

# Risk-Stratified Postnatal Care of Newborns with Congenital Heart Disease Determined by Fetal Echocardiography

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**Background:** Advances in fetal echocardiography have improved recognition of congenital heart disease (CHD). Imaging protocols have been developed that predict delivery room (DR) risk and anticipated postnatal level of care (LOC). The aim of this study was to determine the utility of fetal echocardiography in the perinatal management of CHD.

**Methods:** A retrospective analysis of fetal and postnatal records was conducted. The anticipated LOC was assigned by fetal echocardiography (LOC 1, nursery consult/outpatient follow-up; LOC 2, stable in DR with transfer to cardiac hospital; LOC 3 or 4, DR instability/urgent intervention needed). Prenatal diagnoses and LOC assignment were compared with postnatal diagnoses, treatment, and short-term outcomes.

**Results:** From 2004 to 2012, 8,101 fetuses were evaluated; 7,405 were normal. Of 696 with CHD, 101 terminated, 40 died in utero, and 37 received palliative care. LOC was assigned in the remaining 518. Of 219 LOC 1, 195 (89%) had postnatal follow-up. Only two required transfer for intervention (LOC 1 sensitivity, 0.9; LOC 1 positive predictive value, 0.99). Of 260 assigned LOC 2, 229 (88%) had follow-up. Of these, 200 (87%) were transferred for surgery or intervention. The median time to admission was 195 min. Twenty-two patients (10%) assigned LOC 2 did not require intervention; however, seven (all with D-transposition of the great arteries) required catheter intervention before surgery. Hospital survival was 86% (LOC 2 sensitivity, 0.97; LOC 2 positive predictive value, 0.87). All LOC 3 and 4 patients had follow-up. Thirty-four (87%) needed urgent intervention, with 100% DR and 87% hospital survival (LOC 3 and 4 sensitivity, 0.83; LOC 3 and 4 positive predictive value, 0.87).

**Conclusions:** Fetal echocardiography enables accurate postnatal risk stratification in CHD, with the exception of D-transposition of the great arteries. LOC 1 assignment facilitated outpatient follow-up; LOC 2 assignment facilitated transfer for intervention. LOC 3 and 4 patients underwent stabilizing intervention or surgery with good short-term outcomes. Given the inability to predict need for intervention in D-transposition of the great arteries, all such patients should be assigned as LOC 3 or 4. Fetal echocardiography with LOC assignment should be used in the planning of postnatal care in CHD. (*J Am Soc Echocardiogr* 2015;28:1339-49.)

**Keywords:** Fetal echocardiography, Fetal cardiology, Congenital heart disease

Improvements in fetal cardiac imaging have led to an increased number of newborns diagnosed prenatally with congenital heart disease (CHD). High-resolution fetal echocardiography with analysis of serial studies to assess disease severity and progression has enabled the prediction of clinical course in utero and during delivery. As a consequence, specialists in fetal medicine are now be-

ing asked to manage fetuses as distinct patients, with the transition to postnatal life an important part of individualized care.<sup>1</sup> Available data suggest that fetal diagnosis may improve outcomes in severe CHD by allowing the planning of specialized care to prevent the postnatal hemodynamic instability that occurs during transition.<sup>2-6</sup> For most newborns, however, only routine resuscitation is required in the delivery room (DR), thus allowing stabilization in the local hospital and either outpatient follow-up or nonurgent hospital transfer to a cardiac center.<sup>7</sup> Care protocols at our institution for risk assessment at delivery have been developed on the basis of published data<sup>2,8-24</sup> and clinical experience for fetuses with CHD. The primary aims of this study were to assess the accuracy of fetal echocardiography to correctly diagnose CHD and predict postnatal anticipated care and resuscitation in the DR and perinatal period, and to determine the effectiveness of risk-stratified DR care protocols for the postnatal management of newborns diagnosed in utero with CHD.

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**Abbreviations**

<b>CHD</b> = Congenital heart disease
<b>CNMC</b> = Children's National Medical Center
<b>DR</b> = Delivery room
<b>D-TGA</b> = D-transposition of the great arteries
<b>HLHS</b> = Hypoplastic left heart syndrome
<b>IAS</b> = Intact atrial septum
<b>LOC</b> = Level of care
<b>PPV</b> = Positive predictive value
<b>RFO</b> = Restrictive foramen ovale
<b>TOF</b> = Tetralogy of Fallot
<b>VSD</b> = Ventricular septal defect

**METHODS**

Since 2004 as part of clinical practice, fetuses diagnosed with CHD have been assigned an anticipated postdelivery "level of care" (LOC) with commensurate care plan determined by fetal echocardiographic findings suggestive of postnatal hemodynamic compromise and/or need for intervention or surgery in the DR or perinatal period (Table 1). This study was a retrospective analysis of the LOC protocol created at our institution to "prospectively" determine risk for compromise and need for specialty care at delivery.

**Subjects**

Records of all fetuses diagnosed with CHD and evaluated in the Fetal Heart Program at Children's National Medical

Center (CNMC) from November 2004 to March 2012 were reviewed. Patients were identified by searching the fetal cardiac database. Fetal and postnatal echocardiograms and maternal and neonatal electronic medical records were reviewed, and data were collected after patient identifiers were removed. The review was approved with a waiver of the requirement for informed consent by the hospital institutional review board.

**Fetal Determinants of LOC**

Fetal echocardiographic criteria for disease severity and LOC assignment were determined using published data<sup>8-24</sup> when available (Table 2) and multidisciplinary discussion including experts in obstetrics, neonatology, and cardiology in all others. Results of the last fetal echocardiographic examination before delivery were used for final delivery planning.

Fetuses with mild cardiac disease, such as isolated shunt lesions, mild valve abnormalities, and benign arrhythmias requiring only telemedicine consultation or outpatient cardiology follow-up, were assigned to LOC 1. Fetuses with CHD requiring DR stabilization by the neonatologist on site with subsequent hospital transfer for subspecialty care including catheter intervention or surgery were assigned to LOC 2. These babies most often had ductal-dependent circulation requiring the initiation of a prostaglandin infusion before transfer to our hospital for catheter or surgical intervention. Ductal-dependent flow was determined on the basis of the finding of reversed flow documented by color Doppler in either the ductus arteriosus (ductal-dependent pulmonary flow) or foramen ovale and/or distal aortic arch (ductal-dependent systemic flow)<sup>15,16</sup> (Figures 1a and 1b). Other diagnoses assigned to LOC 2 included nonsustained tachycardias or arrhythmias controlled in utero requiring postnatal treatment, cardiomyopathies without heart failure, and any defect in which prediction of a stable postnatal transition was uncertain. Fetuses with severe CHD requiring planned and coordinated delivery with a specialized CNMC care team in the DR were assigned to LOC 3 or 4, depending on the severity of the cardiac diagnosis and the

