CERPO
Centro de Referencia Perinatal Oriente
Facultad de Medicina, Universidad de Chile

Diagnóstico prenatal de hipoplasia pulmonar

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MAPA DE RUTA:

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DIAGNÓSTICO DE HIPOPLASIA PULMONAR

- Introducción
- Definición
- Embriología del desarrollo pulmonar fetal
- Fisiopatología
- Clasificación
- Ultrasonografía
- RM

Introducción

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- Alteración del desarrollo del parénquima pulmonar tanto como su vasculatura.
- Rara condición que afecta a 9-11/10.000 NV.
- Se asocia a elevada mortalidad perinatal: 71-95% de los casos.
- Gold Standard: Resonancia nuclear magnética, en casos de hernia diafragmática congénita.
- No se debe incluir la hipoplasia pulmonar, como hallazgo aislado, dentro de las anomalías congénitas de mal pronóstico vital, considerar el volumen pulmonar y la enfermedad de base.

Consenso de la rama de genética de la Sociedad Chilena de Pediatría sobre las anomalías congénitas del mal pronóstico vital. Rev. chil. pediatr. vol.87 no.5 Santiago oct. 2016.
Jourdan E. Triebwasser. Prenatal prediction of pulmonary hypoplasia. Seminars in Fetal & Neonatal Medicine (2017) 1-5, http://dx.doi.org/10.1016/j.siny.2017.03.001.

Definición

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- Desarrollo defectuoso pulmonar con disminución en el número de células
- Inicialmente diagnóstico histológico:
  - Tejido pulmonar con peso <40% del esperado, autopsia.
- Lung/Body weight index <0,015 (<28sem)+RAC <1DS

Embriología

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- Etapas del desarrollo pulmonar:
  - Embrionaria
  - Pseudoglandular
  - Canalicular
  - Sacular
  - Alveolar

Jourdan E. Triebwasser. Prenatal prediction of pulmonary hypoplasia. Seminars in Fetal & Neonatal Medicine (2017) 1-5, http://dx.doi.org/10.1016/j.siny.2017.03.001.

Fisiopatología

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- Poner alteraciones según etiología y etapa que se altera.
- Los movimientos respiratorios y la presión intraamniótica desempeñan un papel fundamental en el desarrollo pulmonar normal.

- Displasias esqueléticas: Compresión extrínseca torácica impide el adecuado desarrollo y expansión del parénquima pulmonar

Posibles complicaciones de hipoplasia pulmonar

- Broncospasmo
- Hemoptisis
- Infecciones respiratorias recurrentes
- Obstrucción de las vías respiratorias centrales
- Insuficiencia cardiaca
- Hipertensión pulmonar
- Edema pulmonar relacionado con la altitud

Clasificación

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- Primaria:
  - Unilateral
  - Bilateral
- Secundaria:
  - Ocupación cavidad torácica (más frecuente)
  - Oligohidroamnios
  - Caja torácica pequeña
  - Compromiso funcional (neuro-muscular)

Clasificación

- Subsegmentaria
- Segmentaria
- Lobar
- Pulmonar unilateral
- Pulmonar bilateral

A. Salcedo Posadas. Hipoplasia pulmonar: causa de errores diagnósticos. Acta Pediatr Esp. 2006; 64: 260-268.

Clasificación

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- Stocker: Congenital Pulmonary Airway Malformation (CPAM)
  - Tipo 0
  - Tipo 1
  - Tipo 2
  - Tipo 3
  - Tipo 4
- Carece de utilidad para seguimiento y determinar pronóstico.

Ultrasonografía

- Ecografía 2D
- Ecografía 3D
- Ecografía funcional

Estandarización de evaluación ultrasonográfica ERNICA

- Para hernia diafragmática congénita.
- Considera al O/E LHR como predictor independiente de sobrevida y morbilidad a corto plazo.
- Tiene como objetivo establecer una predicción de resultado perinatal individual.

Francesca María Russo. Proposal for standardized prenatal ultrasound assessment of the fetus with congenital diaphragmatic hernia by the European Reference Network on Rare Inherited and Congenital Anomalies (ERNICA). Prenatal Diagnosis. Volume38, Issue9, August 2018. Pages 629-637.

