Journal of Pediatric Surgery 49 (2014) 853–858

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

AAP Papers

Fetal MRI lung volumes are predictive of perinatal outcomes in fetuses with congenital lung masses

Irving J. Zamora [a,b], Fariha Sheikh [a,b], Christopher I. Cassady [a,c], Oluyinka O. Olutoye [a,b,e], Amy R. Mehollin-Ray [a,c], Rodrigo Ruano [a,d], Timothy C. Lee [a,b], Stephen E. Welty [a,d], Michael A. Belfort [a,e], Cecilia G. Ethun [a,b], Michael E. Kim [a,b], Darrell L. Cass [a,b,e,*]

[a] Texas Children's Fetal Center, Texas Children's Hospital, Houston, TX
[b] The Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, TX
[c] Department of Radiology, Baylor College of Medicine, Houston, TX
[d] Department of Pediatrics, Division of Neonatology, Baylor College of Medicine, Houston, TX
[e] Department of Obstetrics and Gynecology, Baylor College of Medicine, Houston, TX

ARTICLE INFO

Article history:
Received 10 January 2014
Accepted 27 January 2014

Key words:
Congenital lung malformation
Risk stratification
CCAM
CPAM
Fetal MRI
Fetal lung volumes
Perinatal outcomes

ABSTRACT

Purpose: The purpose of this study was to evaluate fetal magnetic resonance imaging (MRI) as a modality for predicting perinatal outcomes and lung-related morbidity in fetuses with congenital lung masses (CLM).
Methods: The records of all patients treated for CLM from 2002 to 2012 were reviewed retrospectively. Fetal MRI-derived lung mass volume ratio (LMVR), observed/expected normal fetal lung volume (O/E-NFLV), and lesion-to-lung volume ratio (LLV) were calculated. Multivariate regression and receiver operating characteristic analyses were applied to determine the predictive accuracy of prenatal imaging.
Results: Of 128 fetuses with CLM, 93% (n = 118) survived. MRI data were available for 113 fetuses. In early gestation (<26 weeks), MRI measurements of LMVR and LLV correlated with risk of fetal hydrops, mortality, and/or need for fetal intervention. In later gestation (>26 weeks), LMVR, LLV, and O/E-NFLV correlated with neonatal respiratory distress, intubation, NICU admission and need for neonatal surgery. On multivariate regression, LMVR was the strongest predictor for development of fetal hydrops (OR: 6.97, 1.58–30.84; $p = 0.01$) and neonatal respiratory distress (OR: 12.38, 3.52–43.61; $p \leq 0.001$). An LMVR >2.0 predicted worse perinatal outcome with 83% sensitivity and 99% specificity (AUC = 0.94; $p < 0.001$).
Conclusion: Fetal MRI volumetric measurements of lung masses and residual normal lung are predictive of perinatal outcomes in fetuses with CLM. These data may assist in perinatal risk stratification, counseling, and resource utilization.

Congenital lung masses are rare and encompass a wide spectrum of malformations of the developing fetal lung. Large fetal lung masses compress surrounding thoracic structures. Compression from the mass on normal lung architecture increases the likelihood for pulmonary hypoplasia and respiratory failure following birth [1]. Compression from these lesions on the mediastinum and heart may decrease cardiac venous return and pose a risk for fetal hydrops and fetal demise [2,3]. To date, ultrasound measurement of the CCAM-volume ratio (CVR) has been the primary predictor of prenatal and postnatal outcomes in fetuses with CLM [4,5]. Fetal MRI has been established as an adjunct to ultrasound in the imaging of fetuses with congenital lung malformations (CLM) as early as 18 weeks gestation [6,7]. Compared to ultrasonography, fetal MRI may be superior at characterizing the boundaries of the malformed lung and how it relates to the normal lung lobar anatomy and surrounding thoracic structures [8–10]. Recently, it has been shown that fetal MRI may be superior in differentiating between the various types of CLMs, including bronchopulmonary sequestration, congenital lobar emphysema, congenital pulmonary airway malformations (CPAM), and bronchogenic cysts [11].

