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Mini Review

Fetal Magnetic Resonance Imaging in the Prenatal Evaluation of Congenital Diaphragmatic Hernia

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Abstract

Congenital diaphragmatic hernia (CDH) is a developmental anomaly in which abdominal organs penetrate into the thorax cavity through a diaphragmatic defect.

The thorax cavity has an existing dimension, and its occupation by herniated abdominal content may compress the thoracic organs resulting in pulmonary hypoplasia and pulmonary hypertension, which are the main causes of neonatal mortality in these patients. In the daily clinical practice CDH is diagnosed by ultrasonography (US).

Fetal magnetic resonance imaging (MRI) has become an important advance in the diagnosis of congenital diaphragmatic hernia because it enables to evaluate the severity of pulmonary hypoplasia and to confirm or exclude liver herniation, which are the major prognostic factors. It can also estimate the survival rate and the need for extracorporeal membrane oxygenation (ECMO) at birth. Fetal MRI contributes in a better selection of candidates for intrauterine treatment (tracheal balloon occlusion) with the intention of decreasing severe complications such as pulmonary hypertension or chronic pulmonary insufficiency, and improving neonatal survival. In this article the authors review the different MRI findings in CDH and the parameters that assist in establishing the prognosis and perinatal management.

ABBREVIATIONS

CDH: Congenital Diaphragmatic Hernia; US: Ultrasonography, MRI: Magnetic Resonance Imaging; ECMO: Extracorporeal Membrane Oxygenation; SSFS: Single Shot Fast Spin Eco; FIESTA: Fast Imaging Employing Steady-State Acquisition; LAVA: Liver Acquisition Volume Acceleration; LHR: Lung-To-Head Ratio; TFLVO: Total Fetal Lung Volume; TFLVE: Expected Total Fetal Lung Volume; RFLV: Relative Fetal Lung Volume; LH: Liver Herniation; %LH: Percentage of Liver Herniation; Litr: Liver/Thoracic Volume Ratio; FBV: Fetal Body Volume; PPH: Persistent Pulmonary Hypertension; PPHHI: Pulmonary Hypertension Index; PA: Pulmonary Artery; FETO: Fetal Endotracheal Balloon Occlusion

INTRODUCTION

CDH is a developmental anomaly in which abdominal organs penetrate into the thorax cavity through a normal or pathologic diaphragmatic defect. The diaphragm closes to the eight weeks of gestation and completely divides the pleural and peritoneal cavities. Any diaphragmatic defect, premature bowel migration or intestinal rotation abnormality can lead to a CDH [1].

The incidence of CDH varies between 1/2,500 and 1/5,000 cases per year depending on whether live births are included or not [2].

85% of the diaphragmatic hernias occur on the left side , 13% on the right side and 2% bilaterally [3].

Nearly 40% of the cases have other congenital anomalies associated [4], and when this occurs the survival rate is less than 15% [5].

The severity of pulmonary hypoplasia and liver herniation are the major prognostic factors. The liver´s position is an independent risk factor not related to the estimated fetal lung volume; therefore liver herniation is associated with a worse prognosis [6].

MRI is a non-invasive modality complementary to the initial US examination and makes possible to evaluate these prognostic factors (pulmonary hypoplasia severity and liver herniation) by calculating a series of volumes obtained in the ultrafast sequences images.

CDH is a developmental anomaly in which abdominal organs penetrate into the thorax cavity through a diaphragmatic defect. In left-sided hernias it is frequent to find herniation of ipsilateral viscera (stomach, small intestine, omental fat and left hepatic

lobe), while in the right-sided hernias the right hepatic lobe generally herniate. Retroperitoneal structures such as the kidney and pancreas rarely herniate.

The liver has intermediate signal intensity on T2-weighted images and a modest hyperintensity on T1-weighted images that distinguish it from the lung. The small intestine appears as small tubular or rounded structures gathered together, with high signal on T1 weighted imaging from week 20 of gestation. From week 30 of gestation meconium can be seen in the ileon distal portion hyperintense on T1-weighted images and hypointense on T2-weighted images, and as a result of this colon loops are high signal on T1-weighted images and low signal on T2-weighted images as the foetus grows and meconium is accumulated inside colon loops [7,8].

