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Discordant prenatal ultrasound and fetal MRI in CDH: wherein lies the truth?☆

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ABSTRACT

Purpose: Prenatal risk assessment of congenital diaphragmatic hernia (CDH) relies on prenatal ultrasound (U/S) and fetal magnetic resonance imaging (MRI). When the modalities differ in prognosis, it is unclear which is more reliable.
Methods: Retrospective chart review identified cases of prenatally diagnosed CDH from 4/2010–6/2018 meeting inclusion criteria. Demographic, radiologic, and postnatal outcomes data were collected.
Ultrasound- versus MRI-based prognosis (mild, moderate, and severe) was compared with clinical outcomes. Kappa measures compared congruency in disease severity scaling between imaging modalities, while logistic regression and receiver operating characteristics curves compared the ability of each modality to predict outcomes.
Results: Forty-two patients met criteria. Both U/S- and MRI-based prognosis categories differentiated for survival. MRI categories differentiated for ECMO use, surgical repair, and defect type. O/e TFLV better discriminated for survivors and defect type than o/e LHR. Seventeen (40.5%) had discordant prenatal prognostic categories. In 13/17 (76.5%), o/e TFLV predicted higher severity when compared to o/e LHR, but sample size was insufficient to compare accuracy in cases of discordance.
Conclusions: Clinical outcomes suggest fetal MRI may more accurately predict severe pulmonary hypoplasia compared to prenatal ultrasound. Our analysis suggests fetal MRI is a valuable adjunct in the prenatal evaluation of CDH.
Level of Evidence: Level III.
Type of Study: Retrospective Review.

Congenital diaphragmatic hernia (CDH) complicates 1.9 to 2.3 in 10,000 births and is associated with high perinatal morbidity and mortality [1,2]. Currently, 68% percent of cases are diagnosed in utero, and while survival rates range based on severity of disease, patients diagnosed prenatally are associated with worse outcomes [higher proportion of larger defect sizes, increased mortality, more frequent utilization of Extracorporeal Membrane Oxygenation (ECMO)] compared to those with postnatal diagnoses [3].

Data obtained from prenatal ultrasound (U/S) and fetal magnetic resonance imaging (MRI) have been studied as surrogate measures of fetal lung volume to predict the degree of pulmonary hypoplasia critical to morbidity and mortality in CDH. Lung-to-head ratio (LHR) and observed-to-expected LHR (o/e LHR), both calculated from ultrasound, are the most commonly utilized and best validated measures, favored for easy accessibility and low cost [4,5]. Based on the antenatal CDH registry, Deprest et al. proposed stratifying isolated left-sided CDH patients into mild, moderate, and severe prognostic categories based on their o/e LHR and liver position [6]. More recently, as many patients are also undergoing fetal MRI as part of their prenatal evaluation, total fetal lung volume (TFLV) and observed-to-expected TFLV (o/e TFLV) have been validated as important adjuncts for prenatal diagnosis and prognosis [7–10]. These values have also been used to stratify patients into mild, moderate, and severe prognostic categories [8].

It is unknown how often prenatal U/S and fetal MRI assessments differ in their prediction of severity of pulmonary hypoplasia and associated outcomes, and which is the more reliable test in the context of a discrepancy. Accurate diagnosis and prognosis of CDH is critical to allow for comprehensive counseling and planning of pre- and postnatal interventions [11,12]. We hypothesized that in cases of discordant prognoses, fetal MRI would more accurately predict clinical outcomes compared to prenatal ultrasound.

☆ Annotation of changes: Institutional Review Board approval at University of Michigan (HUM00031524)

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1. Material and methods

1.1. Study base

The study was approved by the Institutional Review Board (IRB 00031524). Cases of prenatally diagnosed CDH were identified between April 2010 and June 2018. Cases that had documented fetal MRI-based lung volumetric data and sonographic LHR measurements within a week of each other were included in analysis. LHR measurements, using the longest diameter method, were obtained by Registered Diagnostic Medical Sonographers with specialized training in high-risk obstetric scanning and reviewed by experienced Maternal Fetal Medicine (MFM) physicians. In post-hoc analysis, a single MFM physician blinded to previous data re-reviewed each ultrasound to obtain a trace-based LHR measurement from the same image used for the longest-diameter-based LHR measurement. TFLV was calculated by a dedicated Pediatric Radiologist by multiplying the area of manually outlined lung boundary excluding pulmonary hila by the slice thickness and summing the consecutive slice volumes. Observed-to-expected TFLV was calculated using the formula for expected TFLV published in Meyers et al. [13].