The utility of fetal MRI in assessing volume measurements of CLM both in terms of the mass itself, as well as the uninvolved, normal lung, has not been previously examined. Therefore, the purpose of this study was to evaluate fetal MRI as a modality for predicting perinatal outcomes, including the development of fetal hydrops, mortality, neonatal respiratory distress and lung-related morbidities in fetuses with CLM.

1. Materials and methods

1.1. Study cohort

Permission to conduct this study was obtained from the institutional review board (H-29695) of Baylor College of Medicine,

* Corresponding author at: Texas Children's Hospital, 6701 Fannin St. Suite 1210, Houston, TX 77030. Tel.: +1 832 822 3135; fax: +1 832 825 3141.
E-mail address: dcass@bcm.edu (D.L. Cass).

http://dx.doi.org/10.1016/j.jpedsurg.2014.01.012
0022-3468/

Houston, TX. The records of all patients referred to the Texas Children's Fetal Center with a congenital lung malformation over a 11-year period from January 2002 to December 2012 were reviewed retrospectively. Fetuses that died owing to non–lung-related comorbidities and those without at least one available fetal MRI were excluded. Data collected from the charts included patient demographics, gestational age at diagnosis and at birth, mortality, fetal course including development of fetal hydrops (defined as presence of serous fluid in two or more body cavities) and need for fetal intervention, and postnatal course including the presence of neonatal respiratory distress (defined as any supplemental oxygen requirement beyond the initial resuscitation period), need for intubation, duration of intubation, NICU admission, need for urgent operation and hospital length of stay. All fetal MRI images were reviewed and lung mass volume ratio (LMVR), observed/expected normal fetal lung volumes (O/E-NFLV), and lesion-to-lung volume ratio (LLV) were calculated.

1.2. Total fetal lung volume and lung mass volume ratio measurements

A fetal MRI scan was performed at the time of the initial consultation for most patients referred for a CLM. For most patients this scan was performed before 26 weeks gestation. A subset of patients had a second fetal MRI performed later in gestation (>26 weeks). All lung volumes were calculated on contiguous axial single shot fast spin echo (SSFSE) T2-weighted MR images free from motion by using a freehand region of interest (ROI) tool. The CLM was defined by its hyperintense signal on T2-weighted images and the lesion area was outlined on contiguous sections (Fig. 1). The sum of all measurements was multiplied by the section thickness to obtain a volume in cubic centimeters, which was then divided by the head circumference in centimeters to derive the lung mass volume ratio (LMVR) corrected for gestational age [12]. The total fetal lung volume (TFLV) was measured using the same method. To obtain the observed normal total fetal lung volume (ONTFLV), the volume of normal lung was measured, excluding the volume of the lung mass. This ONTFLV was used to calculate the O/E-NFLV by dividing the measured value by the mean expected TFLV for the respective gestational age of each fetus [13]. The lesion/normal total lung volume ratio was then calculated by dividing the measured lung lesion volume by the ONTFLV, and labeled the "lesion-to-lung volume ratio."