MRI protocol

Studies are performed with MR in high magnetic field strength. In our center studies are obtained in 1.5 T imaging units (Optima MR450w 1.5T GE Healthcare, USA),with multichannel coils with high spatial resolution and ultrafast sequences, which allows minimizing artefacts secondary to fetal movements and enables to achieve MR imaging without sedation (Figure 1).

The main sequences used are the following:

• T2-weighted sequences, such as single shot fast spin eco (SSFSE T2) and balanced sequences, for instance fast imaging employing steady-state acquisition (FIESTA), show excellent tissue contrast and exhibits the amniotic fluid with high signal, useful in the study of the lung, urinary and intestinal tract. Moreover, balanced sequences facilitate performing vascular studies without intravascular contrast agents, revealing hyperintense fetal vessels (Figure 2).

• T1-weighted sequences, such as three-dimensional gradient dual echo and liver acquisition volume acceleration (LAVA), are used to study the liver and intestinal loops, both of which are visualized hyperintense.

Pulmonary hypoplasia evaluation

The best pulmonary hypoplasia prognostic index in US examination is the ratio between the lung and the head circumference or lung-to-head ratio (LHR). A LHR greater than 1.6 is correlated with a ≥ 83% rate of survival; a LHR between 1 and 1.6 has a 66% survival rate; and a LHR between ≥0.8 and <1 has a 16% rate of survival [9]. The observed-to-expected LHR ratio is obtained as the quotient between the measured LHR and the expected LHR for a given gestational age, expressed in percentage. There are equations for calculating the expected LHR and tables that establish the vital prognosis of CDH [10]. Poor postnatal survival rates have been found on expectantly managed fetuses with isolated, left-sided CDH when the LHR at 22–28 weeks'gestation was less than 1.0, which is equivalent to an observed-to-expected LHR of ≤ 25%. Both normal fetuses and in those with CDH the LHR changes with gestational age at assessment, whereas the observed to expected LHR is independent of gestational age. Furthermore, the data show that in both left- and right-sided CDH, measurement of observed-to-expected LHR provides useful prediction of survival [10,11].

