

[09-090]

Does fetal position affect right lung measurements in left congenital diaphragmatic hernia?

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OBJECTIVE: To assess agreement of right trace lung areas obtained with the fetal spine at the 6:00 and at the 3:00 or 9:00 (3:00|9:00) positions in cases of left congenital diaphragmatic hernia.

METHODS:

Interim method-agreement analysis was performed with the trace lung area (mm^2) obtained with the spine at the 6:00 and 3:00|9:00 positions. Additional endpoints include lung-to-head-ratio (LHR) and observed/expected LHR calculated in each position. For each endpoint we calculated the mean paired difference (Bland-Altman bias), SD and SE of differences, a 90% confidence interval for the mean difference, 95% limits of agreement (LoA) with confidence intervals.

RESULTS:

Nine fetuses contributed paired observations. Agreement between 6:00 and 3:00|9:00 methods was close for each endpoint, with 6:00 values lower on average. Mean paired differences (6:00 – 3:00|9:00) were: lung area -5.81 mm^2 (90% CI, -18.83 to 7.21; 95% LoA, -46.98 to 35.35); LHR -0.020 (90% CI -0.084 to 0.044 ; LoA -0.221 to 0.181); O/E LHR -1.41pp (90% CI -4.20 to 1.38 ; LoA -16.41 to 7.42). No systematic bias was statistically detectable.

CONCLUSIONS: Initial results suggest little difference between lung area measurements obtained at 6:00 and 3:00|9:00; however, prospective definition of equivalence margins and a larger sample are required before equivalence testing.

[09-091]

The best formula to diagnose fetal growth restriction in fetuses with congenital diaphragmatic hernia

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Objectives: to assess the performance of three ultrasound-based estimated fetal weight (EFW) formulas in predicting small-for-gestational-age (SGA) neonates

Methods: Retrospective review of patients with CDH between 2014 and 2024. We excluded fetuses with major associated anomalies. Receiver operating characteristic (ROC) curve analyses were performed using EFW percentile scores at the last available third trimester ultrasound, derived from three formulas (Hadlock, Hornarvar, and Siemer), with birth weight SGA as outcome. For each formula, the area under the curve (AUC), optimal cut point, sensitivity, and specificity were calculated.

Results: 415 CDH were included. 35/415 (8.3%) were SGA. ROC analysis demonstrated the highest discriminatory performance for the Hadlock formula, with an AUC of 0.92 and an optimal percentile cutpoint of 4.7, yielding a sensitivity of 0.71 and specificity of 0.96.

Conclusions: Among the ultrasound-based EFW formulas evaluated, the Hadlock formula demonstrated the best performance for prediction of SGA, with excellent discrimination and high specificity. While the Hornarvar formula showed high sensitivity, its low specificity limits clinical utility. The Siemer formula showed intermediate performance. These findings suggest that Hadlock formula can be used for CDH and the optimal cut off for EFW to identify those who are actually SGA at birth is 10%

[09-092]

Cerebroplacental ratio to evaluate brain sparing in fetuses with severe congenital diaphragmatic hernia

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Objective: Evaluate cerebroplacental ratio (CPR) in fetuses with mild/moderate versus severe CDH.

Methods: Retrospective study of fetuses with CDH seen 2013-2024. For fetuses > 20 weeks, middle cerebral artery and umbilical artery pulsatility index (MCA-PI and UA-PI) were obtained at initial visit and CPR calculated. Observed/expected lung-to-head-ratio (O/E LHR) was measured and pregnancies divided into mild/moderate versus severe groups. Dopplers compared to reference values and then compared between groups. Pregnancy characteristics and outcomes compiled, and multivariable logistic regression conducted. **Results:** Of 406 patients, 350 (86.2%) had adequate MCA-PI, UA-PI and O/E LHR measurements after 20 weeks. Of this group, 284 (81.1%) had mild/moderate and 66 (18.9%) had severe CDH. Fetuses with severe CDH had lower MCA-PI, higher UA-PI and lower CPR z scores versus fetuses with mild/moderate CDH. 13 (19.7%) fetuses with severe CDH versus 20 (7%) with mild/moderate CDH had a CPR less than the 5th percentile. Multivariable logistic regression revealed that severe CDH and FGR were independent risk factors for low CPR while CDH side was not.

Conclusion: Although MCA-PI, UA-PI and CPR are not markedly different in fetuses with CDH versus population means, severity of CDH has an impact suggesting a subtle “brain-sparing” effect with severe disease.

[09-093]

Prenatal imaging characteristics and outcomes of left versus right-sided congenital diaphragmatic hernia

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Objectives: To compare prenatal imaging characteristics and neonatal outcomes between left- and right-sided congenital diaphragmatic hernia (CDH).