anticipated complexity of the staffing needed for DR stabilization, taking into account the predicted likelihood that an urgent intervention would be required. In instances when specialized medical care was anticipated for stabilization and the need for an urgent catheterization or surgical intervention was a possibility but not a certainty (LOC 3), delivery at the hospital adjacent to CNMC was planned. If it was anticipated that an urgent interventional catheterization or surgical procedure would be required (LOC 4), every effort was made to deliver at CNMC in the cardiac operating room. Babies assigned to LOC 3 or 4 most often had hypoplastic left heart syndrome (HLHS) and a restrictive foramen ovale (RFO) or intact atrial septum (IAS) or D-transposition of the great arteries (D-TGA) and an RFO and/or abnormal ductus arteriosus. Other diagnoses included uncontrolled sustained tachyarrhythmias or any severe CHD with heart failure. Fetuses with HLHS and RFO or IAS were stratified into LOC 3 versus LOC 4 on the basis of pulmonary venous flow pattern.<sup>9,10</sup> LOC 3 was assigned if the pulmonary vein forward/reversed velocity-time integral flow ratio was  $>3$  and  $<5$  and LOC 4 if this ratio was  $<3$ . Fetuses with D-TGA and any abnormality of the atrial septum (including a hypermobile, tethered, bowing, or intact atrial septum) and/or ductus arteriosus were assigned to LOC 3 versus LOC 4 on the basis of the specific features of the atrial septum and flow in the ductus arteriosus<sup>11-13</sup> (Figure 2a and b). Complete heart block with low ventricular rate, uncontrolled severe tachycardias, and diseases expected to have compromise in the DR, such as severe tetralogy of Fallot (TOF) with absent pulmonary valve or severe Ebstein's anomaly, were assigned to LOC 3 if cardiac dysfunction was present and to LOC 4 if hydrops fetalis was documented.<sup>17-24</sup>

For each LOC, written recommendations were prepared for the obstetric and neonatal teams for DR and postnatal management, including delivery location, DR staff, neonatal care, cardiac-specific care, and either outpatient follow-up or hospital transfer to CNMC. Delivery letters summarizing the CHD diagnosis, expected clinical findings, recommendations, and important phone numbers were sent to the delivery hospital at 30 weeks and again near term. For LOC 1, a call was made to arrange outpatient follow-up if the baby had not been scheduled 1 week after the due date or was unexpectedly transferred for care. For LOC 2, 1 week before the expected delivery date, the local neonatologist was called to review the care plan, and the CNMC transport team was notified. For LOC 3 and 4, delivery planning included formulation of a detailed multisubspecialty care algorithm with predelivery simulation and postdelivery debriefing for all patients.

Decisions regarding timing, place, and mode of delivery were made considering family preference when possible and in consultation with the obstetrician and the neonatal team. For LOC 1, spontaneous delivery was most often planned. For LOC 2, decisions regarding spontaneous delivery versus need for elective induction near term ( $\geq 39$  weeks) were made on the basis of family preference regarding place of delivery (local hospital vs facility closer to CNMC) and the opinion of the on-site physicians, who often favored a planned delivery date to help facilitate the coordination of care. For LOC 3 and 4, decisions regarding elective induction near term versus a planned cesarean section were based on the complexity of the staffing anticipated in the DR for stabilization of the infant.

**Data Collection and Analysis**

Fetal data collection included (1) cardiac diagnosis at final evaluation before delivery; (2) LOC assignment with proposed delivery

**Table 1** Definition of LOC assignment and coordinated action plan

LOC	Definition	Example CHD	Prenatal planning	Delivery	DR recommendations
1	CHD without physiologic instability in first weeks of life	1. Shunt lesions (e.g., ASD, VSD, AVSD) 2. Benign arrhythmias	Arrange outpatient cardiology evaluation	Spontaneous vaginal delivery	Routine DR management
2	CHD with physiologic stability in DR but requiring postnatal intervention/surgery before discharge	1. Ductal-dependent lesions or lesions with complex physiology likely to require neonatal intervention/surgery (e.g., HLHS, PA/IVS, truncus arteriosus) 2. Nonsustained or controlled tachyarrhythmias	Create plan of care for DR stabilization and neonatal management by local hospital with transport to CNMC	Spontaneous vaginal delivery vs induction near term	Neonatologist in DR; initiate PGE at low dose for ductal-dependent lesions
3	CHD with expected instability requiring immediate specialty care in DR before anticipated stabilizing intervention/surgery	1. HLHS/RFO 2. D-TGA/RFO 3. Severe Ebstein's anomaly with dilated right ventricle and low RV pressure 4. TOF/APV with RV and/or LV dysfunction and cardiac shift 5. Sustained tachyarrhythmias or CHB with heart failure	Create plan of care to include specialized CNMC team in DR and interventional/surgical team on standby	Planned induction usually at 39 wk with "bailout" C/S if necessary for care coordination	Neonatologist and CNMC specialists in DR; stabilizing medications predetermined by care plan
4	CHD with expected instability requiring immediate specialty care and urgent intervention/surgery in DR to improve chance of survival	1. HLHS/IAS 2. D-TGA/severe RFO or IAS with abnormal DA flow 3. Severe Ebstein's anomaly or TOF/APV with hydrops 4. Tachyarrhythmias/bradyarrhythmias with hydrops	Create multidisciplinary plan of care to include CNMC delivery if possible with specialized care team in DR and interventional/surgical team ready	Planned C/S at CNMC usually at 38–39 wk or sooner if there is evidence of fetal distress or hydrops Maternal risk determined by obstetrician (only low-risk women deliver at CNMC)	Specialized care team in DR Stabilizing medications/equipment predetermined by care plan

APV, Absent pulmonary valve; ASD, atrial septal defect; AVSD, atrioventricular septal defect; CHB, complete heart block; C/S, cesarean section; DA, ductus arteriosus; LV, left ventricular; PA/IVS, pulmonary atresia with intact ventricular septum; PGE, prostaglandin E; RV, right ventricular.

plan including place of delivery, intervention anticipated at delivery, and recommendations for outpatient follow-up or hospital transfer; and (3) recorded delivery information including place of delivery, time from delivery to outpatient follow-up or admission to the cardiac intensive care unit, time to intervention or surgery, intervention or surgery performed, and survival to outpatient follow-up or discharge from hospital after intervention. For LOC 1 in which outpatient follow-up was recommended, return for follow-up was documented as the primary clinical end point. For LOC 2, in which stabilization by the delivery hospital with ambulance transport for definitive intervention was planned, time from birth to admission and survival to hospital discharge were documented as the primary clinical end points. For LOC 3 and 4 in which comprehensive delivery coordination of care with cardiology specialists in the DR was planned, DR survival, time from birth to intervention, and survival to hospital discharge were documented as the primary clinical end points.