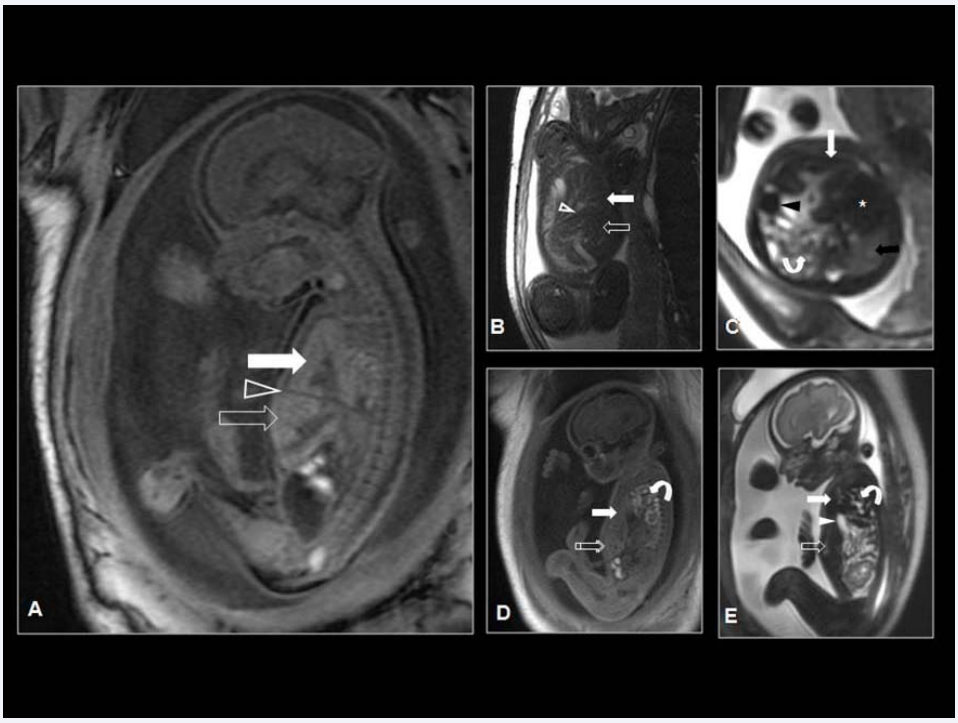

Figure 1 (A) Sagittal 3D LAVA MR image, (B) Coronal FIESTA MR image, (C) Axial SS FSE T2-weighted image, (D) Sagittal 3D LAVA MR image and (E) Sagittal SS FSE T2-weighted image. 29 week-fetus presenting a right hepatic lobe herniation (solid white arrow) which is rotated to the left and rests on the diaphragm (empty white arrowhead). The left hepatic lobe (empty white arrow) presents a normal location. MR images also show herniation of ileum (white curved arrow) and colon (solid black arrowhead), and gallbladder herniation (solid white arrowhead). The heart is shifted to the left (white asterisk). RFLV: 24.45%.

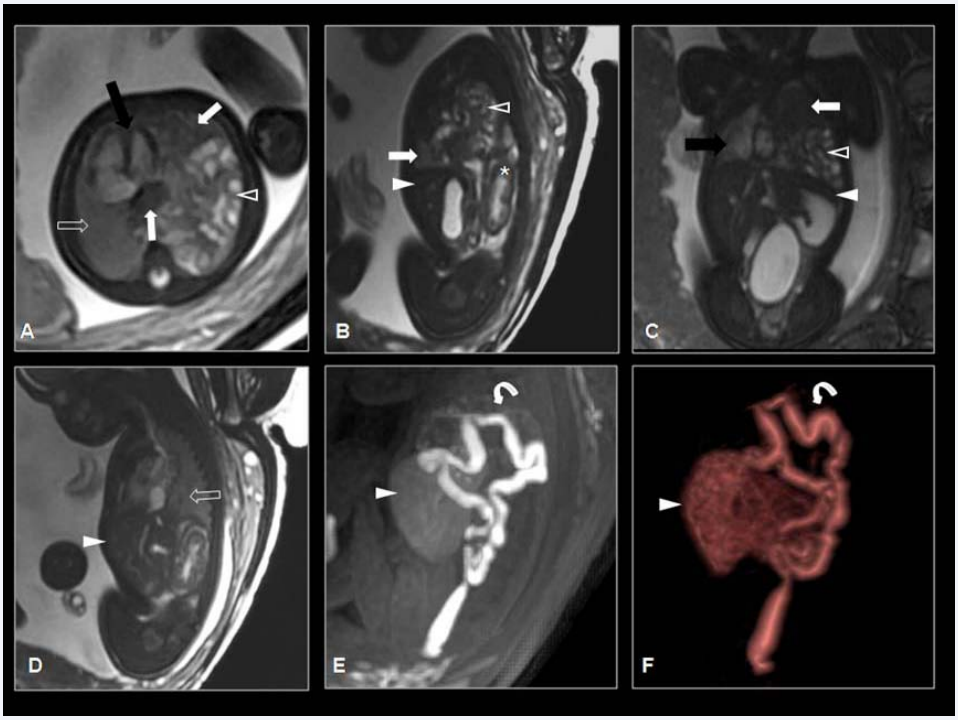

Figure 2 (A) Axial FIESTA MR image, (B), sagittal FIESTA MR image, (C) coronal FIESTA MR image, (D) sagittal FIESTA MR image, (E) sagittal 3D LAVA MIP reconstructions. (F) sagittal 3D LAVA volume rendering reconstruction. 30 week-fetus with herniation of small intestine (hyperintense on T2-weighted images,empty white arrowheads), splenic angle and transverse colon (hyperintense on T1-weighted images, curved white arrows) and partially the left kidney (white asterisk). Ahypoplastic left lung (solid white arrows), a normal right lung (empty white arrows) and a right-shifted heart (black arrows) without hepatic herniation (solid white arrowheads) are seen. RFLV: 44.47%.

MRI allows quantifying the lung volume on the same side and on the opposite side of the hernia, by which the observed total fetal lung volume (TFLVo) is obtained. Rypens et al., established an equation in MRI studies to achieve the expected total fetal lung volume (TFLVe) for a given gestational age: TFLVe = 0.0033 x $g^{2.36}$ (where "g" is the gestational age in weeks) [12].