Methods: Retrospective study of fetuses diagnosed with CDH between 2012 and 2025. Cases undergoing fetoscopic tracheal occlusion and ventral CDH cases were excluded. Prenatal ultrasound and MRI as well as neonatal outcomes were compared by CDH laterality.

Results: Among 286 cases, 234 (81.8%) were left-sided and 52 (18.2%) right-sided. Right-sided CDH demonstrated significantly greater liver herniation at both evaluations (initial: 39.0% vs 19.9%, $p < 0.001$; second: 38.9% vs 19.2%, $p < 0.001$). Despite this difference, MRI-derived lung volumes were similar between groups (initial o/e TFLV: 35.5% vs 33.7%, $p = 0.53$; second o/e TFLV: 33.4% vs 32.2%, $p = 0.75$). Ultrasound-derived o/e LHR was higher in right-sided CDH, and interval change in o/e LHR differed significantly (+22.5 vs -1.0, $p = 0.002$). Neonatal outcomes were similar but with higher rates of pulmonary hypertension (93.3% vs 81.0%, $p = 0.10$). Survival did not differ significantly between groups (61.1% vs 71.7%, $p = 0.21$).

Conclusions: Right-sided CDH is associated with greater liver herniation but similar MRI-derived lung volumes. Differences in longitudinal o/e LHR trends suggest ultrasound measurements may behave differently depending on defect laterality. Neonatal outcomes did not differ between the two groups.

[09-094]

Isolated versus non-isolated congenital diaphragmatic hernia: does it matter?

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Objectives: To compare prenatal characteristics, genetic evaluation, and neonatal outcomes between isolated and non-isolated congenital diaphragmatic hernia (CDH).

Methods: Retrospective study of fetuses diagnosed with CDH 2012 and 2025. Cases were classified as isolated or non-isolated CDH based on the prenatal or postnatal presence of additional structural anomalies or molecular finding. Fetuses undergoing fetal endoscopic tracheal occlusion (FETO) were excluded.

Results: A total of 293 fetuses were included; 176 (60%) had non-isolated CDH and 117 (40%) isolated CDH. Baseline demographics were similar between groups. Non-isolated cases were more likely to undergo genetic counseling and testing ($p < 0.05$). Initial observed-to-expected lung-to-head ratio (o/e LHR) was lower in non-isolated cases (35.9 ± 15.7 vs 44.2 ± 18.6 , $p = 0.014$). Distribution of CDH defect type differed significantly ($p = 0.003$), with type C defects more common in non-isolated CDH. Neonatal outcomes were similar. Pulmonary hypertension was common in both groups, with a trend toward higher prevalence in non-isolated CDH (86.1% vs 77.8%, $p = 0.16$), and survival rates were comparable (68.7% vs 69.3%, $p = 0.92$).

Conclusions: Non-isolated CDH is associated with lower prenatal lung measurements and increased genetic evaluation, but neonatal outcomes including survival and ECMO use were similar.

[09-095]**Non-isolated congenital diaphragmatic hernia: outcomes in genetic versus structural causes**

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Objectives: To examine imaging and outcomes in cases of non-isolated congenital diaphragmatic hernia (CDH) in subgroups according to structural, genetic, or structural+genetic comorbidity.

Methods: Retrospective study of fetuses with non-isolated CDH between 2012 and 2025. Cases were categorized as structural, genetic, or structural+genetic. Prenatal imaging findings and neonatal outcomes were compared across groups.

Results: A total of 210 non-isolated CDH cases were included: 101 (48.1%) structural, 31 (14.8%) genetic, and 78 (37.1%) structural+genetic. The structural+genetic group was evaluated at an earlier gestational age (median [IQR]: 26.0 [23.1, 29.1] vs 28.4 [25.1, 33.4] vs 26.8 [23.6, 29.1], $p = 0.031$). Initial observed-to-expected lung-to-head ratio (o/e LHR) was lowest in structural+genetic group (median [IQR]: 28.0 [21.0–30.2] vs 33.5 [27.0–45.5] vs 37.5 [26.0–46.0], $p = 0.049$). Postnatal defect size was largest in the structural+genetic group (median [IQR]: 85.0 [75.0–90.0] vs 70.0 [50.0–87.0] vs 55.0 [20.0–80.0], $p = 0.019$). Despite these differences, ECMO utilization, pulmonary hypertension, and survival were similar across groups.

Conclusions: Non-isolated CDH cases demonstrate substantial heterogeneity, highlighting the importance of genetic testing and counseling along with prenatal imaging. Cases with structural+genetic findings show lower o/e LHR but similar short-term neonatal outcomes compared with other non-isolated subgroups.

