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在线全文

产前磁共振在先天性肺囊性疾病胎儿预后评估中的应用研究*

贾 阳[1,2]，鲍 莉[1,2]，徐 蓉[1,2]，谢林均[1,2]，叶 璐[2,3]，郭应坤[1,2]，陈 慧[2,4△]

1. 四川大学华西第二医院 放射科（成都 610041）；2. 出生缺陷与相关妇儿疾病教育部重点实验室(四川大学)（成都 610041）；
3. 四川大学华西第二医院 超声科（成都 610041）；4. 四川大学华西第二医院 生殖内分泌科（成都 610041）

【摘要】 **目的** 回顾性分析先天性肺囊性疾病胎儿产前磁共振(magnetic resonance imaging, MRI)图像，探讨产前MRI检查评估胎儿先天性肺囊性疾病的可行性，初步探索产前MRI对先天性肺囊性疾病胎儿预后的预测价值。**方法** 收集2018年5月–2023年3月四川大学华西第二医院经产前超声怀疑胎儿先天性肺囊性疾病并行MRI检查确诊者。测量胎儿肺部肿块的体积及肺头比(cystic volume ratio, CVR)、双侧肺肝信号强度比值，结合随访结果分析MRI评估胎儿先天性肺囊性疾病的可行性。采用logistic回归模型评价病灶体积、CVR、患侧-健侧肺肝信号强度比值差值与不良预后是否有关。采用受试者工作特征(receiver operating characteristic, ROC)曲线评估MRI参数对于预测胎儿预后的价值。**结果** 最终纳入47例先天性肺囊性疾病胎儿，其中预后良好30例，预后不良17例。预后良好组与预后不良组间胎儿患侧-健侧肺肝信号强度比值差值的差异有统计学意义(P<0.05)，且健侧肺肝信号强度比值高于患侧肺肝信号强度比值。CVR〔比值比(odds ratio, OR)=1.058，95%置信区间(confidence interval, CI)为1.014～1.104〕、患侧-健侧肺肝信号强度比值差值(OR=0.814，95%CI为0.700～0.947)与先天性肺囊性疾病胎儿出生不良预后相关。此外，ROC曲线分析结果显示，联合应用病灶体积/患侧肺体积及患侧-健侧肺肝信号强度比值差值观察预测先天性肺囊性疾病胎儿预后较单一参数判断更为准确，其曲线下面积为0.988，截断值为0.33，对应的敏感度为100%，特异度为93.3%，95%CI为0.966～1。**结论** 基于产前MRI获得的病灶体积、病灶体积/患侧肺体积、病灶体积/总肺体积、CVR、患侧-健侧肺肝信号强度比值差值预测先天性肺囊性疾病胎儿的不良预后有一定价值，但在联合指标中病灶体积/患侧肺体积及患侧-健侧肺肝信号强度比值差值的预后效能更好。

【关键词】 先天性肺囊性腺瘤样畸形 支气管肺隔离症 支气管囊肿 磁共振成像

Application of Fetal Magnetic Resonance Imaging in Prognosis Assessment of Fetuses With Congenital Pulmonary Cystic Diseases

JIA Yang[1,2], *BAO Li*[1,2], *XU Rong*[1,2], *XIE Linjun*[1,2], *YE Lu*[2,3], *GUO Yingkun*[1,2], *CHEN Hui*[2,4△]. 1. *Department of Radiology*, *West China Second University Hospital*, *Sichuan University*, Chengdu 610041, China; 2. *Key Laboratory of Birth Defects and Related Diseases of Women and Children of the Ministry of Education*, *Ministry of Education*, Chengdu 610041, China; 3. *Department of Ultrasound*, *West China Second University Hospital*, *Sichuan University*, Chengdu 610041, China; 4. *Department of Reproductive Endocrinology*, *West China Second University Hospital*, *Sichuan University*, Chengdu 610041, China