The formula TFLVo/ TFLVe x 100 brings forth the relative fetal lung volume (RFLV) and values less than 80% are considered hypoplasia [13]. In Killian et al., study RFLV values < 14.3% was correlated to 100% fetal mortality rate; RFLV > 32.8% was associated with 100% fetal survival; and values > 44% did not need extracorporeal membrane oxygenation (ECMO) [14]. Tsuda et al., found a significant negative correlation between percent RFLVand duration of oxygen therapy in infants with CDH [15]. Moreover, RFLVof both lungs as well as of the lung contralateral to the CDH seem reliable prenatal predictors of survival, need for ECMO, and development of chronic lung disease, as described by Hagelstein et al. [16],

In addition, there is a statiscally significant correlation betweenRFLV and observed-to-expected ultrasound for left-sided CDH (and the correlation is best before 32 weeks' gestation),bur not for right-sided CDH [17].

Jani et al., have noted that RFLVand the percent herniated liver (%LH) as calculated by MRI appear to offer better predictive value than ultrasound LHRand the observed-to-expected LHR [18].

It is important to highlight that operator experience has an impact on the accuracy of estimation of TFLVo. Strizek et al., stated that in the absence of experience in volumetric measurements, estimation of TFLVo in fetuses with CDH by 3D-ultrasound showshigher variability than MRI measurements, but even in experienced hands variability is greater for 3D-ultrasound [19].

MRI is also able to accurately predict the severity of CDH by means of percentage predicted lung volume (PPLV). To calculate this value, a subtraction of mediastinal volume from total thoracic volume is necessary. Lung volumes were expressed as a percentage of the predicted lung volume (PPLV), definedas the sum of the volumes of the right and left lungs divided by the predicted lung volume, multiplied by 100. Values lower than 15 correlate with a significantly higher risk for prolonged support and/or death, despite aggressive postnatal management [20,21]. Of those with first PPLV was higher than 15%, 31% dropped below 15%, having similar ECMO use as the high-risk cohort, but trending toward greater survival.On the other hand, those with first and final PPLV>15% had significantly less ECMO use and greater survival rate than the high-risk cohort. Serial MRI is recommended for those with initial PPLV>15%, as clinical outcomes tend to mirror the lowest PPLV [21].Furthermore, RFLVand PPLV can undergo various changes during gestation, reflecting the dynamic course of pulmonary hypoplasia. Late TFLVo, early and late RFLVand late PPLV can be predictive factors of neonatal survival that may facilitate prenatal counseling and focus perinatal management [22].

When isolated isolated left-sided CDH is found, the right fetal lung-to-liver signal intensity ratio (LLSIR) has been described as an accurate marker of fetal lung maturity that correlates with postnatal survival and can potentially be used as a prognostic parameter in CDH management, as reported by Yamoto et al., and Nishie et al., [23,24].

Liver herniation evaluation

Liver herniation (LH) is another of the major prognostic factors in CDH, in such a way that, fetuses that present it have a 50% survival rate. LH is an independent risk factor not related to other factors [9]. Hedrick et al. [6], reported that fetuses with LH had 45% survival rate and 85% needed ECMO; while fetuses without LH had 93% survival rate and 25% required ECMO.

In left-sided CDH, percentage of LH (%LH) is calculated as the quotient between the herniated liver volume and the total fetal liver volume,andthe liver/thoracic volume ratio (LiTR) is obtained as the ratio of herniated liver volume to total thoracic volume (excluding the spine). Lazar et al., and Zamora et al., estimated %LH and LiTR in left-sided CDH and determined that a %LH >21% and LiTR > 14% are prognostic factor of neonatal mortality and of ECMO use [25,26]. Ruano et al., stated that the best combination of measurements to predict mortality was RFLVand %LH (with 83% accuracy), although PPLV and LiTR also correlated with mortatilty rate [27].

Cannie et al. [28], concluded that the estimation of the fetal body volume (FBV) by MRI had a better correlation with the fetal pulmonary predictive volume than hepatic volumetric measurements.Stomach herniation has been considered as a prognostic factor in CDH. Kitano et al. [29], studied patients with left-sided CDH, analysing as predictor factors the following: LHR, liver´s and stomach´s position, gestational age at diagnosis and the presence or absence of polyhydramnios. The authors came to the conclusion that LH is the most important prognostic factor followed by stomach herniation into the right chest cavity.

The MRI-based ratio of fetal lung volume to fetal body volume (FLV/FBV)has also been proved topredict neonatal survival and ECMO requirement in children with CDH with high accuracy [30] (Figure 3).

