
<td>0.08</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Interpretation of the table is as follows: for the aortic discriminant score, the values at birth are less than zero overall (p intercept < 0.001), with the biventricular group demonstrating higher values than the univentricular group (−2.03 vs. −3.05, P group = 0.01). The rate of growth overall is positive (P time < 0.001), with a faster growth rate for biventricular patients (P interaction = 0.01). Thus, after 100 days, a typical biventricular patient will have increased his/her aortic discriminant z-score by 1.38, compared with 0.84 for a typical univentricular patient. Prototypical trajectories for the aortic discriminant score are also shown in Figure 2.

* Slope is expressed as the change in dependent variable per 100 days of age.

**Figure 1** Individual growth trajectories for the two aortic scores. Note the suggestion of differing intercepts and rates of growth for the univentricular compared with the biventricular groups for the aortic discriminant score. The horizontal line represents the cut-off value at birth for the prediction of successful biventricular repair. The same degree of differentiation is not seen with the aortic annulus score.
with diagnoses other than critical aortic stenosis. However, trends in the aortic discriminant score did show a difference between those who were eventually managed with a biventricular repair and those who were managed with a single-ventricle type of repair, suggesting that following such trends may assist decision-making in the future. There was a trend towards an increase in z-scores of cardiac structures for infants, who achieved a biventricular circulation. The infants who attained a biventricular repair required more cardiac procedures than those managed by a single-ventricle repair. Furthermore, one of the three survivors with a biventricular repair developed systemic pressures in the pulmonary circulation due to restrictive left ventricular physiology in the context of initial critical aortic stenosis and subsequently died. This outcome has been described previously. Thus, for some infants, aggressive pursuit of a biventricular repair may be detrimental and the challenge remains to identify such cases early enough, so a single-ventricle repair remains an option.

Limitations of our study include the small number of patients. The group described is a select group, drawn from a much larger population of patients with severe left heart disease, and it is likely that future studies will have to be multicentre in nature to provide statistical power. The aortic discriminant score has been applied beyond the neonatal period and for lesions for which it was not initially applied. In the past, final decisions had been applied beyond the neonatal period and for lesions for which it was not initially applied. In the past, final decisions had been applied beyond the neonatal period and for lesions for which it was not initially applied. In the past, final decisions had been applied beyond the neonatal period and for lesions for which it was not initially applied. In the past, final decisions had been applied beyond the neonatal period and for lesions for which it was not initially applied.

Conclusions
Our data, although retrospective, are encouraging that the use of the hybrid procedure may lead to achieving a biventricular circulation in a higher proportion of patients than was thought possible previously and we use a serial application of the aortic discriminant score to assist the decision-making progress. We propose a multicentre prospective study to confirm these findings and to examine long-term outcomes.

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References