△ Corresponding author, E-mail: 646198099@qq.com

【**Abstract**】 **Objective** The aim of this study is to explore the practical value of prenatal magnetic resonance imaging (MRI) in the assessment of congenital cystic lung disease in fetuses, to evaluate the relative size of the lesion and the status of lung development, and to make an attempt at utilizing the strength of MRI in post-processing to obtain assessment indicators of the size of the lesion and the status of lung development, with which predictions can be made for the prognosis that these fetuses may face after birth. We retrospectively collected and analyzed the data of fetuses diagnosed with congenital cystic lung disease. Prenatal ultrasound examination of these fetuses led to the diagnosis that they were suspected of having congenital cystic lung disease and the diagnosis was confirmed by subsequent prenatal MRI. The fetuses were followed up to track their condition at birth (postnatal respiratory distress, mechanical ventilation, etc.), whether the fetuses underwent surgical treatment, and the recovery of the fetuses after surgical treatment. The recovery of the fetuses was followed up to explore the feasibility of prenatal MRI examination to assess fetal congenital pulmonary cystic disease, and to preliminarily explore the predictive value of prenatal MRI for the prognosis of fetuses with congenital pulmonary cystic disease. **Methods** MRI fetal images were collected from pregnant women who attended the West China Second University Hospital of Sichuan University between May 2018 and March 2023 and who were diagnosed with fetal congenital pulmonary cystic disease by prenatal ultrasound and subsequent MRI. Fetal MRI images of congenital cystic lung disease were post-processed to obtain the fetal lung lesion volume, the fetal affected lung volume, the healthy lung volume, and the fetal head circumference measurements. The signal intensity of both lungs and livers, the lesion volume/the affected lung volume, the lesion volume/total lung volume, the cystic volume ratio (CVR),

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△ 通信作者，E-mail: 646198099@qq.com

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and the bilateral lung-liver signal intensity ratio were measured. The feasibility and value of MRI post-processing acquisition indexes for evaluating the prognosis of fetuses with congenital cystic lung disease were further analyzed by combining the follow-up results obtained 6 months after the birth of the fetus. Logistic regression models were used to quantify the differences in maternal age, gestational week at the time of MRI, CVR, and bilateral lung-to-liver signal intensity ratio, and to assess whether these metrics correlate with poor prognosis. Receiver operating characteristic (ROC) curves were used to assess the value of the parameters obtained by MRI calculations alone and in combination with multiple metrics for predicting poor prognosis after birth. **Results** We collected a total of 67 cases of fetuses diagnosed with congenital cystic lung disease by fetal MRI between May 2018 and March 2023, and excluded 6 cases with no normal lung tissue in the affected lungs, 11 cases of fetal induction, and 3 cases of loss of pregnancy. In the end, 47 cases of fetuses with congenital cystic lung disease were included, of which 30 cases had a good prognosis and 17 cases had a poor prognosis. The difference in the difference between the signal intensity ratios of the affected and healthy sides of the lungs and livers of the fetuses in the good prognosis group and that in the poor prognosis group was statistically significant (P<0.05), and the signal intensity ratio of the healthy side of the lungs and livers was higher than the signal intensity ratio of the affected side of the lungs and livers. Further analysis showed that CVR (odds ratio [OR]=1.058, 95% confidence interval [CI]: 1.014-1.104), and the difference between the lung-to-liver signal intensity ratios of the affected and healthy sides (OR=0.814, 95% CI: 0.700-0.947) were correlated with poor prognosis of birth in fetuses with congenital cystic lung disease. In addition, ROC curve analysis showed that the combined application of lesion volume/affected lung volume and the observed difference in the signal intensity ratio between the affected and healthy lungs and liver predicted the prognosis of children with congenital cystic lung disease more accurately than the single-parameter judgment did, with the area under the curve being 0.988, and the cut-off value being 0.33, which corresponded to a sensitivity of 100%, a specificity of 93.3%, and a 95% CI of 0.966-1.000. **Conclusions** Based on the MRI of fetuses with congenital cystic lung disease, we obtained information on lesion volume, lesion volume/affected lung volume, lesion volume/total lung volume, CVR, and bilateral lung-to-liver signal intensity ratio difference, all of which showing some clinical value in predicting the poor prognosis in fetuses with congenital cystic lung disease. Furthermore, among the combined indexes, the lesion volume/affected lung volume and bilateral lung-to-liver signal intensity ratio difference are more effective predictors for the poor prognosis of fetuses with congenital cystic lung disease, and show better efficacy in predicting the poor prognosis of fetuses with congenital cystic lung disease. This provides a new and effective predictive method for further assessment of pulmonary lung development in fetuses with congenital cystic lung disease, and helps improve the assessment and prediction of the prognosis of fetuses with congenital cystic lung disease.