All decisions regarding postnatal care, including catheterization or surgical intervention, were made by the clinical care

team. For LOC 3 and 4 patients, decisions regarding DR intervention were made on the basis of clinical findings such as severe hypoxia, worsening acidosis, hemodynamic instability, unstable rhythm, and/or echocardiographic features suggesting the need for atrial septostomy in newborns with D-TGA or HLHS and RFO or IAS.

Prenatal diagnoses and plans of care were compared with postnatal diagnoses and DR and postnatal events; records of unanticipated events or complications were reviewed to determine the accuracy of fetal diagnoses and prenatal LOC assignment. Contingency table analyses was implemented to determine if actual postnatal care, used as the gold standard, could be predicted by prenatal LOC assignment, computing sensitivity and positive predictive value (PPV) for each LOC. LOC groups were then divided in two ways to determine the sensitivity and specificity of LOC assignment to predict (1) those neonates requiring only cardiology consultation or outpatient follow-up (LOC 1) versus those requiring postnatal care at the cardiac hospital (LOC 2–4) and (2) those neonates needing standard neonatal

**Table 2** Fetal echocardiographic predictors of LOC

CHD diagnosis	Fetal echocardiographic findings	DR recommendation
VSD or AVSD (shunt lesions) Mild valve abnormalities	Isolated cardiac defect with normal FO and DA flow, normal or minimal flow disturbances at valves, and normal heart function (LOC 1)	Routine care, hospital or telemedicine consult
Pulmonary atresia, HLHS, other single ventricles, or cyanotic TOF (ductal-dependent lesions) <sup>15,16</sup>	Ductal-dependent pulmonary circulation (LOC 2): 1. Aorta to pulmonary flow in the DA 2. Reversed orientation of the DA (inferior angle < 90°) Ductal-dependent systemic circulation (LOC 2): 1. Left-to-right atrial flow across the FO and reversed flow in the distal aortic arch	Initiation of prostaglandin
HLHS and variants with intact or restrictive atrial septum <sup>9,10</sup>	1. Moderate obstruction: PV f/r < 5 and > 3 (LOC 3) 2. Severe obstruction: PV f/r < 3 (LOC 4)	Initiation of prostaglandin; plan for immediate intervention to decompress left atrium
D-TGA and variants with restrictive atrial septum <sup>11-13</sup>	FO findings: 1. Hypermobile septum (LOC 3) 2. Angle of septum primum < 30° (LOC 3) 3. Lack of swinging motion of septum or "tethered" septum (LOC 3) 4. Bowing of atrial septum > 50% (LOC 4) 5. Intact (LOC 4) Abnormal DA (with additional RFO, LOC 4): 1. Small with moderate/severe restriction 2. Reversed or accelerated flow	Initiation of prostaglandin If RFO, plan for immediate balloon atrial septostomy in DR If ductal flow abnormal, consider pulmonary hypertension therapy
TOF/APV	Cardiac dysfunction (LOC 3) Hydrops fetalis (LOC 4) Lung findings suggestive of compression or fluid trapping (LOC 4)	Specialized ventilation Consider primed ECMO circuit
Severe Ebstein's anomaly	Cardiac dysfunction (LOC 3) Hydrops fetalis (LOC 4)	Consider measures to decrease pulmonary resistance and support cardiac output
Unstable tachyarrhythmias	Uncontrolled with associated heart failure (LOC 3) Hydrops fetalis (LOC 4)	Consider early delivery if gestational age appropriate Cardioversion or medical therapy in DR
CHB	Low ventricular rate with heart failure (LOC 3) Hydrops fetalis (LOC 4)	Consider early delivery if gestational age appropriate Consider chronotrope vs pacing in DR

APV, Absent pulmonary valve; AVSD, atrioventricular septal defect; CHB, complete heart block; DA, ductus arteriosus; ECMO, extracorporeal membrane oxygenation; FO, foramen ovale; PV f/r, pulmonary vein forward/reversed flow integral.

DR care (LOC 1 and 2) versus those who would benefit from specialized cardiac care in the DR (LOC 3 and 4).

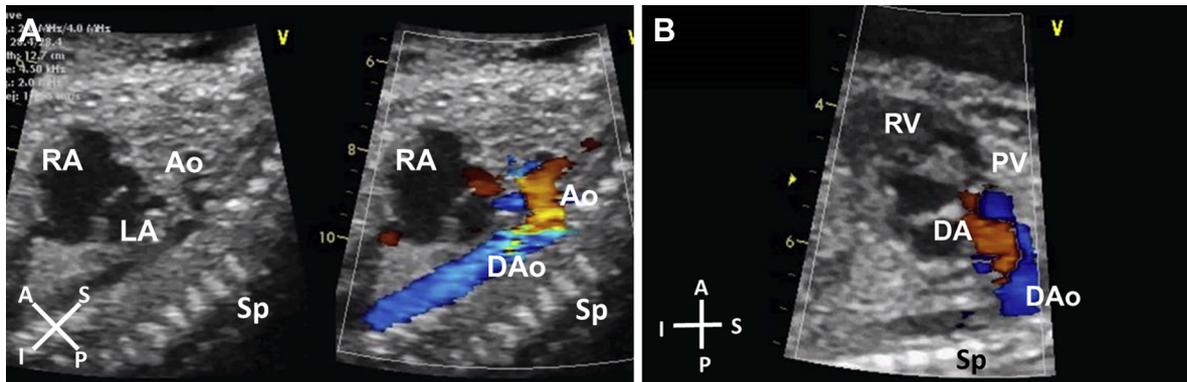
assigned a LOC and 42 of the fetuses (24%) who died in utero or received palliative care.