Cases excluded from final analysis were those fetuses part of a multiple gestation, with a right-sided or bilateral defect, with a major cardiac anomaly as defined by the CDH Study Group (CDHSG) [14], and/or those with a chromosomal abnormality as confounding factors that would affect clinical outcomes. Patients meeting criteria were classified into mild, moderate, and severe pulmonary hypoplasia prognostic categories based on their o/e LHR and liver herniation status as described in Deprest et al. [6]. Patients were also similarly classified by their o/e TFLV percentages as presented in previous literature [8] (Table 1). Maternal and neonatal charts were reviewed, and demographic, radiographic, delivery, operative, and postnatal clinical outcomes data were collected. Patients were also assigned a mortality risk category according to the CDHSG clinical prediction model based on neonatal data obtained within the first few hours of life [15]. The score, based on birthweight, 5-min APGAR score, presence of severe pulmonary hypertension on initial echocardiogram, and the finding of a severe cardiac or chromosomal anomaly, assigned patients to a low, intermediate, or high mortality risk, and was validated in a population-based study [16]. Those for whom a CDHSG score could not be calculated (echocardiogram data missing or not obtained prior to expiring) were excluded from statistical comparison analysis.

1.2. Statistical analysis

Statistical analyses were performed using Stata version 15 (College Station, TX) and GraphPad Prism version 8.0.0 for Mac (San Diego, CA), and the alpha level was set a priori at $p < 0.05$. The analytical sample was described using frequencies, percentages, mean (± standard error of the mean (SEM)), median, and range.

We compared outcomes with regards to the frequency of each CDHSG mortality risk category, ECMO utilization, surgical repair, type of defect (A/B vs C/D), and survival by the prognostic categories derived from prenatal U/S and fetal MRI using Fisher's exact test. In the subset of survivors, we compared post-discharge outcomes including rates of home oxygen use, supplemental tube feeds, and need for pulmonary hypertension medications. Differences in the hospital length of stay amongst survivors based on prenatal prognostic categories were detected using a Kruskal-Wallis Test.

Congruency in the prognostic categories between the two prenatal imaging modalities was compared using kappa measure for agreement. Kappa measure was also used to evaluate congruency between the prenatal image-based prognostic category and the postnatal CDHSG mortality risk category for the 34 patients that had a valid CDHSG risk score. We used ordinal logistic regression to predict the postnatal CDHSG mortality risk category using o/e LHR and o/e TFLV as predictors in separate regression models.

Logistic regression was used to predict outcomes including ECMO utilization, type of defect (A/B vs C/D), surgical repair, and survival using o/e LHR and o/e TFLV values as predictors in separate regression models. The deterministic power for o/e LHR in predicting each binary outcome was compared to that of o/e TFLV by comparing the Receiver Operating Characteristic (ROC) curves and the area under the ROC curve (AUC) according to the method suggested by Hanley and McNeil [17].

In post-hoc analysis, the same statistical analyses as described above were applied utilizing LHR data derived by the trace method.

Table 1
Prognostic category based on o/e LHR and liver position [6] and o/e TFLV [8]

Prognostic Category	o/e LHR (%)	Liver position	o/e TFLV (%)
Severe	15–25	Up or down	<25
Moderate	26–35	Up or down	25–35
	36–45	Up	
Mild	36–45	Down	>35
	>45	Up or down	

o/e LHR: observed-to-expected lung-to-head ratio.
o/e TFLV: observed-to-expected total fetal lung volume.

