Improved Surgical Outcome After Fetal Diagnosis of Hypoplastic Left Heart Syndrome

Wayne Tworetzky, MD; Doff B. McElhinney, MD; V. Mohan Reddy, MD; Michael M. Brook, MD; Frank L. Hanley, MD; Norman H. Silverman, MD

Background—Hypoplastic left heart syndrome (HLHS) is frequently diagnosed prenatally, but this has not been shown to improve surgical outcome.

Methods and Results—We reviewed patients with HLHS between July 1992 and March 1999 to determine the influence of prenatal diagnosis on preoperative clinical status, outcomes of stage 1 surgery, and parental decisions regarding care. Of 88 patients, 33 were diagnosed prenatally and 55 after birth. Of 33 prenatally diagnosed patients, 22 were live-born, and pregnancy was terminated in 11. Of 22 prenatally diagnosed patients who were live-born, 14 underwent surgery, and parents elected to forego treatment in 8. Of 55 patients diagnosed postnatally, 38 underwent surgery, and 17 did not because of parental decisions or clinical considerations. Prenatally diagnosed patients were less likely to undergo surgery than patients diagnosed after birth ($P=0.008$). Among live-born infants, there was a similar rate of nonintervention. Among patients who underwent surgery, survival was 75% (39/52). All patients who had a prenatal diagnosis and underwent surgery survived, whereas only 25 of 38 postnatally diagnosed patients survived ($P=0.009$). Patients diagnosed prenatally had a lower incidence of preoperative acidosis ($P=0.02$), tricuspid regurgitation ($P=0.001$), and ventricular dysfunction ($P=0.004$). They were also less likely to need preoperative inotropic medications or bicarbonate ($P=0.005$). Preoperative factors correlating with early mortality included postnatal diagnosis ($P=0.009$), more severe acidosis ($P=0.03$), need for bicarbonate or inotropes ($P=0.008$ and 0.04), and ventricular dysfunction ($P=0.05$).

Conclusions—Prenatal diagnosis of HLHS was associated with improved preoperative clinical status and with improved survival after first-stage palliation in comparison with patients diagnosed after birth. (Circulation. 2001;103:1269-1273.)

Key Words: prenatal diagnosis ■ hypoplastic left heart syndrome ■ heart diseases
after first-stage palliative surgery, and (3) parental decisions to pursue surgical options.

Methods

Patients
We reviewed all patients with HLHS who were evaluated at our institution between July 1992 and March 1999. We included all fetuses and newborn infants with HLHS, which we defined as normal cardiac topology with concordant atrioventricular and ventriculoarterial relationships, an intact ventricular septum, and hypoplasia of the left ventricle and left heart complex sufficient to preclude biventricular repair. Thus, we did not include patients with other forms of functionally univentricular cardiac defects who underwent a Norwood or Damus type of palliative procedure, such as unbalanced atrioventricular septal defect, double-outlet right ventricle with mitral valve atresia, and aortic atresia with ventricular septal defect. Patients with low birth weight (<2000 g) and patients with associated potentially lethal noncardiac congenital defects were also excluded. At diagnosis, the parents were counseled by an attending pediatric cardiologist and cardiac surgeon. Although cardiac transplantation was mentioned in postdiagnosis counseling as a therapeutic option that could be pursued at other institutions, it was not offered as an option at our institution. To obtain clinical and laboratory data, we reviewed patient records and departmental databases, including records from the referring hospital and transport team for patients referred from other institutions.

Diagnosis and Preoperative Evaluation
Diagnosis was made by standard echocardiography. In patients diagnosed prenatally, the diagnosis was confirmed with postnatal echocardiography. In patients transported to our center after being diagnosed with HLHS elsewhere, the diagnosis was confirmed with echocardiography at our institution. Not all of the postnatally diagnosed infants in this study underwent an echocardiogram before referral. For this reason, the first postnatal echocardiogram performed in our institution was used for analysis of anatomic and functional data, such as assessment of tricuspid regurgitation, ventricular dysfunction, and the degree of restriction of the interatrial communication. Right ventricular function was reported as normal if normal or mildly depressed and as abnormal if moderately or severely depressed by qualitative analysis. Similarly, the degree of tricuspid regurgitation was assessed as being normal if absent or mild and as clinically significant (abnormal) if moderate or severe. Because the echocardiograms were performed on the patient’s admission to the hospital, the cardiologist who interpreted the echocardiogram was blinded to the final outcome.

Operative Management
Stage 1 palliation for HLHS was performed in the standard fashion, with side-to-side anastomosis of the pulmonary trunk and ascending aorta, reconstruction of the ascending aorta and aortic arch with a patch of allograft tissue, atrial septectomy, and placement of a 3.0-, 3.5-, or 4.0-mm systemic-to-pulmonary-arterial shunt from the innominate or right subclavian artery to the right pulmonary artery. The diameter of the ascending aorta was measured intraoperatively.