## RESULTS

From 2004 to 2012, 8,101 fetuses were evaluated; 7,405 were diagnosed as having normal hearts, and no postnatal follow-up was arranged, though three were unexpectedly admitted as neonates with CHD and one was seen as an outpatient. Of 696 with CHD, 15% terminated, 6% died in utero, and 5% were delivered and received palliative care before death. LOC was assigned in the remaining 518 fetuses with CHD and intent to treat. Of these, 463 had postnatal follow-up (Figure 3). Extracardiac anomalies were found in 90 of the fetuses (19%) assigned a LOC and 64 (36%) of the fetuses who died in utero or received palliative care. Genetic abnormalities were confirmed in 97 of the fetuses (20%)

### Accuracy of Fetal Diagnosis

Diagnoses by LOC are listed in Table 3. Overall, the exact fetal cardiac diagnosis matched the postnatal diagnosis in 391 of 463 patients who had postnatal evaluation and care (84% diagnostic accuracy). Differences in diagnoses occurred only in LOC 1 ( $n = 43$ ) and LOC 2 ( $n = 29$ ) patients and were minor and did not affect care in most cases. Common examples of minor discrepancies from pre- to postnatal diagnosis include (1) presence or description of ventricular septal defect (VSD), (2) presence or absence of mild ventricular hypertrophy, (3) presence or absence of minor valve abnormalities, (4) prediction of coarctation of the aorta, and (5) minor anatomic details of complex single ventricles. In only 13 patients (seven LOC 1 and six LOC 2) were there changes in the primary cardiac diagnosis that affected care (97% diagnostic accuracy for major cardiac



**Figure 1** (A) Ductal-dependent systemic circulation. Note reversed flow (red) in the transverse aortic arch. (B) Ductal-dependent pulmonary circulation. Note reversed flow (red) in the main pulmonary artery. A, Anterior; Ao, aorta; DA, ductus arteriosus; D Ao, descending aorta; I, inferior; LA, left atrium; P, posterior; PV, pulmonary valve; RA, right atrium; RV, right ventricle; S, superior; Sp, spine.

defects), though in only four would the prenatal plan have involved more specialized intervention in the DR (Table 4).

### LOC 1 Outcomes

Of the 195 fetuses assigned to LOC 1 who returned for care after delivery (Figure 4, row 1), 170 had cardiology consultations at the delivery hospital. The remaining 25 had confirmation of their diagnoses via telemedicine. Sixteen were unexpectedly transferred to CNMC, though only four for cardiac care (Figure 3). Two of the four had suspicion of coarctation on fetal echocardiography; postnatally, initial echocardiography could not confirm a normal arch. Despite cardiology consultation and reassurance, both were transferred for observation and ultimately discharged without surgery. In contrast, the other two patients transferred for care had changes in diagnosis resulting in need for intervention; one had a fetal diagnosis of possible coarctation that on postnatal evaluation revealed mild left ventricular hypoplasia with mitral and aortic stenosis. The baby required neonatal aortic balloon valvuloplasty. The second had a fetal diagnosis of double-outlet right ventricle with large VSD and mild pulmonary obstruction. Postnatally, the patient was diagnosed with double-outlet right ventricle and severe pulmonary stenosis requiring pulmonary valvuloplasty.

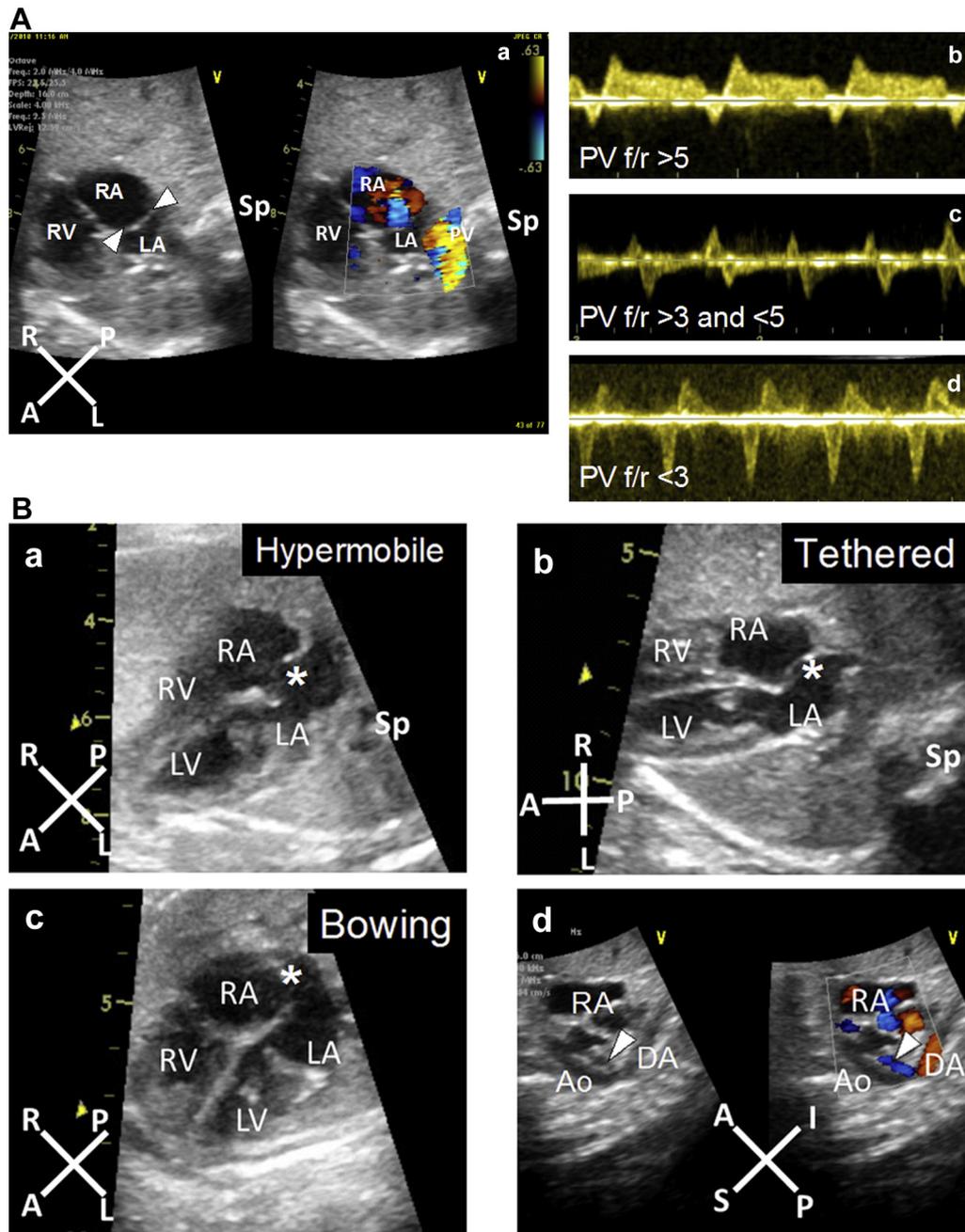
### LOC 2 Outcomes

Of the 229 fetuses assigned to LOC 2 who had care after delivery (Figure 4, row 2), 200 (87%) were transferred and received the intervention anticipated. The median time from delivery to arrival in the cardiac intensive care unit was 195 min (95% CI, 176–217 min). During initial hospitalization, 171 underwent surgery, 18 underwent interventional catheterization, and four received medication and/or cardioversion. Seven were admitted for planned diagnostic testing not available at the local hospital. Survival was 86% for those who were admitted and received the anticipated intervention. Twenty-two of the LOC 2 patients (10%) did not require the expected intervention after transfer to CNMC. Diagnoses included complex single ventricle not ductal dependent ( $n = 6$ ), double-outlet right ventricle with VSD ( $n = 3$ ), suspected coarctation ( $n = 4$ ), mildly unbalanced atrioventricular septal defect ( $n = 2$ ), mild to moderate aortic stenosis ( $n = 2$ ), TOF with atrioventricular septal defect ( $n = 1$ ), TOF with pulmonary atresia and collateral vessels ( $n = 1$ ), cardiac tumor ( $n = 1$ ), mild Shone's complex ( $n = 1$ ),

and complete heart block with adequate ventricular rate ( $n = 1$ ). In contrast, seven patients (3%), all with D-TGA, had unexpected hemodynamic compromise soon after delivery and required intervention for stabilization (Figure 3).