Ultrasonografía

- Tamaño pulmonar:
  - LHR: Inicialmente usado en el segundo trimestre tardío, siendo <1 de mal pronóstico. El pulmón crece más rápido que la circunferencia craneana. Curva de aprendizaje: 72-77 mediciones.

  - O/E LHR: Elimina el impacto de la edad gestacional en la evaluación. Herramienta prenatal para aconsejar a los padres del resultado de la gestación y para definir tratamiento. (TOTAL trial)

  - E LHR= −2.2481 + (0.2712 × EG) – (0.0033 × EG2)

  - https://totaltrial.eu/?id=6

Francesca María Russo. Proposal for standardized prenatal ultrasound assessment of the fetus with congenital diaphragmatic hernia by the European Reference Network on Rare Inherited and Congenital Anomalies (ERNICA). Prenatal Diagnosis. Volume38, Issue9, August 2018. Pages 629-637.

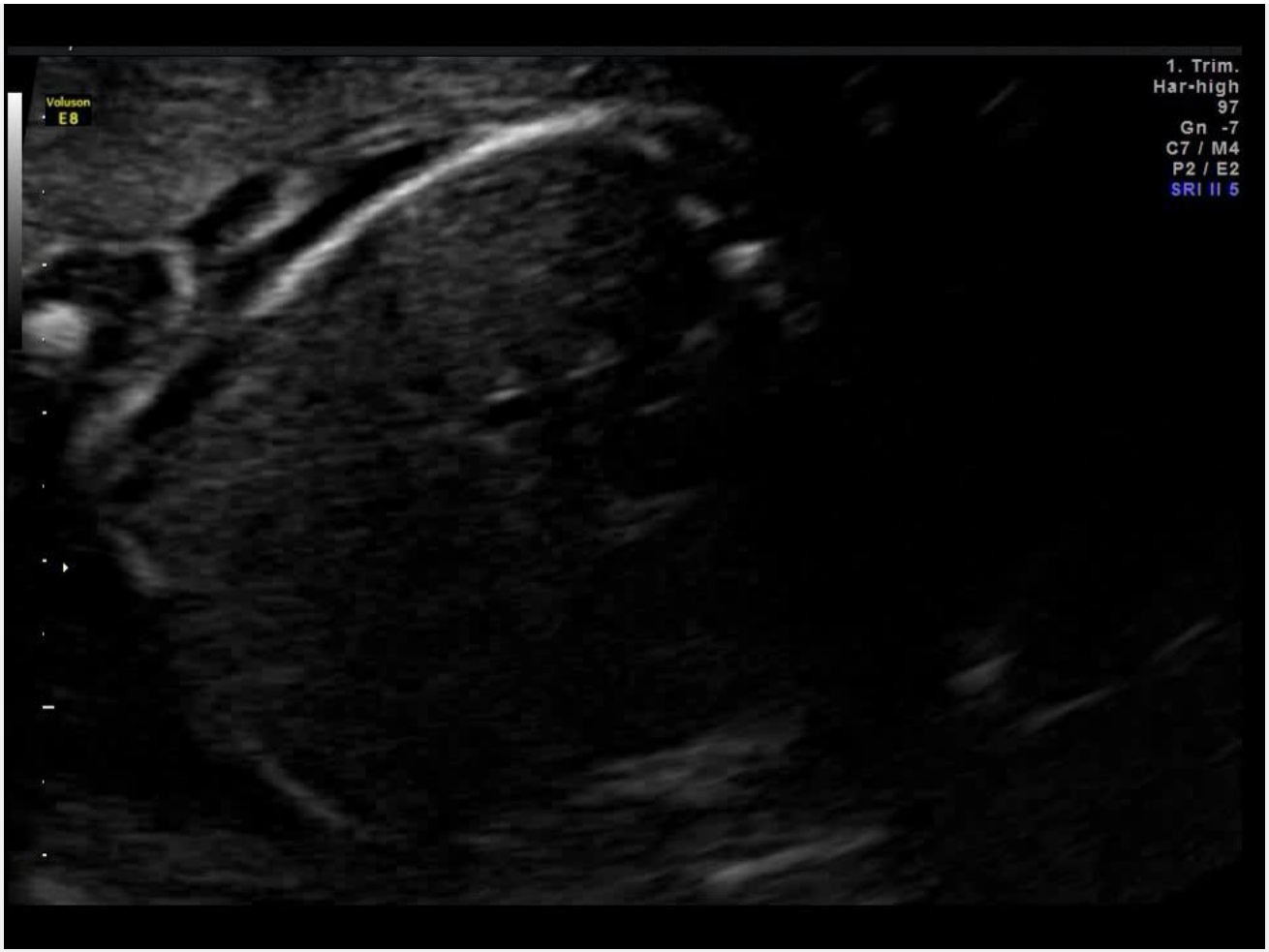
Ultrasonografía

- Posición hepática:
  - Valor predictivo independiente en HDC izquierdas, no así en las derechas.

- Posición gástrica:
  - Método indirecto de determinar severidad en HDC izquierdas, se correlaciona con la porción hepática intratorácica estimada con RM.
  - Correlación independiente de O/E LHR para mortalidad y morbilidad postnatal.

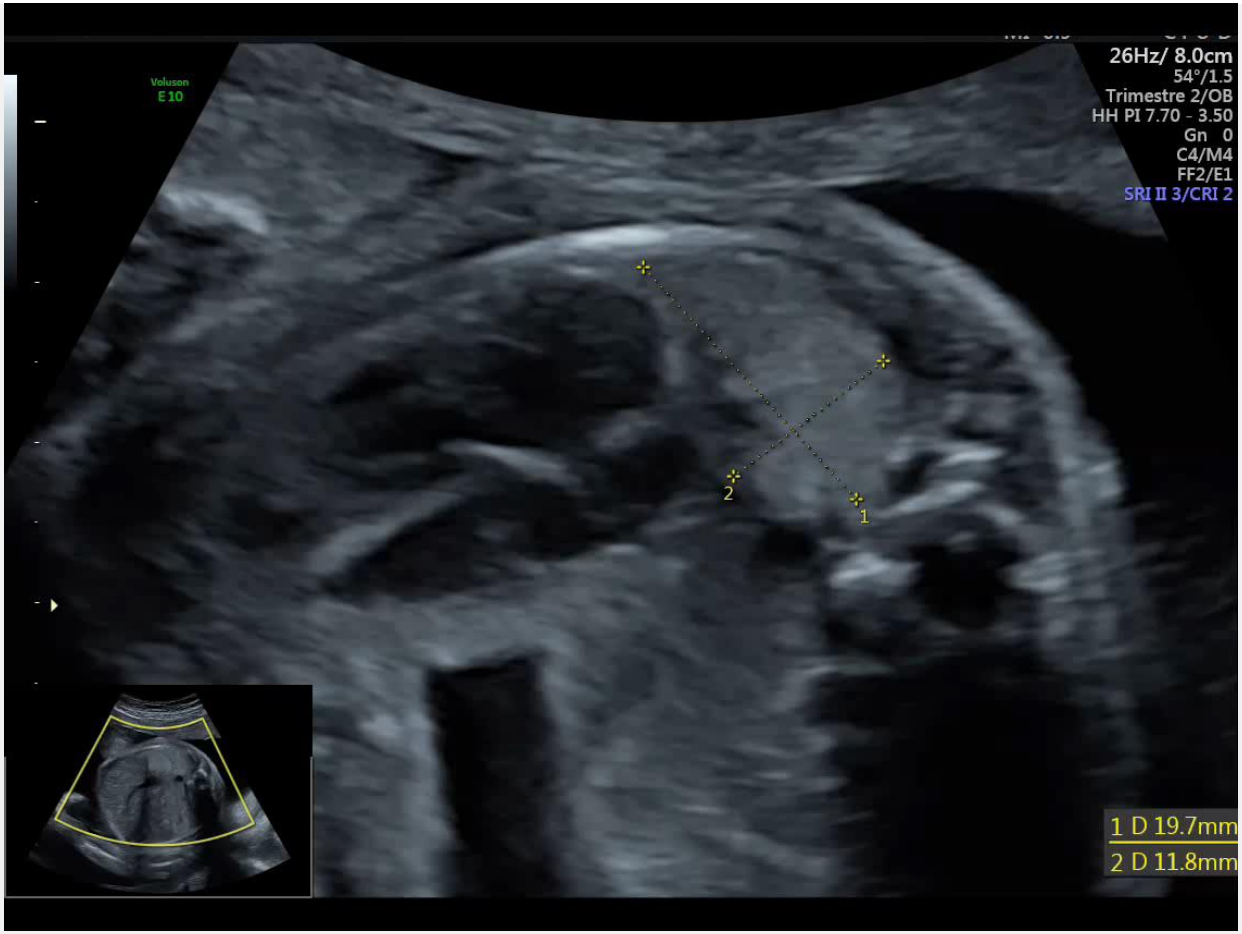
Francesca María Russo. Proposal for standardized prenatal ultrasound assessment of the fetus with congenital diaphragmatic hernia by the European Reference Network on Rare Inherited and Congenital Anomalies (ERNICA). Prenatal Diagnosis. Volume38, Issue9, August 2018. Pages 629-637.