【Key words】 Congenital cystic adenomatoid malformation of lung　Bronchopulmonary sequestration　Bronchogenic cyst　Magnetic resonance imaging

胎儿先天性肺囊性疾病是胎儿期肺部组织发育异常所导致的先天性肺部疾病，其发生率约为4.15∶10 000[1]，其主要包含先天性肺囊腺瘤样畸形、支气管源性囊肿、肺隔离症。超声检查凭借其实用、安全、经济等特点成为产前一线筛查手段，但成像质量易受母亲肥胖、羊水过少、胎儿胸廓等因素限制影响成像质量，尤其是孕晚期成像质量欠佳。胎儿磁共振（magnetic resonance imaging, MRI）作为二线检查，其安全性已得到胎儿MRI中国专家共识认同，其场强、特异性吸收率、噪声等不会对无MRI明确禁忌证的孕妇及胎儿发育造成影响[2]，不受母亲肥胖、羊水过少、胎儿胸廓等因素的影响，并具有多平面成像及软组织分辨率高的特点，与超声测量相比更具优势。产前超声对于病变的主要观测指标是胎儿肺头比（cystic volume ratio, CVR），而MRI在实现病灶准确显示及后处理之外还可以凭借获取肺肝信号强度比值评估胎儿肺部发育不良[3]。这一方法已有多项研究进行探索[3-4]，但少有研究涉及同时测定双侧肺肝信号强度比值评估肺部发育程度。本研究尝试进行双侧肺肝信号强度比值测定，并联合病灶体积共同预测先天性肺囊性疾病胎儿不良预后出现的可能。现报道如下。

1 资料与方法

1.1 一般资料

本研究经四川大学华西第二医院医学伦理委员会批准〔医学科研2022伦审批第(227)号〕。回顾性收集四川大学华西第二医院2018年5月–2023年3月产前诊断为胎儿肺部囊性病变孕妇67例。纳入标准：①胎儿MRI诊断为先天性肺囊性疾病；②临床资料如生后患儿情况、手术记录及患儿预后结局较为完整。排除标准：①MRI图像受运动伪影或其他影响无法准确测量所需参数；②伴发其他系统畸形；③患侧肺部无正常肺组织，无法测量患侧肺肝信号强度比值；④胎儿引产；⑤随访失访者。纳入排除标准如图1所示。

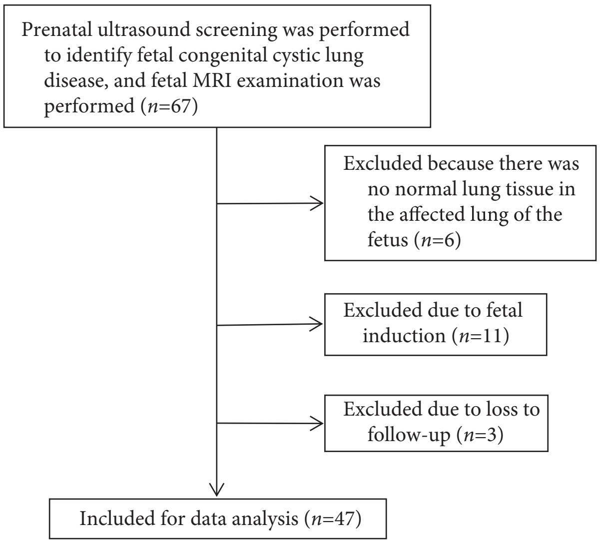

图 1 患者纳入和排除标准

Fig 1 Patient inclusion and exclusion criteria

1.2　检查方法

采用Philips Achieval 1.5T磁共振扫描仪，16通道相控阵体线圈(Sense-XL-Torso)。体位以仰卧位为主，足先进。扫描方式：首先进行定位相扫描，再根据胎儿体位获取横、冠、矢状位T2WI图像。扫描序列及参数：单次激发快速自旋回波(single shot fast spin echo, SS-FSE)序列，重复时间(repetition time, TR)1 500 ~ 1 800 ms，回波时间(echo time, TE)80 ms，层厚5 mm，层间隔0 mm，翻转角90°，视野419 mm×419 mm，矩阵432×432。