2. Results

2.1. Baseline patient characteristics

During the study period, there were 105 cases of prenatally diagnosed CDH. We excluded those with missing prenatal data (n = 24), right-sided CDH (n = 9), chromosomal abnormalities (n = 7), major cardiac anomalies (n = 6), twin gestation (n = 6), history of delivery at a different institution (n = 5), other major comorbid conditions (n = 3), errors in diagnosis (n = 2), or US and MRI with greater than 1 week interval (n = 1). Forty-two patients met criteria: singleton pregnancy with a prenatal diagnosis of a left-sided CDH without chromosomal or major cardiac anomalies and having had a prenatal U/S and fetal MRI within 1 week of each other with lung volumetric analysis. Patient characteristics are summarized in Table 2.

2.2. Prenatal Imaging and classification

Comparison prenatal U/S and fetal MRI were performed on the same day in 40/42 patients (95.2%) at a median gestational age of 30.5 weeks (22–36) and 30.6 weeks (22–36), respectively. Median o/e LHR and o/e TFLV values and ranges are presented in Table 2. The distribution of o/e LHR and o/e TFLV values in each prognostic category are depicted in Fig. 1, with open markers identifying the cases that were discordant in each group. The vast majority of patients (80.9%) on prenatal U/S fell into the mild (45.2%) and moderate (35.7%) prognostic categories based on their o/e LHR and liver position. With fetal MRI, 81.0% of patients were split almost evenly (38.1% and 42.9%) between the mild and severe prognostic categories. There were 17 cases of discordant classification between prenatal U/S and fetal MRI for a 40.5% discordance rate (Kappa score agreement = 59.52%; $\kappa = 0.403 \pm 0.1003$; $p < 0.01$). In the majority of these discordant cases (13/17 or 76.4%), o/e TFLV designated a worse prognostic category than o/e LHR.

2.3. Prognostic categories and clinical outcomes

Overall survival in the entire cohort was 57.1% (24/42). ECMO was utilized in 38.1% (16/42) and 78.9% (33/42) underwent surgical repair of the CDH. In those that survived, median hospital length of stay was 24.5 days (12–149), and upon discharge, 25.0% (6/24) were on supplemental oxygen, 70.8% (17/24) necessitated supplemental feeds (either

Table 2
Patient characteristics.

N = 42 unless otherwise specified	Mean ± SEM / Median (range) / Percentage
Demographics	
- Maternal age at delivery (years)	30.1 (18.4–44.3)
- Maternal race/ethnicity	
- White/Caucasian	74.0
- Black/African-American	12.0
- Other	5.0
- Unknown	9.5
- Fetal gender (% male)	47.6
- Birthweight (kilograms) (n = 41)	3.1 ± 0.08
- GA at delivery (weeks)	38.7 (29.0–41.3)
Prenatal imaging	
- GA at U/S (weeks)	30.5 (22–36)
- o/e LHR (%)	41.5 (15.0–93.0)
- GA at fetal MRI (weeks)	30.6 (22–36)
- o/e TFLV (%)	31 .8 (6.9–59.9)
CDH characteristics	
- Liver up (%)	54.8
- Type A or B (%) (n = 33)	60.6
- Type C or D (%) (n = 33)	39.4

SEM: standard error of the mean.
GA: gestational age.
U/S: ultrasound.
o/e LHR: observed-to-expected lung-to-head ratio.
MRI: magnetic resonance imaging.
o/e TFLV: observed-to-expected total fetal lung volume.
CDH: congenital diaphragmatic hernia.

by nasogastric, nasojejunal, or gastrostomy access), and 33.3% (8/24) continued on medications for pulmonary hypertension.

In comparison analysis of each outcome based on the image-based prognostic category for the entire cohort of 42 patients, there was a significant difference in survival rates by both U/S-based classification and MRI-based classification (Table 3). Rates of ECMO utilization, surgical repair of the CDH, and frequency of defect type (A/B vs C/D) were also significantly different by MRI classification, but not by U/S classification. When assessing congruency between the prenatal image-based prognostic category and the postnatal CDHSG mortality risk category, there was more agreement between the fetal MRI and the CDHSG mortality risk category (Kappa score agreement = 44.12%; p = 0.03) than between prenatal U/S and the CDHSG mortality risk category (Kappa score agreement = 29.41%; p = 0.57).