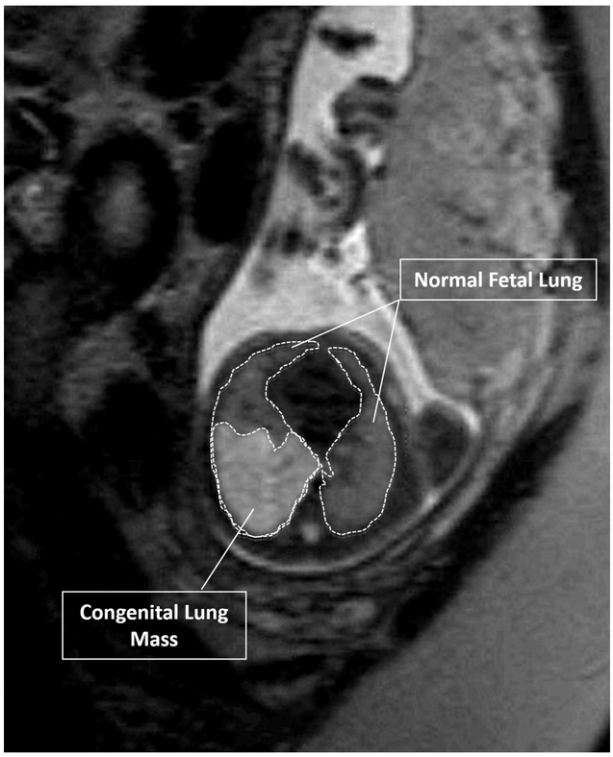

Fig. 1. A representative image of an axial single shot fast spin echo (SSFSE) T2-weighted MR image of a fetus with CLM. Using a freehand region of interest (ROI) tool the lung lesion and normal fetal lung areas were outlined. The lung lesion was identified as the region of most hyperintense signal in the chest.

1.3. Indications for fetal intervention

As previously described [5], the primary indication for fetal intervention at our center was the presence of fetal hydrops, defined as serous fluid in two or more body cavities. Fetuses with hydrops and evidence of heart failure on fetal echocardiography were considered for open maternal-fetal surgery. Fetuses that had large lung masses causing persistent mediastinal compression (PMC) late in gestation were offered an ex-utero intrapartum treatment (EXIT) to lung resection approach [14,15].

1.4. Statistical analysis

Outcomes between groups for categorical variables were compared using Chi-square analysis and Fisher's Exact test. Continuous variables were compared using 2-tailed Student's t-tests for normally distributed data and Mann-Whitney U test for nonnormally distributed data. An alpha of <0.05 was considered statistically significant.

The outcomes examined in this study were stratified according to the gestational age at the time of fetal MRI. For fetal MRIs at <26 weeks, the primary outcome was the development of fetal hydrops, and secondary outcomes were need for fetal intervention and mortality. For fetal MRIs obtained >26 weeks, the primary outcome was the development of neonatal respiratory distress, and secondary outcomes were need for intubation, NICU admission, and urgent surgery in the neonatal period. Mortality was defined as survival status at the time of chart review.

A stepwise multivariate logistic regression was performed for the prenatal categorical outcome of 'development of hydrops.' The covariates examined in the regression model were gestational age at diagnosis, gender, location of the CLM and prenatal imaging parameters obtained at <26 weeks gestational age (GA) including LMVR and O/E-NFLV. A separate stepwise regression model was performed for the postnatal categorical outcome of 'neonatal respiratory distress.' The covariates examined in the regression model were gestational age at diagnosis, gestational age at birth, gender, location of the CLM and prenatal imaging parameters including LMVR and O/E-NFLV. Interactions were evaluated between all the covariates in the regression models.

Receiver operating characteristic curves (ROC) were utilized to determine the predictive accuracy of prenatal imaging for perinatal outcomes. The O/E-NFLV and LMVR measurements obtained at <26 weeks were evaluated with ROC analysis against the outcome of 'development of hydrops' and the O/E-NFLV and LMVR obtained at >26 weeks were evaluated against the outcome of 'neonatal respiratory distress.' Optimal cutoff points of greatest accuracy were derived by graphing the results of the ROC analyses and selecting the point of maximum sensitivity and specificity of each analysis.

2. Results

During the study period a total of 128 fetuses (65 male) were evaluated for CLM, 93% (118) survived, 63% (81) were left sided, and the average gestational age at diagnosis was 22.1 ± 4.2 weeks. Two fetuses died from non–lung mass related causes and were excluded from further analysis – one from complications owing to Trisomy 18 and one from complications owing to congenital heart disease. MRI data were available for a total of 113 fetuses. Of these fetuses, 57