1.3　图像分析

由2名有5年工作经验的胎儿影像学诊断医师分别独立测量CVR及双侧肺肝信号强度比值。使用3D-slicer (5.2.2)于冠状位图像上逐层勾画病灶及双侧肺脏，采用描点法勾勒出每个层面的肺组织，注意避开肺部大血管，自动处理计算得到左肺体积、右肺体积及病灶体积，并测量胎儿头围，计算CVR。见图2。CVR计算使用病灶体积/头围，头围数值获取通过扫描头部层面测量或者图像三维重建测量。使用PACS系统在胎儿冠状位切面选取患侧正常肺组织及其同一水平线上正常肺组织及肝实质均匀的区域，避开无组织边界区域和大血管结构，分别选取3个感兴趣区(region of interest, ROI)，ROI面积截取10 ~ 15 mm^2，将3次测量所得结果取平均值[5]，再通过计算得出患侧肺肝信号强度比值，再用同样方法测量健侧肺肝信号强度比值，获得的信号强度比值的差值即得到患侧-健侧肺肝信号强度比值差值。

1.4　随访

通过查阅病历资料及出生后6个月进行电话随访记录妊娠结局及胎儿出生后情况，根据产前诊断先天性肺

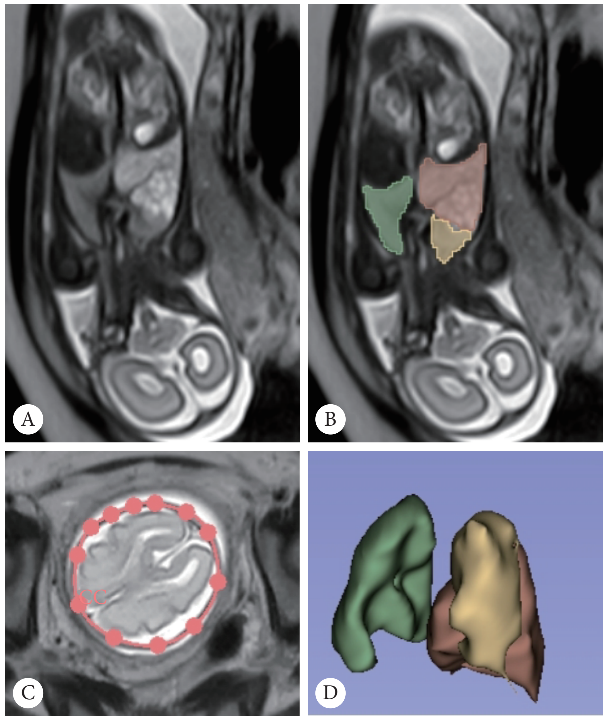

图 2 勾画示意图

Fig 2 Schematic diagram

A, A coronal-plane image of the feus; B, 3D-slicer used the tracing method to outline the lung tissue at each level while avoiding the large blood vessels of the lung; C, fetal head circumference measurement; D, fetal lung 3D reconstruction schematic diagram, with green representing the lung tissue of the healthy side, yellow, the lung tissue of the affected side, and red, the lesion.

囊性疾病胎儿妊娠结局及出生后呼吸、手术干预等状况将其分为预后良好(出生后无明显呼吸系统相关症状，未进行出生时抢救，无须临床干预)及预后不良(出生后出现明显呼吸系统症状，需要进行临床干预，或出现与疾病相关围产期死亡)。随访内容：①妊娠最终结局，包括孕期胎死宫内、引产；②新生儿出生时的呼吸系统症状，是否出现呼吸窘迫综合征，进行气管插管等抢救性治疗；③出生后根据症状及临床医生建议行手术干预治疗。