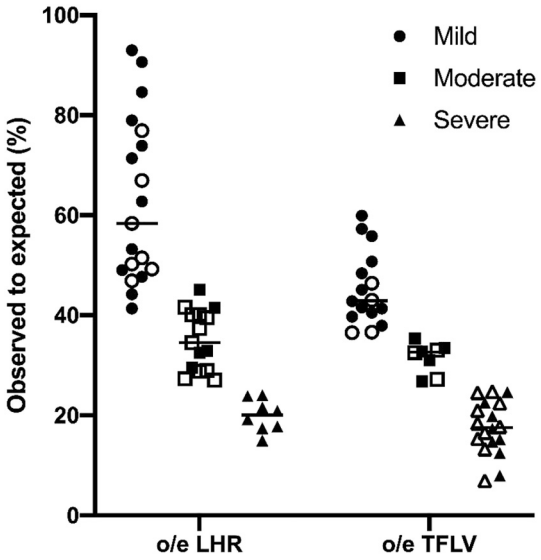

Fig. 1. Graph depicts distribution of o/e LHR and o/e TFLV values in each prognostic category. Solid markers represent concordant cases, open markers represent discordant cases. o/e LHR: observed-to-expected lung-to-head ratio; o/e TFLV: observed-to-expected total fetal lung volume.

Next we performed a subset analysis of survivors only (n = 24), comparing discharge-related outcomes such as hospital length of stay and post-discharge needs by each image-based prognostic category (Table 3). Length of stay was statistically significantly different by prognostic category for both U/S and MRI. As well, need for home oxygen and pulmonary hypertension medications were significantly different by prognostic category for both U/S and MRI; need for supplemental feeds was significantly different by U/S but not by MRI.

On regression analysis, both o/e LHR and o/e TFLV were significant predictors of ECMO utilization, surgical repair, type of defect, and survival (Table 4). The effect of a change in o/e TFLV was greater than the effect of a change in o/e LHR.

ROC curves were created to compare the discriminatory power of each prenatal imaging modality for each binary outcome. O/e TFLV was more discriminatory than o/e LHR in two outcomes: 1) distinguishing survivors from non-survivors (AUC = 0.9213 vs 0.7662; p = 0.04), and 2) identifying defect type A/B from C/D (AUC = 0.9115 vs 0.7346; p = 0.03) (Fig. 2). There was no significant difference in the ROC curves between o/e LHR and o/e TFLV to discriminate ECMO utilization or surgical repair.

The 17 cases in which prenatal image-based prognoses differed between prenatal ultrasound and fetal MRI were reviewed separately and listed with clinical outcomes in Table 5. The sample size was too small for statistical analysis, but outcomes overall appear more consistent with the fetal MRI-based prognostic category than the prenatal U/S-based prognostic category. For example, in the 4 cases designated "Mild" by U/S criteria and "Severe" by MRI criteria, 100% of those offered ECMO (n = 2) utilized ECMO, there were no type A/B defects in the 2 that underwent repair (the 2 other patients transitioned to comfort care and expired within hours of delivery), and there were no survivors. There were five patients in whom the CDHSG mortality risk score could not be calculated: in one case the echocardiogram report was unavailable for review, and in the remaining four, the patients expired within hours of birth prior to obtaining an echocardiogram.

2.4. Post-hoc analysis LHR calculated with the trace method

In post-hoc analysis, when the trace method was utilized to calculate LHR, over half of cases were assigned to the mild category (25/42 or 59.5%), with 12/42 (28.6%) assigned to moderate, and 5/42 (11.9%) assigned to severe (Supplemental Table 1). There were 20 cases of discordant classification between prenatal U/S (trace method) and fetal MRI for a 66.8% discordance rate (Kappa score agreement = 33.2%; $\kappa = 0.287 \pm 0.0945$; $p < 0.01$). In 18/20 (90%) of these discordant cases, the o/e TFLV designated a worse prenatal prognostic category than the o/e LHR. In comparison analysis of outcomes by Fisher's exact test, survival rates were significantly different per prognostic category using the trace method as they were with the longest-diameter method (Supplemental Table 2). In addition, rates of surgical repair were also significantly different per prognostic category with the trace method, which was not the case with the longest-diameter method. Amongst survivors, hospital length of stay, need for home oxygen, and pulmonary hypertension medications at discharge were significantly different per prognostic category with the trace method.