Data Analysis
Data are presented as median and range or mean±SD. Data analysis was conducted for 2 different cohorts: (1) all patients with HLHS, with comparisons made between those diagnosed prenatally and those diagnosed postnatally, and (2) only patients who underwent stage 1 palliative surgery, with comparisons made between those diagnosed prenatally and postnatally, as well as between surgical survivors and nonsurvivors.

Among the entire cohort of patients diagnosed with HLHS, the parental decision regarding treatment (ie, termination of pregnancy, no treatment after birth, or stage 1 palliative surgery) was the primary outcome assessed.
however, there was a similar rate of nonintervention between the 2 groups (8 of 22 versus 17 of 55, \( P > 0.5 \)). All patients who did not undergo surgery died within 7 days and therefore were not included in further analysis.

**Surgical Cohort**

Overall, 52 (60%) of the 88 patients underwent stage 1 palliation. Age at repair was more uniform and significantly younger in those diagnosed prenatally than those diagnosed after birth (5.9 \( \pm \) 6.1 versus 8.2 \( \pm \) 5.1 days, \( P = 0.02 \)) (Figure 2). Overall survival to hospital discharge was 75% (\( n = 39 \)). All of the patients who had a prenatal diagnosis and underwent stage 1 palliative surgery (\( n = 14 \)) survived to hospital discharge, which contrasted with a survival rate of 66% (25/38) among the postnatally diagnosed patients (\( P = 0.009 \)). The 13 postnatally diagnosed patients who did not survive died a median of 5 days after surgery (0 to 34 days).

Among the 52 patients who underwent surgery, those diagnosed prenatally had a significantly lower incidence of preoperative acidosis (lowest arterial pH \( 7.29 \pm 0.1 \) versus \( 7.19 \pm 0.1 \), \( P = 0.02 \)), tricuspid regurgitation (\( P = 0.001 \)), and ventricular dysfunction (\( P = 0.004 \)) (Figures 3 and 4). They were also significantly less likely to need preoperative inotropic medications or bicarbonate (both OR 0.08 [95% CI 0.01 to 0.69], \( P = 0.005 \)) (Figure 4). Only 1 prenatally diagnosed patient became significantly acidic before surgery, most likely as a result of pulmonary overcirculation and systemic hypoperfusion, and needed bicarbonate and inotropic medication. The acidosis was treated rapidly, and the patient underwent surgery the following day. None of the other preoperative or operative variables analyzed were found to differ significantly between prenatally and postnatally diagnosed patients (Table).

In addition to postnatal diagnosis (OR 1.6 [95% CI 1.2 to 2.0], \( P = 0.009 \)), factors that correlated significantly with early mortality included greater preoperative acidosis (arterial pH \( 7.13 \pm 0.2 \) versus \( 7.25 \pm 0.1 \), \( P = 0.03 \)), need for bicarbonate medication preoperatively (OR 2.6 [95% CI 1.4 to 5.0], \( P = 0.008 \)), need for inotropic medications preoperatively (OR 2.1 [95% CI 1.1 to 4.1], \( P = 0.04 \)), and preoperative ventricular dysfunction (OR 2.4 [95% CI 1.03 to 5.5], \( P = 0.05 \)) (Figure 5).

Aside from the aforementioned variables, none of the other preoperative or surgical variables analyzed were found to correlate significantly with early mortality. By multivariable logistic regression analysis of the above factors that were significant by univariable analysis, only postnatal diagnosis remained significantly associated with early mortality (\( P = 0.04 \)).

Two patients, both of whom were diagnosed postnatally, had an intact atrial septum. After cardiovascular collapse and trans-

### Demographic and Surgical Variables in Prenatally and Postnatally Diagnosed Patients Undergoing Stage 1 Palliation of HLHS

<table>
<thead>
<tr>
<th>Variable</th>
<th>Fetal Diagnosis (n=14)</th>
<th>Postnatal Diagnosis (n=38)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at repair, d</td>
<td>5.9 ( \pm ) 1.4</td>
<td>8.2 ( \pm ) 5.1</td>
<td>0.02</td>
</tr>
<tr>
<td>Weight at repair, kg</td>
<td>3.2 ( \pm ) 0.4</td>
<td>3.4 ( \pm ) 0.5</td>
<td>0.16</td>
</tr>
<tr>
<td>Gestational age at birth, wk</td>
<td>38.9 ( \pm ) 1.1</td>
<td>39.6 ( \pm ) 1.4</td>
<td>0.11</td>
</tr>
<tr>
<td>Ascending aortic diameter, mm</td>
<td>3.0 ( \pm ) 1.5</td>
<td>3.4 ( \pm ) 1.7</td>
<td>0.45</td>
</tr>
<tr>
<td>Total support time, min*</td>
<td>134 ( \pm ) 46</td>
<td>158 ( \pm ) 52</td>
<td>0.13</td>
</tr>
<tr>
<td>Circulatory arrest time, min</td>
<td>48 ( \pm ) 8</td>
<td>43 ( \pm ) 17</td>
<td>0.57</td>
</tr>
<tr>
<td>Diameter of systemic-to-pulmonary-artery shunt, mm</td>
<td>3.4 ( \pm ) 0.3</td>
<td>3.4 ( \pm ) 0.2</td>
<td>0.89</td>
</tr>
</tbody>
</table>

