Prenatal diagnosis and outcome of fetal lung masses

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Fetal hydrops;
Fetal surgery;
Prenatal steroids;
Pulmonary mesenchymal neoplasm

Abstract
Aim: The purpose of this study is to evaluate the accuracy of prenatal diagnostic features, particularly congenital cystic adenomatoid malformation volume ratio (CVR), in predicting outcomes for fetuses with lung masses.

Methods: The records and imaging features of all fetuses referred to the Texas Children’s Fetal Center with a fetal lung mass between July 2001 and May 2010 were reviewed retrospectively. Data collected included gestational age (GA) at diagnosis, fetal magnetic resonance imaging findings, CVR, mass size, nature of fetal treatment, surgical findings, pathology, and outcome. Data were analyzed for predicting development of hydrops or the need for fetal therapy using receiver operating characteristic curves.

Results: Of 82 fetuses (41 male) evaluated for a lung mass, 53 (65%) were left-sided (1 bilateral), and the mean (SD) GA at diagnosis was 21.5 (4.3) weeks. Seventy-three fetuses underwent fetal magnetic resonance imaging at a mean (SD) GA of 26.1 (4.6) weeks. Thirteen fetuses (16%) had fetal treatment. Four fetuses with hydrops underwent open fetal surgical resection, and 3 survived. Six fetuses with large lung masses and persistent mediastinal compression near term underwent ex-utero intrapartum therapy-to-resection procedures, and 3 fetuses with hydrops underwent serial thoracentesis. Congenital cystic adenomatoid malformation volume ratio correlated strongly with the development of hydrops and the need for fetal therapy with an area under the receiver operating characteristic curve of 0.96 (P < .0001) and 0.88 (P < .0001), respectively. Of 18 fetuses with a CVR greater than 2.0 compared with 2 (3%) of 60 with a CVR of 2.0 or less, 10 (56%) required fetal intervention (P < .0001).

Conclusion: Congenital cystic adenomatoid malformation volume ratio correlates strongly with the development of fetal hydrops and the need for fetal intervention. A threshold value of 2.0 yields the most powerful statistical results.

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Fetal lung masses are relatively rare, thought to occur in 1 of every 15,000 live births. However, the true incidence is likely higher because many previously undiagnosed lesions are now detected because of the widespread application and improved sensitivity of prenatal ultrasound (US). Fetal lung masses may appear cystic or solid and represent a wide array of developmental malformations including congenital cystic adenomatoid malformation (CCAM)—now referred to as congenital pulmonary airway malformation by some—
bronchopulmonary sequestration, bronchogenic cyst, congenital lobar emphysema, and segmental bronchial atresia [1-3]. There is general agreement as to what lesions should be diagnosed as bronchogenic cyst, congenital lobar emphysema, and extralobar sequestration, but there is disagreement as to the nomenclature used to describe lesions with bronchial atresia [3,4]. Congenital lung masses can also show considerable overlap in their histologic features, leading to the creation of the term hybrid lesion as an example [5]. In nearly all instances, a fetal lung mass is a benign disorder, but pleuropulmonary blastoma, a rare pediatric lung cancer, is an exception [6].

The natural history of a fetal lung mass is variable but generally depends on the size of the mass and the physiologic derangement caused by compression from the mass on surrounding structures [7,8]. These lesions commonly grow during a period from about 18 to 26 weeks of gestation, but most reach a plateau and either stop growing or decrease in size relative to the overall size of the fetus [9,10]. This group of lesions is usually asymptomatic in the fetal and postnatal period. In contrast, a small percentage of these lesions will grow dramatically relative to the confines of the fetal thoracic cavity, which may lead to compression of the mediastinum, vena cava, and heart; impaired right atrial blood return; and findings of fetal hydrops, heart failure, and ultimately, fetal death unless treated. Treatment options for large fetal lung masses with findings of hydrops include medical options (maternal administration of steroids), percutaneous decompression (thoracentesis or thoracoamniotic shunt), and open fetal surgical resection [9,11-13]. To this point, open fetal surgical resection of a lung mass in a hydropic fetus has been performed successfully in only 2 fetal treatment centers, although other centers have reported unsuccessful attempts [9,11,14,15].