With regards to congruency between prenatal image-based prognostic category and the postnatal CDHSG mortality risk category, prenatal ultrasound (trace) was poorly congruent (Kappa score agreement: 21.5%, p = 0.36). On regression analysis, o/e LHR (trace) was a significant predictor of surgical repair and survival (Supplemental Table 3). There was no significant difference in the ROC curves between o/e TFLV and o/e LHR (trace) to discriminate survivors (AUC = 0.9213 vs 0.8102; p = 0.11), surgical repair (AUC = 0.8586 vs 0.8081; p = 0.6), or ECMO utilization (AUC = 0.7572 vs 0.6322; p = 0.12). O/e TFLV

Table 3
Outcome rates by prenatal U/S-based and fetal MRI-based prognostic categories. Percentages are out of the total number of patients in each prognostic category.

		U/S-based Prognostic Category			p Value[a]	MRI-based Prognostic Category			p Value[a]
		Mild (n = 19)	Moderate (n = 15)	Severe (n = 8)		Mild (n = 16)	Moderate (n = 8)	Severe (n = 18)	
CDHSG mortality risk category[b] (%)	Low	5.9	16.7	0	0.73	6.7	12.5	9.1	0.60
	Intermediate	70.6	50.0	60.0		66.7	75.0	45.5	
	High	23.5	33.3	40.0		26.7	12.5	45.5	
ECMO (%)		26.3	40.0	62.5	0.21	12.5	25.0	66.7	**0.003**
Repair (%)		89.5	80.0	50.0	0.09	93.8	100.0	55.6	**0.009**
Defect type A/B (%)[c]		76.5	50.0	25.0	0.09	93.3	62.5	10.0	< **0.001**
Survival (%)		73.7	60.0	12.5	**0.02**	93.8	75.0	16.7	< **0.001**
Survivor discharge data (n = 24)		n = 14	n = 9	n = 1		n = 15	n = 6	n = 3	
Length of stay (days) [d]		21 (12–60)	42 (19–139)	149	**0.03**[e]	24 (12–60)	31.5 (12–74)	139 (90–149)	**0.02**[e]
Home O_2 (%)		7.1	44.4	100.0	**0.03**	6.7	33.3	100.0	**0.003**
Supplemental feeds (%)		50.0	100.0	100.0	**0.03**	60.0	83.3	100.0	0.28
Pulmonary HTN meds (%)		14.3	55.6	100.0	**0.04**	13.3	50.0	100.0	**0.009**

U/S: ultrasound.
MRI: magnetic resonance imaging.
CDHSG: Congenital Diaphragmatic Hernia Study Group.
ECMO: extracorporeal membrane oxygenation.
O2: oxygen.
HTN: hypertension.
[a] Fisher's exact test unless otherwise specified.
[b] Total n = 34. Eight patients were excluded because CDHSG score could not be calculated due to incomplete data. Percentages are based on the number of patients in each image-based prognostic category with a CDHSG score (for U/S: Mild = 17, Moderate = 12, Severe = 5; for MRI: Mild = 15, Moderate = 8, Severe = 11).
[c] Total n = 33. Nine patients were excluded for not having undergone surgical repair. Percentages are based on the number of patients in each image-based prognostic category that underwent repair (for U/S: Mild = 17, Moderate = 12, Severe = 4; for MRI: Mild = 15, Moderate = 8, Severe = 10).
[d] Median and range.
[e] Kruskal Wallis test.

was more discriminatory than o/e LHR (trace) in identifying type A/B defects from type C/D defects (AUC = 0.9115 vs 0.6654; p = 0.006).