*Sum of cardiopulmonary bypass time and circulatory arrest time.
Results and Implications of the Study

This is the first study to demonstrate that patients with HLHS who are diagnosed prenatally have improved survival after first-stage palliative surgery compared with those diagnosed after birth. In our cohort, the improved early survival can most likely be attributed to the more stable preoperative clinical condition of our prenatally diagnosed patients.\(^7,10,11\) HLHS is proportionately one of the most common congenital cardiac defects diagnosed prenatally, because standard 4-chamber views obtained during routine obstetrical ultrasound demonstrate hallmark findings of either a small left side or an echogenic left ventricle.\(^1,2\) In addition, there is usually reversal (left to right) of shunting across the foramen ovale and often retrograde aortic arch flow, all easily recognized by color-flow Doppler.\(^15\)

Prenatal diagnosis of HLHS has clear advantages. It allows time to counsel parents and time for both parents and physicians caring for the patient to plan perinatal management. As at other centers, patients diagnosed prenatally in our experience were caring for the patient to plan perinatal management. As at other centers, patients diagnosed prenatally in our experience were caring for the patient to plan perinatal management. As at other centers, patients diagnosed prenatally in our experience were caring for the patient to plan perinatal management. As at other centers, patients diagnosed prenatally in our experience were caring for the patient to plan perinatal management. As at other centers, patients diagnosed prenatally in our experience were caring for the patient to plan perinatal management. As at other centers, patients diagnosed prenatally in our experience were caring for the patient to plan perinatal management. As at other centers, patients diagnosed prenatally in our experience were caring for the patient to plan perinatal management. As at other centers, patients diagnosed prenatally in our experience were caring for the patient to plan perinatal management. As at other centers, patients diagnosed prenatally in our experience were caring for the patient to plan perinatal management. As at other centers, patients diagnosed prenatally in our experience were caring for the patient to plan perinatal management. As at other centers, patients diagnosed prenatally in our experience were caring for the patient to plan perinatal management. As at other centers, patients diagnosed prenatally in our experience were caring for the patient to plan perinatal management. As at other centers, patients diagnosed prenatally in our experience were caring for the patient to plan perinatal management. As at other centers, patients diagnosed prenatally in our experience were caring for the patient to plan perinatal management. As at other centers, patients diagnosed prenata...
velopmental outcome in patients with HLHS diagnosed in utero, the long-term effects of the potential advantages of fetal diagnosis are not known. Many of the long-term issues facing these patients are complex, multifactorial issues, and an even larger cohort will most likely be necessary to address this question adequately.

Limitations of the Study
There are several limitations to our retrospective study. First, we conducted an institutional rather than a population-based study. Therefore, data regarding the rate of termination of pregnancy for this defect and the decision to pursue surgery at birth in our region are most likely underestimated, because patients may have been diagnosed and counseled elsewhere and may not have been evaluated at our institution. Despite this limitation, we think that a study of this nature can be performed adequately with a retrospective design, insofar as its being conducted at a single center limits the impact of investigator bias that might be introduced in counseling of parents, evaluation of clinical data, and management of patients.

Also, because we were able to evaluate only patients who were referred to our institution, there was the potential for a selection bias. It is possible that only fetal patients with the most optimal cardiac function and anatomy were referred for surgery, whereas the group with a postnatal diagnosis included all comers. For example, a fetus with significant tricuspid regurgitation might not have been referred for surgery because of prenatal counseling at another institution. In the group of patients who were prenatally diagnosed at our institution, however, there were no differences in anatomy or fetal tricuspid regurgitation between patients who ultimately did and did not undergo surgery. The anatomic similarities between the surgical and nonsurgical groups suggest that these factors did not substantially influence counseling or parental decision-making in these patients.

Finally, we acknowledge that right ventricular function is difficult to assess quantitatively by means of echocardiography, and therefore we relied on qualitative assessment of function. Because the data for the study were collected retrospectively, the echocardiographers were essentially blinded to patient outcome, insofar as the studies were performed preoperatively. The echocardiograms used in this study were uniformly the first ones performed at our institution. Patients who were diagnosed prenatally and born at our institution usually underwent an echocardiogram in the first few hours of life. Postnatally diagnosed infants, however, were usually resuscitated before being transferred to our institution. If anything, this reliance on our own institution’s first echocardiogram allowed time for resuscitation, treatment of acidosis, and inotropic support in postnatally diagnosed patients, all factors that may have improved ventricular function before arrival at our center. Nevertheless, patients diagnosed postnatally still had worse ventricular function and more severe tricuspid regurgitation.

Conclusions
Prenatal diagnosis of HLHS affords the opportunity for counseling and perinatal planning. For patients in whom surgical palliation is elected, prenatal diagnosis provides an opportunity to avoid the preoperative hemodynamic and metabolic insult so frequently seen in those diagnosed postnatally. This improved preoperative state may, in turn, contribute to improved survival after first-stage palliation, as was seen to be the case in our experience.

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