Despite several reports from various fetal centers, there are few objective data that correlate prenatal diagnostic features with fetal and postnatal outcomes. Crombleholme et al [16] from the Children’s Hospital of Philadelphia were the first to try to risk-stratify fetuses with different-sized fetal lung masses. These investigators developed the CCAM volume ratio (CVR) in which the volume of the lung malformation is estimated by the formula for a prolate ellipse and then divided by head circumference to try to correct for overall fetal size and gestational age (GA). In their series, a cutoff of 1.6 was found to be significant, and those with an initial CVR greater than 1.6 had a 3- to 4-fold higher rate of hydrops, need for fetal intervention, and fetal or postnatal death. In this study, hydrops was defined as the presence of serous fluid in one or more body cavities, a definition that might limit interpretation of results. In addition, some have criticized the statistical validity of the cutoff point chosen [17]. Since that time, there have been a few reports that have lent support to these observations, but each of these series had relatively small patient numbers [10,11,15].

The purpose of this study was to review a relatively large series of fetuses with lung masses evaluated at a comprehensive fetal treatment center in an effort to further correlate prenatal features with fetal and postnatal outcomes. Specifically, the authors use receiver operating characteristic (ROC) curve analysis to evaluate the statistical validity of CVR and possible cutoff points that may best predict the development of hydrops and the need for fetal intervention.

1. Materials and methods

1.1. Patient population

After approval from the institutional review board of the Baylor College of Medicine (protocol no. H-20983), the case records and diagnostic imaging studies of all fetuses referred to the Texas Children’s Fetal Center between July 1, 2001 and May 30, 2010 with a diagnosis of fetal lung mass were reviewed retrospectively. Fetuses found to have diaphragm hernia (with or without an associated bronchopulmonary sequestration) were excluded. All patients referred to our center underwent comprehensive US and echocardiography, and nearly all patients had 1 or more magnetic resonance imaging (MRI) scans using a protocol described previously [18]. Data collected from the charts included referral diagnosis, GA at diagnosis, GA at consultation in our center, GA at US and fetal MRI, fetal and postnatal treatment, fetal and postnatal complications, and outcome. Imaging findings evaluated included placenta location, lesion size (maximum diameter), the presence or absence of mediastinal shift or displacement of the diaphragm, polyhydramnios, the presence of an anomalous vessel, whether the lesion was predominantly cystic or solid; findings of fetal hydrops including ascites, pleural or pericardial effusion, and scalp or trunk edema, and findings of placentomegaly. For the purposes of this study, fetal hydrops was defined as the presence of serous fluid in more than 1 body cavity (ascites, pleural or pericardial effusion, or scalp or trunk edema), which has been considered the standard obstetric definition of this disorder. Placentomegaly was defined as a thickened placenta that appeared edematous on US and fetal MRI, usually with a thickness of 4 cm or more. Specific echocardiographic findings reviewed included the presence or absence of valvular regurgitation, diastolic dysfunction, Doppler changes with absent or reversal of the atrial wave in the ductus venosus or pulsations in the umbilical vein, and measurements of contractility and ventricular function. The finding of fetal heart failure was defined by a fetal cardiologist and demonstrated by echocardiographic changes that reflected failing right heart function such as worsening of tricuspid regurgitation and reversal of flow in diastole in the ductus venosus and umbilical vein, always in the presence of noncardiac findings of fetal hydrops, as defined above. Maternal mirror syndrome was diagnosed when the mother showed hypertension, proteinuria, or eclampsia in the presence of fetal hydrops.
1.2. CCAM volume ratio and mass size measurement

The CVR was calculated using US features, as described previously [16]. Briefly, the CCAM volume (units of cubic centimeter) is estimated using the formula for a prolate ellipse, with measurements of the lung mass in 3 perpendicular planes. The CVR is obtained by dividing the CCAM volume by the head circumference (measured in centimeters) to correct for differences in overall fetal size and GA. Thus, the CVR is a number that has units of centimeter squared [CVR ($L \times H \times W \times 0.52$/HC)]. Mass size was estimated by US or MRI as the largest perpendicular diameter of the mass in any 1 dimension at any time in gestation.