3. Discussion

In this study we sought to describe the frequency of discordance between prenatal U/S and fetal MRI prognostic categories and determine which imaging modality is more reliably predictive of outcomes. Amongst singleton pregnancies with a prenatally diagnosed isolated left CDH, 40% of cases had differing prognostic categories, and in over 75% of these cases, the o/e TFLV value assigned a more severe prognostic category than the o/e LHR. When each of the image-based prognoses were compared to specific outcomes, o/e TFLV better discriminated for survival and for smaller defect type, and was more congruent with the CDHSG clinical prediction model.

Though more congruent than the U/S-based prognosis, the MRI-based prognosis was congruent with the CDHGSG mortality risk category less than half of the time. The two prognosis categories, though related, are not equal comparisons – the MRI-based measure prognosticates severity of pulmonary hypoplasia based solely on anatomy, whereas the CDSHG clinical tool calculates mortality risk based on evidence-based predictors of mortality. This study cohort specifically excluded those with major cardiac anomalies and chromosomal anomalies, each of which independently confers morbidity and mortality risk [15,18], and are significant contributors to the CDHSG clinical tool equation. A larger more diverse study cohort may yield different results. Petroze et al. [19] in a recent report did not identify any correlation between U/S- and MRI-based imaging parameters and the CDHSG clinical prediction tool. Optimal care of the CDH patient likely will requires synthesizing information obtained from both standardized prenatal imaging and neonatal clinical prediction tools (such as the CDHSG equation and others that incorporate real-time physiologic data) to guide clinical practice.

Fetal lung volume is currently the best surrogate measure we have for quantifying and predicting the degree of pulmonary hypoplasia, a major contributor to morbidity and mortality in CDH. There is no accepted gold standard for the assessment and measurement of fetal lung volumes. Both prenatal ultrasound and fetal MRI are used in varying capacities at different institutions to drive potential candidacy for prenatal interventions [e.g. fetoscopic endoluminal tracheal occlusion (FETO)], choosing a hospital for delivery (e.g. ECMO capability, operative options, and palliative care resources), as well as establishing potential postnatal intervention plans. Accurate prognostic information is also critical for counseling potential parents with regards to outcomes and expectations.

Prenatal ultrasound and measurement of the LHR have been the mainstay of evaluating and monitoring prenatally diagnosed CDH for decades [20]. The modifications of calculating the o/e LHR to counteract the variable growth in lung and head measurements throughout gestation, as well as utilization of the more precise trace method to measure the lung area have improved upon the originally described technique [21,22]. However, the counterpoint to ultrasound's accessibility is interrater variability, and this was demonstrated even amongst North American Fetal Therapy Network (NAFTNet) centers in a recent study [23]. Though some have hypothesized that three-dimensional MRI would be a more accurate volumetric assessment compared to two-dimensional ultrasound, evidence has thus far been conflicting on whether it is clinically superior in predicting outcomes [8,24–27].

Table 4
Logistical regression analyses predicting outcomes based on o/e LHR and o/e TFLV values.

	o/e LHR			o/e TFLV		
	OR	95% CI	p value	OR	95% CI	p value
CDHSG Mortality Risk Category	1.001	0.968–1.037	0.933	0.988	0.936–1.042	0.651
ECMO	0.962	0.926–0.999	**0.047**	0.924	0.870–0.981	**0.01**
Repair	1.059	1.001–1.120	**0.047**	1.158	1.040–1.290	**0.008**
Defect Type (A/B)	1.061	1.006–1.119	**0.006**	1.226	1.074–1.400	**0.001**
Survival	1.058	1.013–1.105	**0.011**	1.220	1.090–1.364	**0.001**

o/e LHR: observed-to-expected lung-to-head ratio.
o/e TFLV: observed-to-expected total fetal lung volume.
CDHSG: Congenital Diaphragmatic Hernia Study Group.
ECMO: extracorporeal membrane oxygenation.