[09-096]

Observed-to-Expected Lung-to-Head Ratio and Outcomes of Isolated Right-Sided Congenital Diaphragmatic Hernia: A Japanese Multicenter Study

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Objectives: To evaluate outcomes of isolated right-sided congenital diaphragmatic hernia (CDH) in Japan and the prognostic value of observed-to-expected lung-to-head ratio (o/e LHR). **Methods:** This multicenter study analyzed the Japanese CDH Study Group registry (15 tertiary centers; 2006–2023). We included singleton pregnancies with prenatally diagnosed isolated right-sided CDH and o/e LHR recorded before 29+6 weeks' gestation. The primary outcome was survival to discharge. Secondary outcomes included ECMO use, patch repair, initial hospitalization duration, 6-month survival, and oxygen-independent survival at 6 months. Following European multicenter studies, cases were divided into two groups (o/e LHR $\leq$ 45% vs. $>$ 45%). Outcomes were compared between these groups using non-parametric tests. **Results:** Among 32 cases, survival to discharge was 8/15 (53.3%) in the $\leq$ 45% group vs. 14/17 (82.4%) in the $>$ 45% group ($p=0.128$). For survivors, hospitalization duration was significantly longer in the $\leq$ 45% group (median 126.5 [IQR 96–182] vs. 72.0 [45–112] days; $p=0.048$). Other secondary outcomes did not differ significantly between groups. **Conclusions:** In this cohort, although survival to discharge did not significantly differ between groups, o/e LHR $\leq$ 45% was associated with significantly longer initial hospitalization. o/e LHR could serve as a valuable indicator for predicting the intensity of postnatal medical intervention in survivors of right-sided CDH.

[09-097]**Natural history of moderate and severe left-sided congenital diaphragmatic hernia: A contemporary multicenter Japanese cohort aligned with TOTAL-trial methodology**

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Objectives:

To describe survival patterns, particularly across baseline observed-to-expected lung-to-head ratio (o/e LHR), in expectantly managed moderate and severe isolated left-sided congenital diaphragmatic hernia (CDH) in Japan, using a framework aligned with the TOTAL trials.

Methods:

We conducted a retrospective multicenter cohort study using the Japanese CDH Study Group registry (15 tertiary centers; 2006–2023). Eligible cases were singleton pregnancies with prenatally diagnosed, isolated left-sided CDH classified as moderate or severe according to TOTAL definitions and managed without fetal intervention. The primary outcome was survival to discharge. Outcomes were summarized descriptively and contextualized against published aggregate results from the TOTAL trials; no inferential comparisons were performed. Exploratory logistic regression with restricted cubic splines was used to visualize survival patterns across baseline o/e LHR.

Results:

A total of 125 cases were included (93 moderate, 32 severe). Survival to discharge occurred in 88 of 124 evaluable cases (71%), including 76% of moderate and 56% of severe cases. Exploratory modeling demonstrated graded increases in survival probability across baseline o/e LHR, with lower survival in the presence of liver herniation.

Conclusions:

Survival patterns across baseline o/e LHR in this Japanese cohort were consistent with those reported in the TOTAL trials.

[09-098]

A Surgical Murine Model of Congenital Diaphragmatic Hernia

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Background: Congenital diaphragmatic hernia (CDH) leads to severe pulmonary pathology, but the mechanism by which this occurs is not fully understood. Nitrofen models are confounded by teratogenicity, and other surgical models occur too late in gestation to evaluate developmental effects. We sought to develop a surgical murine model of CDH to evaluate the isolated effect of visceral herniation on pulmonary development.

Methods: Wild-type C57BL/6 dams underwent laparotomy with uterine exposure at E16.5 (term=19 days). Experimental fetuses underwent transthoracic diaphragm piercing with microsurgical technique. Littermates served as controls. The dams were euthanized at E18.5 and postmortem analysis was performed.

Results: 119 fetuses underwent surgical intervention with 42 serving as controls. In the experimental subjects, there was a 42% rate of intrauterine fetal demise (n=50) and a 19% rate of successful CDH creation (n=23). Experimental subjects that did not have a diaphragmatic defect served as shams. CDH mice had lower lung to body weight ratios (0.02) compared to sham (0.025, $p=0.02$) and control (0.026, $p<0.01$) groups, consistent with pulmonary hypoplasia.

Conclusion: A surgical murine model of CDH is feasible and allows for the study of pulmonary disease and the molecular mechanisms by which it occurs without the confounding teratogenic effects of nitrofen.

[09-099]

In Vivo Characterization of the Nitrofen Rat Model of CDH Using Ultra-High Frequency Ultrasound and Photoacoustic Tracking of Targeted RNA Nanoparticle Delivery

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We aimed to establish a platform for serial phenotyping and real-time tracking of lung-targeted therapeutics using the nitrofen rat model of CDH.