### LOC 3 and 4 Outcomes

All 39 fetuses assigned to LOC 3 or 4 received specialized postnatal cardiac care in the DR (Figure 4, rows 3 and 4). The clinical details and management for 34 of the 39 have been previously reported.<sup>2</sup> Analysis of LOC 3 versus LOC 4 outcomes in this initial study suggested that with specialized cardiac care in the DR and immediate access to the cardiac intensive care unit, catheterization laboratory, or operating room, outcomes were similar whether the delivery occurred at CNMC or the adjacent adult hospital. Given this past analysis, in this study LOC 3 and 4 are reported together. All assigned to LOC 3 were delivered as planned at the adult hospital with cardiac specialists in the DR. Thirteen of the 19 (68%) assigned to LOC 4 were delivered at CNMC; six were delivered at the adult hospital with cardiac specialists and the transport team present in the DR. Overall, 34 of the LOC 3 and 4 patients (87%) received the planned stabilizing intervention. Stabilizing interventions for LOC 3 patients included interventional catheterization ( $n = 13$ ), arrhythmia management ( $n = 1$ ), pacemaker insertion ( $n = 2$ ), and initiation of extracorporeal membrane oxygenation ( $n = 1$ ). Three LOC 3 patients did not require immediate intervention; one with HLHS and RFO had adequate atrial communication and did not require septostomy, and the conjoined twins, both with CHD, were managed medically before separation at 4 months of age. Stabilizing intervention for LOC 4 patients included interventional catheterization ( $n = 15$ ) and specialized medical resuscitation in the two with ectopia cordis. The two LOC 4 patients who did not require immediate intervention had D-TGA with prenatal features suggestive of RFO and abnormal ductus arteriosus. At delivery, the atrial septal communication in both was widely patent, and oxygenation and perfusion were adequate. Overall, median time from birth to stabilizing catheter intervention for LOC 3 and 4 patients was 125 min (95% CI, 101–190 min). For LOC 3, the median time was longer at 190 min (95% CI, 117–590 min) compared with LOC 4 at 101 min (95% CI, 62–135 min) ( $P < .05$ ). All survived delivery. During initial hospital admission, 38 underwent cardiac surgery and one underwent catheter aortic valvuloplasty. Survival



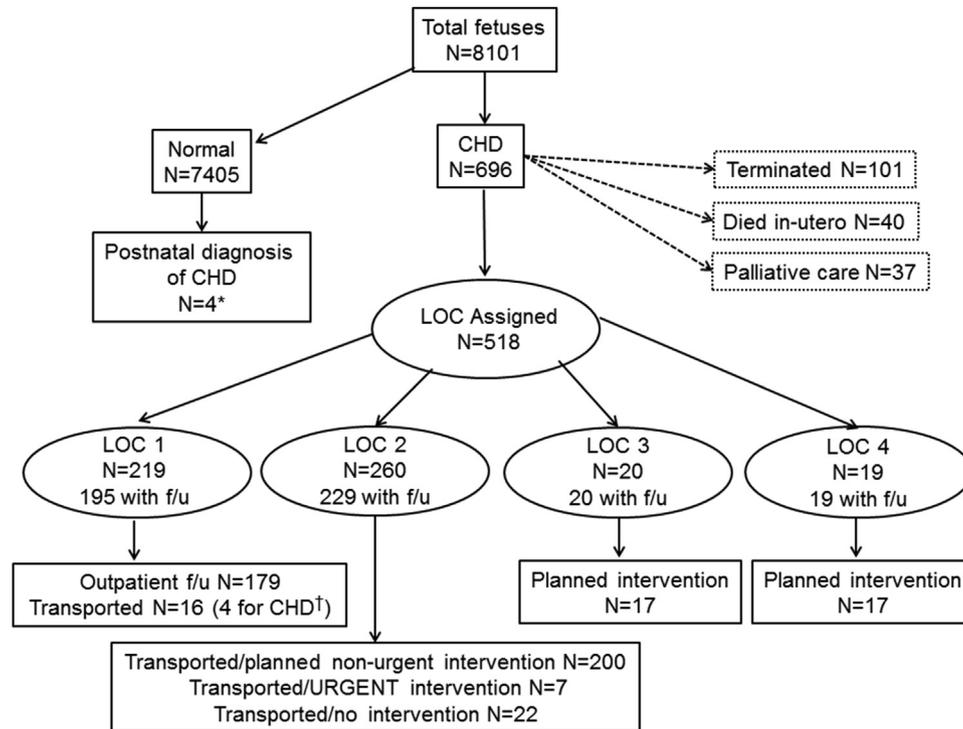
**Figure 2** (A) HLHS LOC coding. (a) Restrictive atrial septum. (b) Pulmonary vein flow, mild restriction: LOC 2. (c) Pulmonary vein flow, moderate restriction: LOC 3. (d) Pulmonary vein flow, severe restriction: LOC 4. Carrots denote atrial septum. (B) D-TGA LOC coding. (a) Hypermobile atrial septum: LOC 3. (b) Tethered atrial septum: LOC 3. (c) Bowing atrial septum: LOC 4. (d) Abnormal ductus arteriosus. Asterisk denotes atrial septum, carrot denotes restrictive ductus arteriosus. A, Anterior; Ao, aorta; DA, ductus arteriosus; I, inferior; L, left; LA, left atrium; LV, left ventricle; P, posterior; PV f/r, pulmonary vein velocity-time integral forward/reversed flow ratio; R, right; RA, right atrium; RV, right ventricle; S, superior; Sp, spine.

to hospital discharge for LOC 3 and 4 patients was 87% (85% for LOC 3 and 89% for LOC 4).