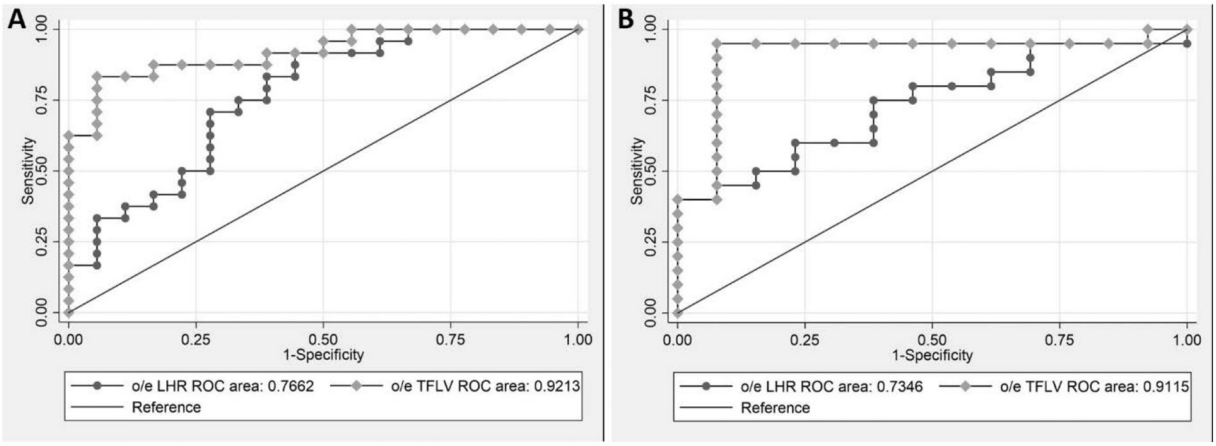

Fig. 2. Receiver operating characteristic (ROC) curves comparing the discriminatory power of o/e LHR versus o/e TFLV for (A) survival and (B) defect size A/B. In both of these examples, o/e TFLV depicts greater area under the curve (AUC) compared to o/e LHR, but more robust statistical analysis will require a larger sample size. o/e LHR: observed-to-expected lung-to-head ratio; o/e TFLV: observed-to-expected total fetal lung volume.

Several groups are also evaluating the clinical utility of applying MRI's ability to characterize the chemical and structural composition of tissue as another measure of lung development and pulmonary hypoplasia. Adding fetal MRI lung signal intensity to the repertoire of prenatal data may be the next step forward in improving our ability to predict outcomes in CDH.

Forty percent of our patients had discordant prognoses based on their prenatal ultrasound and fetal MRI images. Two factors may have contributed to this high discordance rate. We compare data obtained from the prenatal ultrasound that occurred within a week of the fetal MRI (performed between 22 and 36 weeks). Our standard practice evolved throughout the study period such that although the current recommendation is to obtain the fetal MRI between 24 and 28 weeks' gestation, earlier patients had the study performed later. Though LHRs are considered more reliable earlier in gestation [28], and most patients had multiple ultrasounds, re-reviewing earlier ultrasound studies was impractical and would have introduced selection bias to the analysis. We mitigated the effect of gestational age by utilizing the o/e LHR [21]. Secondly, these patients' families were counseled based on LHRs calculated using the longest diameter method. Though our institution has since changed to measure and rely on the trace method, the majority of these cases had their ultrasounds performed before and during the transition. Peralta et al. reported that the trace method was the most reproducible, and that the longest diameter method overestimated lung area by ~45% compared to the trace method [22]. As well, in a recent systematic review in which o/e TFLV was slightly better predictive of survival compared to o/e LHR, this difference disappeared when o/e LHR was calculated with the trace method [8]. We performed post-hoc analysis re-reviewing each U/S to obtain a trace-based LHR to ensure that the U/S technique was not a major contributor to the discordance between U/S and MRI, and also the inferior correlation with clinical outcomes. Interestingly, we found a higher frequency of discordance comparing trace-based prenatal U/S prognosis and fetal MRI prognosis. And in comparison of their correlation with clinical outcomes, trace-based U/S prognosis was not more reliably predictive of outcomes.

Table 5
Discordant cases between prenatal U/S and fetal MRI prognostic categories and outcomes.