CDH was induced via maternal nitrofen gavage at GA 9.5. Pregnant dams underwent serial transabdominal imaging at GA16, GA18, and GA20 using ultra-high frequency ultrasound (VEVO F2 LAZR, 57 MHz). Individual fetuses were tracked longitudinally and correlated with post-harvest phenotypes at GA16, GA18, GA20, and postnatal day 1. Diaphragmatic defects were classified by size, and lung and diaphragm tissues will be analyzed using MALDI mass spectrometry and spatial transcriptomics (Stereo-seq). Photoacoustic imaging will be used to track Cy7-labeled therapeutics following intra-amniotic and fetal intrahepatic delivery.

UHFUS enabled detection of diaphragmatic defects and pulmonary hypoplasia as early as GA16, with reliable longitudinal tracking of individual fetuses through term. Imaging findings correlated with postnatal phenotypes, demonstrating ~50% incidence of diaphragmatic defects and ~90% pulmonary hypoplasia. Photoacoustic imaging will provide a framework to visualize in utero biodistribution of delivered nanoparticles and extracellular vesicles.

We established a longitudinal imaging and molecular profiling platform for this CDH model. This system enables real-time tracking of therapeutic delivery, including lung-targeted 4WJ RNA nanoparticles carrying miR-200b and AF-MSC EVs, and supports evaluation of in-utero rescue strategies.

[09-100]

AF-MSC EVs Restore Metabolic Function after Nitrofen Injury and Inform Development of Targeted miR-200b RNA Nanoparticles; A Potential for Optimization of Pulmonary Function in CDH

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Amniotic fluid mesenchymal stem cell-derived extracellular vesicles (AF-MSC EVs) have been shown to rescue aspects of the nitrofen induced congenital diaphragmatic hernia (CDH)-like phenotype in rodents, though the underlying cellular mechanisms and translatable therapeutic strategies remain unclear.

We assessed cellular metabolism using Seahorse extracellular flux analysis following nitrofen exposure, with or without treatment using amniotic fluid- and placental-derived MSC EVs. EV cargo was profiled via miRNA sequencing. A modular four-way junction (4WJ) RNA nanoparticle was engineered to deliver a miR-200b duplex, incorporating an EpCAM-targeting aptamer and chemical stabilization. Delivery was evaluated following intratracheal (IT) and intravenous (IV) administration in murine lung injury models.

Nitrofen exposure reduced mitochondrial respiration and glycolytic activity in vitro. Treatment with MSC EVs restored oxygen consumption rate and extracellular acidification rate toward baseline levels. miRNA sequencing identified enrichment of miR-200b in AF-MSC EVs, consistent with prior links to CDH rescue. A 4WJ RNA nanoparticle platform enabled lung delivery of miR-200b following both IT and IV administration in injured lungs.

Nitrofen-associated injury causes metabolic impairment reversed with MSC EV treatment. We translate this observation into a scalable 4WJ RNA nanoparticle platform for targeted delivery of miR-200b, providing a strategy to recapitulate EV-mediated therapeutic effects in CDH.

[09-119]

Diagnosis and Treatment Protocols for Congenital Lung Malformations in the Prenatal, Intrapartum, and Neonatal Periods

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Objective: To investigate prenatal diagnosis, integrated intrapartum management, and neonatal surgical indications and outcomes for congenital lung malformations (CLMs). **Methods:** Data from 24 neonates undergoing neonatal surgery at a single center (2019.01–2026.05) were retrospectively analyzed. All cases were prenatally diagnosed CLMs. Some received intrauterine interventions. All were transferred postnatally for treatment. **Results:** Of 24 cases (18 male, 6 female), prenatal diagnosis occurred mostly at 20–24 weeks. Pathological types were mainly congenital pulmonary airway malformation (14, 58.3%) and bronchopulmonary sequestration (7, 29.2%). Maximum prenatal CVR was 6.93. All had respiratory distress postnatally; 18 required respiratory support. Thoracoscopic surgery was performed in 17 (70.8%) and thoracotomy in 7 (29.2%), with a mean operative age of 8.9 days. Two postoperative deaths occurred: one due to giant sequestration with complex vascular malformations, the other to CPAM with bronchopulmonary dysplasia and persistent pulmonary hypertension. One small pneumothorax resolved conservatively. **Conclusions:** Serial CVR monitoring with hydrops assessment and intrauterine intervention planning reduces perinatal risks and avoids unwarranted termination. Neonatal surgical indications include tension pneumothorax from lesion rupture unresponsive to drainage, cardiopulmonary compression preventing respiratory weaning, and progressive mediastinal shift. Prioritizing thoracoscopic surgery improves outcomes.