1.5　统计学方法

使用SPSS26.0软件进行统计学分析。对数据行K-S(Kolmogorov-Smirnov)检验，符合正态分布的计量资料数据用$\bar{x} \pm s$表示，组间差异比较采用独立样本t检验；非正态分布用中位数(四分位间距)表示，组间比较采用Mann-Whitney U检验。利用线性回归中的共线性诊断进行多重共线性分析，排除共线性指标，后续采用logistic回归方程分析非共线性研究指标与胎儿出生后不良预后之间的关系。绘制受试者工作特征(receiver operating characteristic, ROC)曲线，并计算截断值，评价CVR及双侧肺肝信号强度比值预测不良预后的价值。P< 0.05为差异有统计学意义。

2 结果

2.1 一般资料

收集本院从2018年5月–2023年3月产前诊断为胎儿先天性肺囊性疾病的孕妇67例,引产排除11例,患侧肺部无正常肺组织排除6例,失访排除3例,最终纳入47例。孕妇年龄20~44岁,平均年龄(30.06±4.65)岁;MRI检查孕周为20~35周,平均(27.28±3.22)周(从孕妇的末次月经开始推算)。47例患者中,预后不良组共17例,其中行手术治疗12例(70.6%),准备行手术治疗1例(5.9%),未行手术治疗3例(17.6%),胎死宫内1例(5.9%)。预后良好组共30例,出生时及出生后未见明显呼吸系统症状,出生后因无症状未复查17例(56.7%),出生后进行复查13例(43.3%),其中复查未见病灶显示10例(33.3%)。由表1可见,预后不良组病灶体积高于预后良好组($P<0.05$)。预后不良组CVR高于预后良好组($P<0.05$)。预后良好组和预后不良组组内健、患侧肺肝信号强度比值间的差异有统计学意义($P<0.05$),且患侧肺肝信号强度比值明显低于健侧肺肝信号强度比值。

2.2 logistic回归分析不良预后的危险因素

经多重共线性分析,排除共线性指标如病灶体积、病灶体积/患侧肺体积、病灶体积/总肺体积,将孕妇年龄、检查孕周、CVR及患侧-健侧肺肝信号强度比值差值纳入二元logistic回归分析,结果见表2。其中,孕妇年龄及检查孕周对不良预后无明显预测价值,而CVR〔比值比(odds ratio, OR)=1.058,95%置信区间(confidence interval, CI)为1.014~1.104〕、患侧-健侧肺肝信号强度比值差值(OR=0.814,95%CI为0.700-0.947)与不良预后有关。

2.3 ROC曲线分析单独或联合指标预测不良预后的效能

结果见图3和表3。CVR预测不良预后的曲线下面积(area under the curve, AUC)为0.884,截断值为0.20,对应的敏感度为94.1%,特异度为70.0%;患侧-健侧肺肝信号强度比值差值预测不良预后的AUC为0.108,截断值为0.17,对应的敏感度为5.9%,特异度为96.7%;病灶体积/患侧肺体积预测不良预后的AUC为0.845,截断值为0.28,对应的敏感度为94.1%,特异度为66.7%;而病灶体积/患侧肺体积+患侧-健侧肝信号强度比值差值联合预测不良预

表 1 预后良好组及预后不良组基线资料

Table 1 Baseline data of the good prognosis group and the poor prognosis group

Characteristic	Good prognosis group (*n*=30)	Poor prognosis group (*n*=17)	*P*
Maternal age/yr.	29.93±4.72	29 (27, 33)	0.991
Gestational age/week	26 (25, 28)	27.94±3.38	0.308
Lesion volume/cm^3	3.20 (1.59, 6.02)	14.62 (6.06, 18.98)	<0.001
Lesion volume/lung volume of affected side	0.19 (0.11, 0.44)	0.92 (0.38, 2.58)	<0.001
Lesion volume/total lung volume	0.10 (0.05, 0.17)	0.38 (0.19, 0.67)	<0.001
CVR	0.13 (0.06, 0.27)	0.57 (0.25, 0.79)	<0.001
Lung-liver signal intensity ratio of affected side	1.91 (1.68, 1.99)	1.88±0.59	0.894
Lung-liver signal intensity ratio of healthy side	1.93 (1.60, 2.04)	2.09±0.54	0.250
Lung-liver signal intensity ratio difference	−0.07 (−0.08, −0.16)	−0.20±0.14	<0.001

The data are presented as $\bar{x}\pm s$ or median (P_{25}, P_{75}).