1.3. Indication for fetal intervention

The indication for fetal intervention in our center was fetal hydrops, and the indication for open fetal surgery was hydrops with evidence of evolving fetal heart failure on echocardiography. Percutaneous treatments, thoracocentesis or thoracoamniotic shunt, were offered if there were a dominant macrocyst, significant mediastinal deviation, and evidence of evolving fetal hydrops (ascites, pleural or pericardial effusion, and skin edema). Administration of 2 doses of betamethasone was offered to all mothers carrying a fetus with a large lung mass and early signs of hydrops. Fetal hydrops alone, in the presence of preserved cardiac function, was not considered an adequate indication for open fetal surgery. Open fetal surgery was only offered after extensive multidisciplinary counseling regarding the potential risks and goals of therapy. The age and psychosocial support available to the mother were considered in this process. Occasionally, a mother was deemed a poor candidate, and open fetal surgery not offered despite appropriate fetal indications. All counseling was objective and nondirective and followed guidelines outlined by our bioethicist Dr. Laurence McCullough, who has published several articles about this process [19].

An ex-utero intrapartum therapy-to-resection strategy was used in the delivery of fetuses with persistently large fetal lung masses late in gestation with evidence of mediastinal compression or hydrops. For these patients, fetal MRI was useful to identify the lobar location and the relationship of the lesion to surrounding thoracic structures and to the volume of uninvolved normal lung. In general, our EXIT protocol and technique followed that described by Hedrick et al [20].

1.4. ROC curve analysis

All values are expressed as the mean ± SD, unless noted otherwise. Statistical analysis was performed using the Fisher exact test and ROC curves. $P < .05$ was considered significant. The initial CVR and mass size measurements were evaluated with ROC curve analysis against 4 outcome variables: the development of fetal hydrops or heart failure, the need for fetal intervention, and mortality. Optimal cutoff points were determined by graphing the ROC curve and comparing the sensitivity, specificity, and positive (PPV) and negative (NPV) predictive values of each potential cutoff point.

2. Results

During the study period, 82 fetuses (41 male) were evaluated for a confirmed fetal lung mass in the absence of diaphragmatic hernia. Fifty-three fetuses (65%) had left-sided lesions, 28 (34%) had right-sided lesions, and 1 fetus had bilateral lesions identified. The mean age at diagnosis, known for 77 fetuses, was 21.7 ± 4.5 weeks, and the mean age at consultation in our center was 27.1 ± 5.1 weeks of gestation. Seventy-three fetuses had at least 1 fetal MRI performed at 26.1 ± 3.1 weeks of gestation, and 21 fetuses had a second MRI performed at 33.2 ± 3.1 weeks of gestation. A systemic vessel supplying the lesion was identified prenatally by Doppler or MRI in 28 (34%) of the 82 fetuses. Overall, 75 (91%) of 82 fetuses survived. Of the 7 who died, 6 died (in utero or shortly after birth) because of complications from a very large lung malformation, whereas 1 died postnatally after care was withdrawn because of the finding of trisomy 18 in the presence of an average-sized congenital lung malformation (CVR, 1.4) and a large muscular ventricular septal defect.

2.1. CCAM volume ratio

The CVR measurement, available in 78 fetuses, correlated strongly with fetal and postnatal outcome. Four fetuses evaluated early in the study period did not have a CVR calculated, and adequate imaging studies to gain this information were not available. One of these fetuses with an unknown CVR was treated with serial fetal thoracocentesis for a large pleural effusion, marked mediastinal compression, and early signs of hydrops. For the remaining 78 fetuses, the initial CVR was calculated to be 1.4 ± 1.6 (range, 0.01-9.4) at a mean GA of 27.1 ± 5.1 weeks (range, 20-38 weeks) and correlated strongly with the development of hydrops, fetal heart failure, the need for fetal intervention, and overall mortality (Table 1). Based on an analysis of the sensitivity, specificity, PPV, and NPV for each outcome variable tested, the single most useful threshold value was 2.0. With regard to hydrops, heart failure, fetal intervention, mortality, and fetal intervention or mortality, the threshold value of 2.0 showed 92% and 89%, 88% and 86%, 83% and 88%, 86% and 83%, and 82% and 93% sensitivity and specificity, respectively. The statistical results for other potential threshold values (0.75, 1.4, 1.6, and 2.2) with regard to hydrops are shown in Table 2. With regard to hydrops and heart failure, a CVR greater than 1.4 had 100% sensitivity and NPV, meaning that no fetus with a CVR of 1.4 or less...
Fetal lung masses