#### Accuracy of LOC Assignment

Overall, LOC assignment by fetal echocardiography correctly predicted postnatal care in 427 of the 463 patients (92%) who underwent postnatal evaluation and care. For LOC 1, sensitivity was

90%, with a postnatal PPV of 99%. For LOC 2, sensitivity was 97%, with a postnatal PPV of 87%. For LOC 3 and 4, sensitivity was 83%, with a postnatal PPV of 87%. In 36 patients, LOC assignment was incorrect. Of note however is that for our anticipated care plans, the primary goal was to minimize the “false negatives” or the number of patients in whom more care was needed than was anticipated (patients to the right of the shaded cells,  $n = 9$ ). Although a large number of “false positives” is not ideal given that



**Figure 3** Fetal outcome flow diagram. \*Of those thought to be normal, three had coarctation of the aorta requiring surgery, and one had a small VSD. †Of the four LOC 1 patients with CHD transferred, only two required cardiac intervention.

these patients have a higher LOC planned than is needed (numbers to the left of the shaded cells,  $n = 27$ ), this is less likely to result in a bad clinical outcome (Figure 4).

The accuracy of fetal echocardiography to identify neonates needing only outside hospital consultation or telemedicine at the delivery hospital (LOC 1) versus those requiring transfer for specialty care (LOC 2–4) had sensitivity of 99% and specificity of 90%. Only two patients were classified incorrectly. As described previously, one was diagnosed prenatally with possible coarctation and was transferred for management of aortic stenosis with a borderline left ventricle. The other had a fetal diagnosis of double-outlet right ventricle and VSD and was transferred because of cyanosis from severe pulmonary stenosis.

The accuracy of fetal echocardiography to identify neonates needing standard neonatal DR care (LOC 1 and 2) versus those who would benefit from specialized cardiac care in the DR (LOC 3 and 4) had sensitivity of 81% and specificity of 99%. The only neonates predicted to require standard DR care who required postnatal cardiac specialty care all had D-TGA. Six were known to have D-TGA in utero; however, the atrial septum did not meet prenatal criteria for LOC 3 or 4 planning. In one patient, the in utero diagnosis was double-outlet right ventricle with a VSD. The diagnosis of D-TGA was made postnatally after the baby presented with severe hypoxia and acidosis. Six of the seven patients underwent balloon septostomy within the first 2 days of life (mean, 29.4 hours; range, 18–44.0 hours) because of a persistent need for mechanical ventilation with supplemental oxygen and/or inotropes to maintain blood pressure. The one patient thought to have a double-outlet right ventricle required an urgent septostomy, which was done on arrival in the intensive care unit at 4.9 hours of life (worse blood gas had pH of 7.2 and  $pO_2$  of 25 mm Hg). In contrast, five of the 39 patients thought to need specialized care prenatally required only standard DR care.

The conjoined twins with CHD transitioned normally, and one with HLHS and two with D-TGA had adequate atrial communication and did not require septostomy.

### Fetuses with TOF

Subanalysis of the 47 fetuses with TOF and patent pulmonary valve revealed that prediction of ductal dependence and need for neonatal surgery was excellent. Thirty were assigned to LOC 1 (predicted acyanotic TOF in all) and 17 were assigned to LOC 2 (predicted cyanotic ductal-dependent TOF in 14). No babies assigned to LOC 1 required transfer for cyanosis. Thirteen of the 17 (76%) assigned to LOC 2 were transferred and underwent neonatal repair. Three assigned to LOC 2 were transferred to facilitate diagnostic testing only and did not undergo neonatal surgery. Sensitivity was 100% and specificity was 97% for prediction of need for prostaglandin infusion and neonatal repair in TOF.

### Fetuses with Suspected Coarctation of the Aorta

Subanalysis of fetuses with coarctation of the aorta revealed that significant postnatal arch obstruction was difficult to predict with certainty in utero. Seventeen fetuses identified to have “possible arch obstruction” because of findings of a mildly dilated right heart and a small aortic isthmus were assigned to LOC 1 with a plan for hospital consultation or telemedicine to be performed at the delivery hospital. Only three of the 17 (18%) had coarctation, and only one required transfer, not for coarctation but for mitral and aortic stenosis. In contrast, 15 of the 19 patients (79%) who were thought to have “true coarctation” and assigned to LOC 2 because of findings of a dilated right heart with a size discrepancy between the right and left heart and a small distal arch with juxtaductal narrowing and reversed isthmus flow were confirmed to have coarctation postnatally. Of note

**Table 3** Cardiac diagnoses by LOC

LOC 1	LOC 2	LOC 3 or 4
<i>n</i> = 219	<i>n</i> = 260	<i>n</i> = 39
<i>n</i> = 195 with follow-up	<i>n</i> = 229 with follow-up	<i>n</i> = 39 with follow-up
AVSD ( <i>n</i> = 41)	Ductal-dependent SV ( <i>n</i> = 70)	D-TGA with RFO ( <i>n</i> = 17)
VSD ( <i>n</i> = 39)	HLHS ( <i>n</i> = 48)	HLHS/variants with RFO/IAS ( <i>n</i> = 11)
TOF ( <i>n</i> = 30)	VSD with coarctation or IAA ( <i>n</i> = 19)	Critical AS with LV dysfunction ( <i>n</i> = 2)
TOF with PA ( <i>n</i> = 1)	Isolated coarctation ( <i>n</i> = 19)	CHB with low HR ( <i>n</i> = 2)
Possible coarctation ( <i>n</i> = 17)	TOF ( <i>n</i> = 17)	Ectopia cordis ( <i>n</i> = 2)
Non-ductal-dependent SV ( <i>n</i> = 13)	TOF with PA ( <i>n</i> = 10)	Conjoined twins with CHD ( <i>n</i> = 1)
RV hypertrophy ( <i>n</i> = 11)	Truncus arteriosus ( <i>n</i> = 8)	TOF/APV with CLE ( <i>n</i> = 1)
Dilated coronary sinus ( <i>n</i> = 9)	PA/IVS ( <i>n</i> = 8)	Complex PA with RFO ( <i>n</i> = 1)
Mild PS or AS ( <i>n</i> = 7)	D-TGA ( <i>n</i> = 6)	Complex arrhythmia with VT ( <i>n</i> = 1)
Irregular heart rhythm ( <i>n</i> = 6)	Unbalanced AVSD/coarctation ( <i>n</i> = 6)	
Myocardial tumor ( <i>n</i> = 6)	D-TGA with VSD ( <i>n</i> = 4)	
Cardiac malposition ( <i>n</i> = 4)	Ebstein's anomaly ( <i>n</i> = 4)	
Atrial septal defect ( <i>n</i> = 4)	VSD ( <i>n</i> = 2)	
VSD/possible coarctation ( <i>n</i> = 2)	Controlled arrhythmias ( <i>n</i> = 3)	
Tricuspid regurgitation ( <i>n</i> = 2)	AS or PS/no heart failure ( <i>n</i> = 3)	
Small pericardial effusion ( <i>n</i> = 1)	Myocardial tumor ( <i>n</i> = 1)	
Vascular ring ( <i>n</i> = 1)	Dilated cardiomyopathy ( <i>n</i> = 1)	
Absent ductus venosus ( <i>n</i> = 1)		