表 2 二元logistic回归分析筛选胎儿不良预后影响因素

Table 2 Binary logistic regression analysis was performed to screen the influencing factors of poor fetal prognosis

Index	*B*	SE	Wald	*P*	OR	95% CI
Maternal age	0.005	0.130	0.002	0.967	1.005	0.779-1.297
Gestational age	0.060	0.176	0.117	0.733	1.062	0.752-1.499
CVR	0.056	0.022	6.732	0.009	1.058	1.014-1.104
Lung-liver signal intensity ratio difference	−0.206	0.077	7.123	0.008	0.814	0.700-0.947

B: partial regression coefficient; SE: standard error; OR: odds ratio; CI: confidence interval.

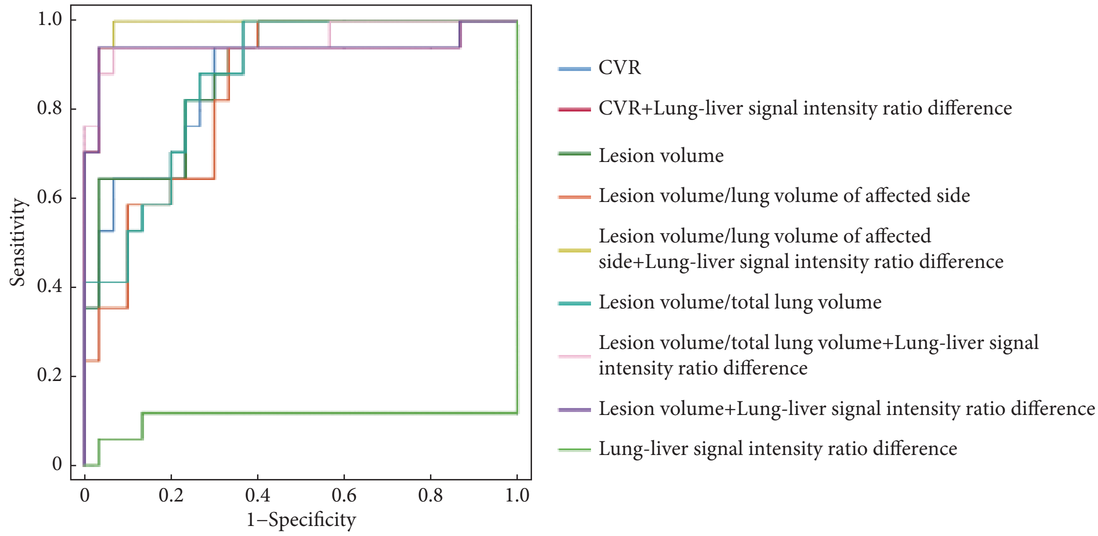

图 3 单独指标或联合指标的ROC曲线分析

Fig 3 ROC curve analysis for individual or combined indicators

表 3　单独或联合指标预测不良预后的AUC值

Table 3　The AUC value of single or combined indicators for predicting poor prognosis

Test result variables	Cutoff value	Sensitivity	Specificity	AUC	95% CI
Lesion volume/cm^3	13.98	0.647	0.967	0.888	0.797-0.980
Lesion volume/lung volume of affected side	0.28	0.941	0.667	0.845	0.737-0.953
Lesion volume/total lung volume	0.12	1	0.059	0.871	0.773-0.968
CVR	0.20	0.941	0.700	0.884	0.792-0.977
Lung-liver signal intensity ratio difference	0.17	0.059	0.967	0.108	0-0.249
Lesion volume+Lung-liver signal intensity ratio difference	0.43	0.941	0.967	0.941	0.843-1
Lesion volume/lung volume of affected side+Lung-liver signal intensity ratio difference	0.33	1	0.933	0.988	0.966-1
Lesion volume/total lung volume+Lung-liver signal intensity ratio difference	0.19	1	0.633	0.871	0.773-0.968
CVR+Lung-liver signal intensity ratio difference	0.40	0.941	0.967	0.941	0.843-1

AUC: area under the curve; CI: confidence interval; CVR: cystic volume ratio.