Table 1  Association of CVR and outcome variables using ROC curve analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>+ Group</th>
<th>− Group</th>
<th>AUC</th>
<th>SE</th>
<th>95% CI</th>
<th>z Statistic</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrops</td>
<td>12</td>
<td>66</td>
<td>0.96</td>
<td>0.02</td>
<td>0.89-0.99</td>
<td>19.7</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Heart failure</td>
<td>9</td>
<td>69</td>
<td>0.94</td>
<td>0.03</td>
<td>0.86-0.98</td>
<td>13.5</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Fetal intervention</td>
<td>12</td>
<td>66</td>
<td>0.88</td>
<td>0.05</td>
<td>0.79-0.94</td>
<td>7.9</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Mortality</td>
<td>7</td>
<td>71</td>
<td>0.88</td>
<td>0.05</td>
<td>0.79-0.94</td>
<td>7.9</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>FI + mortality</td>
<td>17</td>
<td>61</td>
<td>0.92</td>
<td>0.03</td>
<td>0.84-0.97</td>
<td>12.2</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

AUC indicates area below ROC curve; CI, confidence interval; FI, fetal intervention; FI + mortality, those fetal patients who received fetal intervention and/or died.

There were 60 fetuses with a CVR 2.0 or less at presentation (Table 3). One fetus in this group had an initial CVR of 0.8 at 22 weeks of GA, which later increased to 2.8 by 35 weeks of gestation. This infant, delivered by an EXIT-to-resection strategy because of persistent mediastinal compression, had a large extralobar sequestration and recovered uneventfully after resection. Another infant in this group (CVR, 1.5) presented at 36 weeks of gestation with an unusual tumor. The mother developed polyhydramnios late in gestation, and US showed a 6.5-cm solid, rounded right-sided lung lesion with signs of hydrops and early cardiac changes. At EXIT procedure, vascular access above the diaphragm was achieved followed by a decompressive right thoracotomy to relieve tamponade and to improve ventilation. The mass was then resected; the child recovered and has done well since. Pathology showed a rare pulmonary mesenchymal neoplasm. The single death in this group had complications related to trisomy 18, as described previously.

2.2. Fetal lung mass size

Fetal lung mass size (a single measurement of the maximum diameter of the mass, not corrected for fetal gestation), available in 80 of 82 patients, also correlated strongly with fetal hydrops, fetal heart failure, the need for fetal intervention, and mortality, with an area below the ROC curve of 0.91 ± 0.04, 0.92 ± 0.04, 0.91 ± 0.03, and 0.83 ± 0.07, respectively, and P < .0001 for all parameters. With regard to hydrops and fetal intervention, a mass size threshold value of greater than 5.2 cm showed a sensitivity and specificity of 83% and 88% and 92% and 90%, respectively.
2.3. Open fetal surgery

Four fetuses with large lung lesions, hydrops, and evolving heart failure underwent open fetal surgery resection. The first with a large microcystic left-sided lesion was seen early in the development of our Fetal Center and was thus referred to the Children’s Hospital of Philadelphia. The fetus developed ascites, worsening skin edema, and Doppler changes on echocardiography for which a fetal left lower lobectomy was performed at 22 5/7 weeks of gestation. Pathology showed a fetal CCAM with a systemic vessel. The hydrops resolved, and the child was delivered 11 weeks later. He is alive and well at 8 years with a normal developmental outcome. The next 3 fetal patients underwent open fetal surgery at the Texas Children’s Fetal Center for similar indications. One fetus with a giant left-sided mass, a CVR of 4.4, frank hydrops, and significant fetal echocardiographic changes underwent open fetal surgery resection of a left upper lobe mass at 22 2/7 weeks. The hydrops resolved within 10 days, and the child was born 10 weeks later. He is alive and well at 4-year follow-up with normal neurodevelopmental and pulmonary outcomes. Another fetus with a giant right-sided mass, a CVR of 2.6, ascites, skin edema, and worsening function of the right side of the heart had fetal resection of a large extralobar sequestration at 24 weeks of GA. The hydrops resolved, and the child was delivered 9 weeks later. The infant’s course has been complicated by significant tracheobronchomalacia and respiratory insufficiency for which ventilation and tracheostomy were required. She is now doing well at 3-year follow-up, off the ventilator, and nearing decannulation. There is mild motor delay but no deficit in cognitive neurodevelopmental outcome. A third patient was referred at 25 weeks with a large right-sided microcystic lesion with frank hydrops and ascites and placentomegaly. Despite successful open fetal surgical removal of the mass, the fetus became bradycardic and asystolic and died intraoperatively. It is likely that our intervention was timed too late in the pathophysiologic sequence, and placentomegaly may be a contraindication to efforts at open fetal surgery in most cases.