Estandarización de evaluación ultrasonográfica ERNICA



Francesca María Russo. Proposal for standardized prenatal ultrasound assessment of the fetus with congenital diaphragmatic hernia by the European Reference Network on Rare Inherited and Congenital Anomalies (ERNICA). Prenatal Diagnosis, Volume38, Issue9, August 2018, Pages 629-637.

Estandarización de evaluación ultrasonográfica ERNICA



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Estandarización de evaluación ultrasonográfica ERNICA

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Ultrasonografía

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Table 4—Statistical analysis of accuracy of biometric parameters at different sonographic planes in high-risk fetuses. The results are compared to the autopsy data[a]

	Clavicle (%)		Four-chamber view (%)		Diaphragm (%)		
	AP	Trans	AP	Trans	AP	Trans	Length (%)
Sensitivity	12	42	57	44	41	27	29
Specificity	90	55	42	50	66	37	66
PPV	66	66	75	66	70	50	71
NPV	39	31	25	28	37	18	25

[a]All values in the table are percentages.
PPV, Positive predictive value; NPV, negative predictive value; AP, anterior–posterior diameter; trans, transverse diameter.

Table 12—Statistical analysis of the accuracy of sonographic measurements in different diagnoses in high-risk fetuses judged to be pathological when sonographic measurements were >2 SEE below the means established for normal controls[a]

	Sensitivity (%)		Specificity (%)		PPV (%)		NPV (%)	
	AP	Trans	AP	Trans	AP	Trans	AP	Trans
PROM	75	50	80	60	75	50	80	60
Hydrothorax	1	80	0	0	83	80	0	0
Potter	36	30	50	0	80	60	12	0

[a]All values in the table are percentages.
PPV; Positive predictive value; NPV, negative predictive value; AP, anterior–posterior diameter; trans; transverse diameter.

Kai-Sven Heling. Reliability of prenatal sonographic lung biometry in the diagnosis of pulmonary hypoplasia. Prenat Diagn 2001; 21: 649–657.

Ultrasonografía

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Table 13—Review of the literature focusing on papers presenting sensitivity and specificity for sonographic lung biometry