后的AUC为0.988, 截断值为0.33, 对应的敏感度为100%, 特异度为93.3%, 预测效能较单一指标效果更好。

3　讨论

MRI检查作为产前诊断的二线检查, 其良好的空间分辨力和软组织分辨力是其独特的优势, 并能显示胎儿全貌, 有助于图像后处理获取胎儿肺部体积数据。

胎儿肺囊性疾病的量化指标中, 最为广泛应用的是CVR。超声检查计算CVR, 可借此数据进行病灶体积变化的动态评估。现有多中心数据表明, CVR是先天性肺囊腺瘤样畸形胎儿围产期结局的最佳预测因子[6-10], 胎儿先天性肺囊性疾病, 尤其是先天性肺气道畸形中CVR可以动态反映随孕周的变化趋势[11-14], 发现CVR在孕20～30周呈现高值, 峰值出现在孕25周, 此后开始下降, 以孕30周后更为明显。而部分胎儿于妊娠32～34周出现逐渐消退[8-9]。监测CVR对病灶评估具有一定价值[15-18]。本研究显示, CVR预测不良预后的AUC为0.884, 对应的敏感度为94.1%, 特异度为70.0%, 能够对胎儿不良预后进行预测, 但近年来越来越多的研究中尝试结合其他指标提升不良预后的预测效能, 如肺肝信号强度比值评估肺部发育程度、CVR值分层预测患儿预后, 但少有研究同时测量双侧肺肝信号强度比值。

肺肝信号强度比值多用于评估胎儿肺部发育成熟度, 随着孕周推移, 胎儿肺发育逐步成熟, 肺部组织内液体量增多, 胎儿肺部T2WI信号逐渐增高。而肝脏作为胎儿主要造血器官, 其因组织内含铁而在T2WI上呈稍低信号, 因此肺肝信号强度比值随胎龄增大而增大[11-12]。多项研究评估肺部发育程度选取单侧肺组织。BALASSY等[19]

尝试选取膈疝胎儿双侧肺肝信号强度比值评估肺部发育,然而双侧肺肝信号强度比值无明显差异。由于肺部发育随着孕周出现变化,取双侧肺肝信号强度比值差值更能反映双肺发育差异性。而病变体积随着孕周增大亦存在变化,CVR测值通过胎儿孕周发育头围增长相对性量化病灶体积变化趋势,但其阈值判断仍旧是胎儿先天性肺囊性疾病研究热点,且部分病灶在孕周较大时显示欠佳,因此本研究尝试用不同评估病变相对大小的方式与传统测量CVR进行比较,同时结合肺肝信号强度比值评估双肺发育程度及发育差异,病灶相对大小及肺部发育程度联合评估,旨在获取更高预测价值的预测方案。本研究发现双侧肺肝信号强度比值在预后良好与预后不良组间无明显差异,但患侧-健侧肺肝信号强度比值差值在预后良好与预后不良组间则有明显差异,其联合病灶体积/患侧肺体积共同预测胎儿预后存在一定价值,其AUC为0.988,对应的敏感度为100%,特异度为93.3%,预测效能远高于单项指标。

综上所述,基于MRI测量病灶体积、病灶体积/患侧肺体积、病灶体积/总肺体积、CVR、患侧-健侧肺肝信号强度比值差值均具有一定预测价值,但单个指标预测效能有限,而联合病灶体积/患侧肺体积及患侧-健侧肺肝信号强度比值差值的预测效能更高,更有助于预测胎儿出生后呼吸症状及临床干预情况。因病灶存在一定的消退趋势,且孕中晚期对于病变的反映更为准确,此阶段应当重视定期复查的价值。本研究仍存在不足之处:如数据来自单中心,未来计划纳入多中心大样本量数据进行研究;未与肺发育正常胎儿进行对比,课题组计划收集肺发育正常胎儿数据纳入后续研究。近年来关于胎儿肺部MRI生物学测量研究逐渐增多,建立多中心、大样本量数据库,可以建立正常标准值范围为后续开展胎儿肺部疾病研究提供参考。

* * *

作者贡献声明 贾阳负责初稿写作,鲍莉负责数据审编,徐蓉负责研究方法,谢林均负责监督指导,叶璐负责监督指导,郭应坤负责经费获取,陈慧负责审读与编辑写作。所有作者已经同意将文章提交给本刊,且对将要发表的版本进行最终定稿,并同意对工作的所有方面负责。

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