2.4. Histologic findings

The final pathologic diagnosis was available for 55 of 82 fetal patients because of surgical resection or autopsy (Table 4). Five infants are awaiting neonatal surgical follow-up; 20 children with small asymptomatic lesions are being followed postnatally without surgical resection (in 2, no lesion is visible by computed tomographic scan), 1 infant with trisomy 18 had care withdrawn at an outside facility with no autopsy, and 1 infant was lost to follow-up after 6 months. For those infants in which the pathology is known, there was a strong concordance with the final pathologic diagnosis and the need for fetal intervention. Only those fetuses found to have extralobar sequestration, CCAM, or mesenchymal neoplasm received fetal treatment.

3. Discussion

It seems intuitive that the size of the fetal lung mass correlates with outcome. Larger rapidly growing masses may compress the mediastinum and esophagus, leading to impaired fetal swallowing and polyhydramnios and, ultimately, fetal death. This process was elucidated by Rice et al [8] in a sheep model in which balloon tissue expanders were gradually inflated in the thorax of 120-day-old fetal lambs. As the balloon was expanded, these fetal lambs developed signs of hydrops with ascites and pleural and pericardial effusions that resolved when the expanders were deflated.

The term nonimmune hydrops describes anatomical findings that are seen with right-sided heart failure. Passive congestion from elevated right atrial pressures may lead to ascites, pleural and pericardial effusions, scalp edema, anasarca, and placental growth. Fetal echocardiography would seem to be the most accurate method to detect fetal heart failure, but to date, echocardiographic findings remain poorly characterized in those with large lung masses. Theoretically, it may be possible for ascites or scalp edema to occur without heart failure because the mass

<table>
<thead>
<tr>
<th>Pathology diagnosis</th>
<th>No.</th>
<th>Open fetal resection</th>
<th>EXIT-to-resection</th>
<th>Thoracentesis</th>
<th>Fetal intervention (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BA</td>
<td>14</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>ELS</td>
<td>13</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>46</td>
</tr>
<tr>
<td>ILS/BA, with vessel</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>CCAM</td>
<td>8</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>88</td>
</tr>
<tr>
<td>BC</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>CLE</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mesenchymal neoplasm</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Foregut abnormality</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

BA indicates bronchial atresia (no systemic vessel); ELS, extralobar pulmonary sequestration; ILS/BA, intralobar pulmonary sequestration or bronchial atresia with systemic vessel; BC, bronchogenic cyst; CLE, congenital lobar emphysema.
could compress the cysterna chyli or thoracic duct directly while caval blood return is maintained. Indeed, we have seen a number of fetuses with marked ascites, some with accompanying scalp edema that never progressed to frank heart failure. Such fetuses may have met the criteria for fetal surgery, but we now feel that, in the absence of echocardiographic changes, these are best managed by close observation (ie, US 3 times per week). If there is further progression of hydrops or Doppler changes on echocardiography, then fetal surgery may be indicated. There were some fetuses with hydrops and even early heart failure that showed resolution later in gestation. Whether this was caused by direct effects from steroids or a spontaneous resolution of rapid mass growth is not known.

The size of the fetal lung mass, assessed by direct measurement of the maximum diameter or by CVR, correlated strongly with our indices of poor outcome (eg, presence of ascites, the need for fetal intervention and survival, etc). Threshold values of 5.2 cm for mass size and 2.0 for CVR were found to be most significant. Fetuses with smaller lung masses or those with a CVR 2.0 or less predictably do well in general, with a likelihood of survival nearly a third of these fetuses may still die. In this study, CVR was found to be a stronger prenatal predictor than mass size alone.