APV, Absent pulmonary valve; AS, aortic stenosis; AVSD, atrioventricular septal defect; CHB, complete heart block; CLE, congenital lobar emphysema; HR, heart rate; IAA, interrupted aortic arch; LV, left ventricular; PA/IVS, pulmonary atresia with intact ventricular septum; PS, pulmonary stenosis; RV, right ventricular; SV, single ventricle; VT, ventricular tachycardia.

however is that three of the 7,405 fetuses (0.04%) diagnosed as normal were admitted as neonates with coarctation (one in isolation, two with additional CHD), highlighting the fact that false negatives, though rare, do occur even with comprehensive fetal cardiac imaging.

### Fetuses with HLHS

Subanalysis of the 59 fetuses with HLHS revealed that 48 were assigned to LOC 2 and 11 to LOC 3 or 4. All assigned to LOC 2 did not require intervention, and 10 of 11 (91%) assigned to LOC 3 or 4 underwent stabilizing atrial septoplasty. Using pulmonary vein Doppler flow patterns,<sup>9,10</sup> sensitivity was 100% and specificity 97% for prediction of need for urgent intervention in HLHS.

### Fetuses with D-TGA

Subanalysis of fetuses with D-TGA showed that the ability to predict need for postnatal intervention was inadequate using current published criteria.<sup>11-13</sup> For fetuses with D-TGA, the presence of any foramen ovale abnormality predicted the need for urgent balloon septostomy in 15 of 17 (88%) assigned to LOC 3 or 4. Of note however is that seven of 10 thought to have a "reassuring" foramen ovale with no features suggestive of postnatal restriction required balloon septostomy. Four of the fetuses with D-TGA had significant ductal restriction and concerning foramen ovale; three were assigned to LOC 4 and one to LOC 3. In three of the four (75%), urgent septostomy was performed. Sensitivity for prediction of need for atrial septostomy in patients with D-TGA was 68%, and

specificity was 60%. It is important to emphasize that fetal echocardiographic findings both missed and overcalled need for atrial septostomy and urgent care at delivery.

### Fetuses with a Normal Echocardiogram

Of the 7,405 fetuses thought to be normal with no planned follow-up, four required postnatal cardiac care. Three were admitted as neonates with CHD requiring surgery: one with coarctation, one with VSD and coarctation, and one with an aortopulmonary window and coarctation. One patient was seen as an outpatient for a small VSD. None of the remaining 7,401 were known to have had any follow-up or hospitalization for cardiac care.

## DISCUSSION

Disease-specific transitional care recommendations have been created and are accepted in clinical practice.<sup>7</sup> In general, babies with mild valve abnormalities or left-to-right shunt lesions are stable in the DR and may be discharged for outpatient follow-up. Those with more complex defects, including those with ductal-dependent pulmonary or systemic flow, are usually stable in the DR, but they require prostaglandin infusion and hospital transfer for surgical repair. In contrast, babies with D-TGA are often not stable and may require urgent intervention to open the atrial septum, and newborns with HLHS and RFO or IAS require urgent specialty care, including catheter intervention to stabilize the circulation. The diagnostic challenge

**Table 4** Noteworthy discrepancies in fetal diagnosis and effect on postnatal care plan

Fetal diagnosis	Diagnosis change	LOC	Change in postnatal care plan
VSD	TOF	1	No change
Dilated right atrium and ventricle	Transitional AVSD	1	No change
AVSD with possible coarctation	Unbalanced AVSD with mild left ventricular hypoplasia	1	No change
VSD	Normal	1	No follow-up needed (↓)
Transitional AVSD	Dilated coronary sinus	1	No follow-up needed (↓)
Coarctation	Mitral and aortic stenosis with mild left ventricular hypoplasia	1	Aortic valvotomy (↑)
Double outlet right ventricle	Double outlet right ventricle with severe pulmonary stenosis	1	Pulmonary valvotomy (↑)
Aortic stenosis with poor left ventricular function	Atrial flutter with poor left ventricular function	2	Patient transferred for cardioversion (if diagnosis was known, would have planned DR cardioversion) (↑)
HLHS	VSD with mild left ventricular hypoplasia and coarctation	2	No change
Truncus arteriosus	Truncus with IAA	2	No change
Coarctation	Atrial septal defect	2	Outpatient follow-up (↓)
VSD with coarctation	Normal	2	No follow-up needed (↓)
Double outlet right ventricle	D-Transposition of the great arteries	2	Balloon septostomy (↑)

AVSD, Atrioventricular septal defect; IAA, interrupted aortic arch; ↓, postnatal care required less than LOC predicted; ↑, postnatal care required more than LOC predicted.

	# of fetuses with f/u	Actual LOC 1: # with postnatal outpatient follow-up	Actual LOC 2: # with postnatal transfer for surgery or intervention	Actual LOC 3: # requiring postnatal urgent stabilizing intervention	Actual LOC 4: # requiring postnatal emergent stabilizing intervention
Prenatal LOC 1: CHD expected to be stable in 1st weeks of life though outpatient f/u needed	195	193	2	0	0
Prenatal LOC 2: CHD expected to be stable in DR though surgery/cath required	229	22	200	6	1
Prenatal LOC 3: CHD with risk of compromise in DR; Team on standby	20	0	3	6	11
Prenatal LOC 4: CHD expected to be compromised in DR; Team ready	19	0	2	1	16

**Figure 4** Predicted LOC versus actual postnatal care. Rows represent prenatal LOC assignment, columns represent actual care given. Note that numbers in shaded cells represent numbers of patients in whom prenatal LOC matched postnatal care. Numbers to the left of the shaded cells represent patients in whom the care planned was not needed, whereas numbers to the right of the shaded cells represent patients in whom a higher LOC was needed. Note that for LOC 3, urgent stabilization denotes intervention required within the first hours of life. For LOC 4, urgent stabilization is required in the DR.