On the other hand, Lally et al., pointed out that the size of the diaphragmatic defect seems to be the a major factor influencing outcome in infants with CDH, and it is also likely to correlate with the degree of pulmonary hypoplasia [31].

Pulmonary hypoplasia assessment

CDH is associated with neontal respiratory failure due to pulmonary hypoplasia and persistent pulmonary hypertension (PPH) that condition life expectancy [32]. PPH is the consecuence of the abnormal transition from the fetal to neonatal circulation. The persistence of an elevated pulmonar vascular resistence causes right-left shunt of deoxygenated blood to the systemic circulation and produces arterial hypoxia, right ventricular failure with systemic hypotension and obstructive shock [33]. Infants with CDH are often resistant to treatment with inhaled nitric oxide [34] and end up needing ECMO [35]. Russo et al.,´s meta-analysis determined that fetal lung volume and liver herniation predicts the need of ECMO but not the degree of PPH [36].

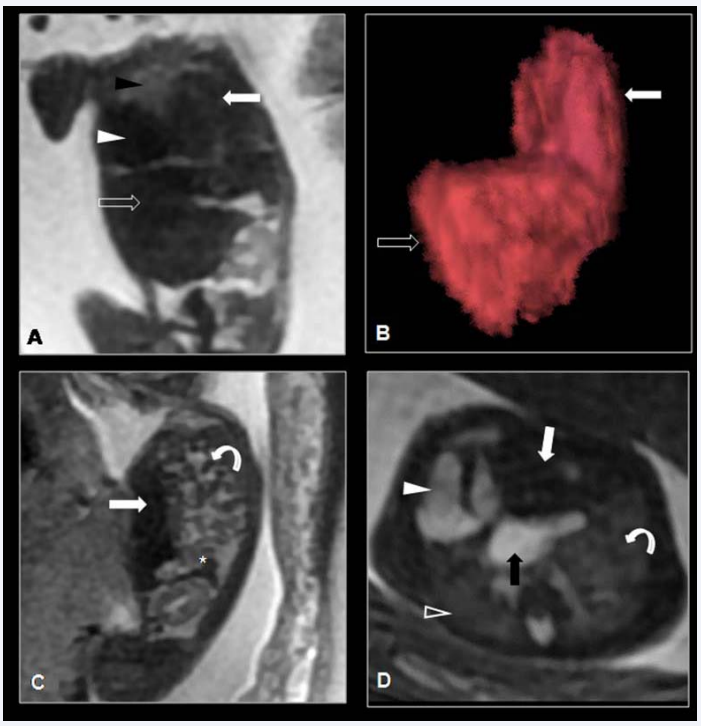

Figure 3 (A) Coronal SS FSE T2-weigthed image, (B) coronal 3D LAVA volume rendering reconstruction, (C) sagittal SSFSE T2-weigthed image and (D) axial FIESTA MR image. 21 –week fetus with left-sided diaphragmatic hernia. A left hepatic lobe herniation is observed (solid white arrows), with normal left adrenal gland (asterisk) and right hepatic lobe (empty white arrow) .The heart is shifted to the right hemithorax (solid white arrowheads) and there is stomach (black arrow) and jejunum-ileum herniation (curved white arrows). A hypoplastic left lung (black arrowhead) and a displaced the right lung (empty white arrowhead) are observed. RFLV: 32.8%.