Prenatal U/S-based Prognostic Category	Fetal MRI-based prognostic category	Total (n = 17)	CDHSG mortality risk category	ECMO (%)	Defect type A or B (%)	survival (%)
Mild	Moderate	3	3 interm	33.3 (1/3)	66.7 (2/3)	66.7 (2/3)
Mild	Severe	**4**	1 interm 1 high 2 n/a[a]	50.0 (2/4)[b]	0 (0/4)[b]	0 (0/4)
Moderate	Mild	**4**	2 interm 1 high 1 n/a[a]	0 (0/4)[c]	75.0 (3/4)[c]	75.0 (3/4)
Moderate	Severe	**6**	1 low 1 interm 2 high 2 n/a[a]	83.3 (5/6)[d]	0 (0/6)[d]	33.3 (2/6)

U/S: ultrasound
MRI: magnetic resonance imaging
CDHSG: Congenital Diaphragmatic Hernia Study Group
ECMO: extracorporeal membrane oxygenation
O2: oxygen
HTN: hypertension
[a] CDHSG score unable to be calculated due to incomplete data
[b] Two patients were not offered ECMO for failing to meet physiologic criteria, transitioned to comfort care, and expired prior to surgical repair.
[c] One patient was not offered ECMO for birthweight < 1500 grams, transitioned to comfort care, and expired prior to surgical repair.
[d] One patient was not offered ECMO for failing to meet physiologic criteria, transitioned to comfort care, and expired prior to surgical repair. 1 other patient had a cardiac arrest at the time of ECMO cannulation, was subsequently transitioned to comfort care, and expired prior to surgical repair.

A few studies have theorized possible contributing factors as to why ultrasound and MRI may be discordant. Prenatal ultrasound only measures the unaffected contralateral lung, whereas fetal MRI measures total lung volumes including both the affected ipsilateral and unaffected contralateral lung. In cases of severe CDH, the contribution of the affected ipsilateral lung may be quite small, but one study attributed inconsistencies between the 2 imaging modalities in the assessment of total lung volumes to the proportion of ipsilateral lung volume seen on MRI [24]. The same study demonstrated that LHR routinely underestimates *actual* lung volume because herniated viscera cause lateral compression of the contralateral lung. According to this explanation, however, fetal MRI should give a larger lung volumes and a greater o/e TFLV compared to the LHR and o/e LHR which is not consistent with our data. We found that in the majority of discordant cases, o/e TFLV demonstrated smaller volumes and thus poorer prognosis. Another particular limitation to ultrasound is its ability to differentiate between lung and liver. The echogenicity of the two structures can appear similar, thus, even if its presence or absence in the thoracic cavity can be determined, the extent of herniation may be difficult to assess [29]. Thus in cases of left-sided CDH, the reliability with which the unaffected-yet-compressed right lung (versus liver) can be accurately distinguished and measured may lead to overestimation of lung volumes.

Limitations to this current study include the retrospective approach, a limited sample size of a particularly severe cohort of CDH likely reflective of being a referral center, as well as the post-hoc nature of the trace-

based analysis, with the original ultrasounds not having been read by a single dedicated MFM. Assessment of congruency between the image-based prognosis categories and the validated CDHSG mortality risk score was also limited by the small sample size, as we also excluded patients with cardiac anomalies and chromosomal anomalies, both factors that additionally confer mortality risk points to the score. Further, we did not have the statistical power to evaluate which prenatal imaging modality was more reliable specifically in the discordant cases. A multi-institutional survey is in the planning stages to assess current practices amongst NAFTNet centers for the prenatal evaluation of CDH with the hopes of establishing future investigation of prenatal ultrasound and fetal MRI concordance amongst all North American fetal centers.

4. Conclusion

Accurately assessing prognosis is critical to prenatal counseling of families with fetuses diagnosed with CDH. We found 40% of patients who underwent both prenatal U/S and fetal MRI demonstrated discordant prognoses. Clinical outcomes demonstrate fetal MRI and specifically o/e TFLV may more accurately predict severity of pulmonary hypoplasia with regards to survival and defect type compared to prenatal ultrasound and o/e LHR. Our analysis suggests fetal MRI-based volumetric analysis is a valuable adjunct in the prenatal evaluation and counseling of CDH.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jpedsurg.2019.11.007.

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Declarations of interest

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