for fetal cardiologists is to identify the in utero predictors of DR compromise on the basis of specific findings rather than the generalized CHD diagnosis. Coordination of care and DR planning can then

be individualized such that the best outcome is achieved. Our results suggest that fetal echocardiography is accurate for diagnosing CHD and predicting postnatal LOC, in particular for distinguishing those

patients who require only routine neonatal care and outpatient follow-up (LOC 1) from those who need transfer and specialized care (LOC 2–4), as well as for those who will be stable in the DR (LOC 1 and 2) versus those that will require specialized DR care (LOC 3 and 4). This is imperative for clinical management given that it is critical to determine those newborns who can be stabilized at the local delivery hospital and then be discharged for outpatient evaluation or transferred for care versus those who will require specialized intervention at delivery. Predelivery planning to determine the appropriate delivery site is important given that many tertiary care hospitals with specialized pediatric cardiac care have a large catchment area, and it is not feasible to bring all patients with CHD in to deliver either on site or, in the case of children's hospitals, at the nearby adult hospital. In addition, in some instances it is the family's preference to deliver locally given the stress and burden involved with delivering in an unfamiliar place far from home. We have found this to be true in our clinical practice, and as long as we believe that clinical care will not be affected, we try to honor these requests for LOC 1 and 2 patients. In contrast, in situations in which specialized urgent catheter or surgical intervention is anticipated, coordination of care that includes delivery by either induction or cesarean section with all necessary personnel in the DR can be planned. This is especially important for children's hospitals that do not have a DR on site, but it can be useful as well for hospitals that have both a DR and cardiac program to best ensure that the interventionist or surgeon is present and ready if needed.

The LOC protocol developed and used at CNMC has been reported previously by our group.<sup>2</sup> In all fetuses diagnosed with CHD, LOC is assigned by the fetal cardiologist, and recommendations are created for postnatal management (Table 1). For most newborns, only routine DR resuscitation is required. Delivery care in these cases is directed toward education of the local physicians regarding what is expected, making certain that support is offered by phone or telemedicine conferencing. In addition, an outpatient follow-up plan is created so that no infant is lost to care. This has resulted in 99% of patients receiving the appropriate care at the delivery hospital (only two of 195 needed transfer for intervention) with 89% returning for specialty follow-up.

For more complex CHD, most that rely on ductus arteriosus and foramen ovale patency for postnatal stability, determination of the in utero predictors that identify those who will require intervention to maintain the circulation postnatally is critical. Most infants can be stabilized by a neonatologist, with initiation of a prostaglandin infusion if needed, before transfer for catheter or surgical intervention. Despite studies suggesting that distance from the cardiac hospital may affect outcomes,<sup>25</sup> our strategy, which includes ongoing education, maintaining a direct line of communication between the neonatologist and CNMC specialists, and making recommendations for care and coordination of transport services, has resulted in successful management and hospital transfer of 87% of patients assigned to LOC 2. Only seven of 229 (3%) unexpectedly required rapid transport, all of whom had D-TGA. In contrast, 22 (10%) were transferred and did not undergo surgery during initial hospitalization, though in some, the transfer was to facilitate diagnosis and ensure comprehensive medical care and follow-up. Of note, however, is that our results represent a single site experience. Additional studies will determine if this strategy can be applied across centers.

Fetuses with HLHS or D-TGA deserve special attention given the risk for compromise or death that may occur if the foramen ovale is restrictive or closed at delivery. In these patients, LOC 3 or 4 assignment may be necessary. Fetuses with HLHS and RFO or IAS have little

or no egress for pulmonary venous blood after delivery. Our experience supports previous reports<sup>9,10</sup> that abnormal pulmonary vein flow is useful (sensitivity, 100%; specificity, 97%) for determining whether delivery at either CNMC or the adjacent adult hospital with the catheterization team on standby is warranted. Newborns with D-TGA also require foramen ovale patency to allow the delivery of pulmonary venous blood to the systemic circulation. In our experience, postnatal compromise was not reliably predicted for fetuses with D-TGA by assessment of the anatomy and flow across the foramen ovale and ductus arteriosus. Although the criteria previously reported<sup>11–13</sup> had a PPV of 88%, sensitivity and specificity were inadequate. Given our early experience using these criteria, which resulted in several babies' requiring unexpected rapid transport by ambulance or helicopter, and the potentially dire consequences of not being prepared for urgent catheter intervention, it has become our practice to assign all fetuses with D-TGA to LOC 3 or 4, making preparations for urgent balloon septostomy if it is needed. Of note is that for defects such as these, LOC 3 and 4 often may be treated as the same entity if the DR is in the cardiac hospital and the interventionist is always available.

There are minimal reported data available for specialty DR care in severe TOF with absent pulmonary valve, severe Ebstein's anomaly, and unstable arrhythmias. In our experience, the presence of heart failure and/or hydrops suggests that cardiovascular support will be required at delivery. For TOF with absent pulmonary valve, fetal magnetic resonance imaging findings suggestive of significant lung disease may also be useful.<sup>23</sup> These patients are assigned to LOC 3 or 4 with a plan that includes multidisciplinary support from cardiology, surgery, and cardiac intensive care.

This study had several limitations. First, there are no long term follow-up data to determine if the LOC method improved outcomes beyond the neonatal period. This was not our goal. The LOC protocol was created to improve preoperative or pre-outpatient cardiology visit care for newborns with CHD. We believe we have shown this to be true for both our outpatients and for the babies who require neonatal cardiac care. Also, we have no way to determine whether the prenatal LOC assignment influenced the postnatal care that occurred. Although we believe this not to be the case, and all decisions regarding care were made by the postnatal medical team, the intended plan of care on the basis of fetal diagnosis has the potential to introduce bias into postnatal management. Third, we do not have information on all patients who were lost to follow-up despite attempts to contact families to determine postnatal care and outcomes. Given distant referral practice patterns, we know that some assigned to LOC 1 were seen by another cardiology group. For those assigned to LOC 2, reasons for not returning included choosing another center for surgery or moving out of the area. There were also likely some unconfirmed terminations or fetuses who died in utero. It is important to note that no patients assigned to LOC 1 or 2 were admitted to our hospital for unanticipated cardiac care, though four thought to be normal were found to have CHD postnatally. Finally, this study had no control group. Although these data would be useful, it was not feasible for us to gather DR information from outside hospitals in patients without a prenatal diagnosis.

## CONCLUSIONS

Improvements in fetal imaging and postnatal care of babies with CHD have created opportunities for pediatric cardiac specialists to offer new and innovative procedures to improve outcomes. The role of

the fetal cardiologist has expanded, such that the fetus must now be considered a patient, with DR management an important part of care. Postnatal care planning for fetuses with CHD includes coordination of care for DR and postnatal management, as well as planned outpatient follow-up or hospital transfer when needed. Our experience suggests that fetal echocardiography can successfully predict postnatal risk and improve perinatal care for newborns diagnosed in utero with CHD. This is relevant in a medical era that includes new technologies for improved diagnostic capabilities for fetal cardiac disease, establishment of centers of excellence for advanced pediatric cardiac care, and improved multidisciplinary collaboration through education and telemedicine partnerships.

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