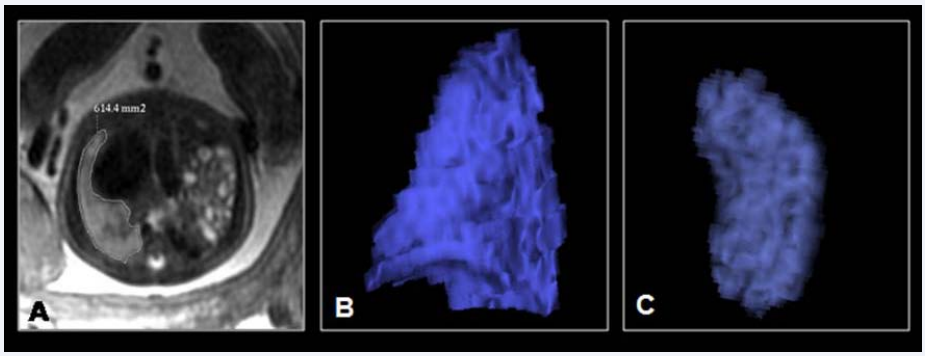

Figure 4 (A) Axial SS FSE T2-weighted image. 29 week-fetus where left-sided diaphragmatic hernia is observed without liver herniation. Pulmonary parenchyma area was measured in each slice in both lungs to obtain a right and left pulmonary volume. (B) 3D Volume Rendering reconstruction of the right pulmonary volumen: 18.17 cc. (C) 3D Volume Rendering reconstruction of the left pulmonary volumen: 6.44 cc. TFLVo was 24.61cc and TFLVe using Rypens´s formula was 55.34 cc. RFLV: 44.47%.

Vulentin et al. [37], settled a new pulmonary hypertension index (PPHHI) by obtaining the diameter of the right and left pulmonary artery (PA), diameter of the aorta and the length of the cerebelum vermis from fetal MR imaging. They calculated the PPHHI (PPHHI = (diameter of left PA/length of the cerebelum vermis) x 10) and the McGoon modified index (McGoon modified index = (diameter of right PA + diameter of left PA)/ diameter of the aorta) finding a negative correlation between PPHHI and McGoon index and pulmonary hypertension.

Early treatment with fetal endotracheal balloon occlusion

Early treatment with fetal endotracheal balloon occlusion (FETO) is considered in the following cases: liver herniation, LHR <1 and in the absense of chromosomal or associated abnormalities. FETO is a minimally invasive therapy in which the endotracheal balloon must be inflated for 3 or 6 weeks, and must be performed in the weeks 26-29 of gestation (Figure 4). Fluid retention in the lung accelerates lung maturation and decreases the risk of pulmonary hypertension. FETO must be placed before week 29 of gestation and then be withdrawn by fetoscopy after balloon deflation in week 34, ex-utero-intraparturm, or by tracheoscopy or percutaneous puncture in the newborn. When the balloon is removed, there is almost 50% loss of the relative lung volume (RLV), but is 40% higher than the previous RLV of the fetus. Placement of FETO after week 29 of gestation does not increase the RLV after the balloon is removed [38].

In the study of Jani et al. [39], 97% of the treated patients were born alive and 50% survived to discharge from hospital after surgery. FETO increased survival rates in left-sided CDH from 24.1% to 49.1%, and from 0% to 35.3% in right-sided CDH.

Ruano et al. [40], studied cases of severe isolated CDH with LHR <1 and liver herniation of which 71% were left and 29% were right. Of the 19 fetuses treated with FETO between the weeks 26 and 30 of gestation the overall survival rate at 6 months was 52.6% compared to 5.3% of the fetuses that were managed conservatively.

Araujo et al., published a systematic review and meta-analysis concerning FETO procedure in severe CDH (LHR< 1.0 and/or observed/expected LHR < 0.26 and > 1/3 LH), concluding that thisprocedure increasesneonatal survival at 30 days and 6 months. Nevertheless, the observed a higher rate of premature rupture of membrane, preterm birth < 37 weeks, and decreased the gestational age at delivery by 2 weeks [41].

A study performed by Nawapun compared changes in lung and liver volumes in fetuses with isolated CDH either expectantly managed or treated in utero by means of MRI. The LiTR did not change in either group. RFLVdid not increase with gestationin expectantly managed fetuses, while there was an increase 2.6 times largerfetuses undergoing tracheal occlusion. Gestational age at tracheal occlusion was an independent predictor of the RFLV. The net rate seems to initially increase and plateau at a maximum of 1.5% per week by 35 to 45 days after occlusion [42].

Although the endoluminal balloon utilized for FETO contains a metallic component, Victoria et al., have demonstrated that the risks of performing MRI at 3 T or less in a patient who has this occlusion balloon in place are acceptable [43].

CONCLUSION

Fetal MRI is capable of identifying CDH and compromised abdominal organs with precision due to the use of ultrafast sequences and high tissue contrast. Furthermore MRI allows calculating the pulmonary volume and the lung´s signal intensity to determine the severity of pulmonary hypoplasia; idsentifies liver herniation and the degree of severity, helping to assess the neonatal prognosis.

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