Even smaller lung masses should still be followed because some may increase in size later than expected by the usual natural history. In this series, 4 fetal lung masses increased in size at more than 26 weeks of gestation.

The outcomes achieved in this series compare favorably with those of other fetal centers. Boston reported a survival of 63% for a group of 8 fetal lung masses with a CVR greater than 1.6 in contrast to 100% survival for 4 fetuses with smaller lesions [10]. Philadelphia reported 56% survival for 16 fetuses with a CVR greater than 1.6 [16]. In our series of 21 fetuses with CVR > 1.6, survival was 76%.

Open fetal surgery can be performed safely with good outcome for hydrotic fetuses with giant fetal lung masses. Recent reports from San Francisco and Philadelphia show survival in 13 (57%) of 23 and 13 (54%) of 24 fetuses, respectively [9,14]. Our initial experience in 3 fetuses shows comparable survival. We feel that intervention was too late in the fetus who died because of progression of thoracic tamponade. Recently, fetal medicine centers in Cincinnati and Tokyo have reported failed attempts at fetal resection for such lesions in 3 and 1 fetuses, respectively [11,15]. However, it is highly likely that these fetuses would have died anyway. In summary, the current overall survival (from the aforementioned centers) appears to be 28 (52%) of 54.

We can only speculate why some fetal lung malformations grow dramatically and cause fetal hydrops and heart failure, whereas most do not. Factors that regulate the balance between cell proliferation and apoptosis, such as the protein platelet-derived growth factor, may play a role in this pathogenesis [21,22]. In the present series, we found a strong correlation between fetal and postnatal symptoms and pathologic diagnosis after resection. Those fetuses with true CCAM, confirmed histologically, had a much higher rate of fetal hydrops and fetal intervention at 88%. Those with an extralobar sequestration also had a high rate of the need for fetal intervention, with nearly 50% receiving fetal treatment. Interestingly, there was no fetus found to have the diagnosis of bronchial atresia, bronchial atresia with systemic vessel (intralobar sequestration), bronchogenic cyst, or congenital lobar emphysema that showed signs of fetal hydrops or required fetal intervention. There has been no fetus that has been found to have congenital lobar emphysema that has required fetal intervention in any of the published reports. Interestingly, these lung abnormalities can appear quite large on prenatal imaging. They are usually seen in the left upper or right middle or upper lobes and can have CVR measurements that exceed 3 [23]. However, these lesions usually stay proportional or decrease relative to the size of the developing fetus and do not cause findings of hydrops. Postnatally, these overexpanded lobes may trap air, causing mediastinal deviation and respiratory symptoms, and the patient may benefit from excision in the neonatal period. These infants are likely best delivered in facilities with immediate access to neonatal surgical care.

References

Discussion

Richard Ricketts (Atlanta, USA): Can you explain a little more about steroid use, when is it indicated and at what stage of gestation?

Darrell Cass: That is an excellent question. The answer is we don’t know. Some centers have reported the resolution of “hydrops” in fetuses treated with steroids, but those centers have defined hydrops as fluid in one body cavity rather than two. Indeed, we have seen fetuses with large lung masses, CVRs greater than 4, marked mediastinal deviation, ascites and even some signs of scalp edema that had good cardiac function on echo and so we did not treat them. We gave steroids and the babies did fine with later EXIT procedures. In the past these babies may have undergone fetal surgery. Did steroids change things? We don’t know. Steroids take a number of days to work by whatever mechanism. I don’t believe they are harmful, but neither do I believe that they are curing these conditions. We need to be consistent in our definition of hydrops and I think ECHO is going to be the most important tool for when to intervene.

Paul Losty (Liverpool, UK): Mike Harrison thinks the steroids work by inducing apoptosis. In this part of the world, quite a few of these lesions melt away but I didn’t see any reference to this in your manuscript.

Darrell Cass: Of 82 fetal lung masses only 2 seemed to disappear and these lesions were likely a mucous plug or bronchial obstructions that somehow resolved itself.