Authors	*n*	Fetal data	Biometric parameter	Sensitivity (%)	Specificity (%)	Autopsy proven?
Johnson *et al.* (1988)	26	PROM, oligohydramnios	TC/AC	94	60	Clinical and autopsy
Nimrod *et al.* (1988)	45	PROM <30 GW, oligohydramni os <34 GW	TC	88	96	Clinical and autopsy
Fong *et al.* (1998)	18	PROM <30 GW	TC/AC	90	86	Clinical and autopsy
Songster *et al.* (1989)	26	PROM	TC	80	92	Clinical and autopsy
Vinzileos *et al.* (1989)	13	Renal anomalies, PROM, Oligohydramnios	TC, HA, HC, TA, (TA−HA) × 100/TA	85 (TA−HA) × 100/TA	85 (TA−HA) × 100/TA	Yes
Roberts and Mitchell, (1990)	20	PROM	Lung length	90	92	Clinical and autopsy
D'Alton *et al.* (1992)	16	PROM <26 GW	TC/AC	75	100	Clinical and autopsy
Ohlsson *et al.* (1992)	58	PROM <30 GW, renal anomalies, skeletal malformations	TC, TC/AC	55–80	90–100	Clinical and autopsy
Maeda *et al.* (1993)	21	NIHF, renal anomalies, CDH, genetic anomalies, PROM <30 GW	Lung area	75	100	Clinical and autopsy
Yoshimura *et al.* (1996)	21	Renal anomalies, skeletal malformation, PROM	TC, TA, TC–HA, LA, TC/AC, TA/HA	80 (LA)	100 (LA)	Yes
Bahlmann *et al.* (1999)	19	CDH	Diameter lung area	100	100	Yes
Present study	29	PROM, hydrothorax, Potter	a.p. and transverse diameter	75/50, 1/80, 36/30, respectively	80/60, 0/0, 50/0, respectively	Yes

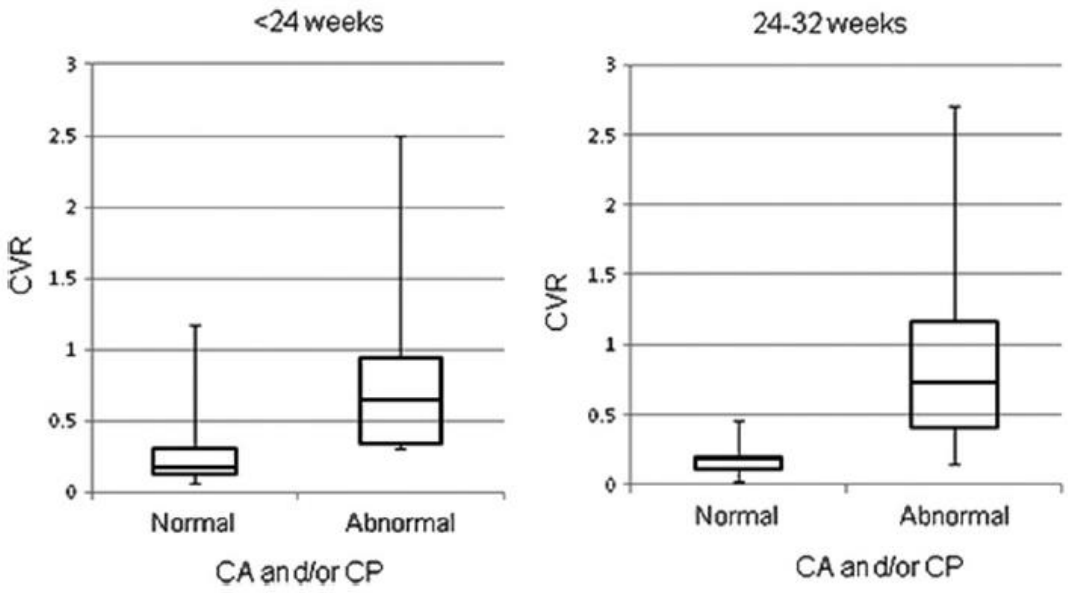
HA, Heart area; TA, thoracic area; TC, thoracic circumference; HC, heart circumference; GW, gestational week; LA, lung area.

PRENATAL SONOGRAPHIC LUNG BIOMETRY IN PULMONARY HYPOPLASIA

Kai-Sven Heling. Reliability of prenatal sonographic lung biometry in the diagnosis of pulmonary hypoplasia. Prenat Diagn 2001; 21: 649–657.

Eje y posición cardíaca

Figure 3. Box-and-whisker plots showing the relationship between the CVR and CA and/or CP abnormalities before 24 weeks and between 24 and 32 weeks for all lesions. The horizontal line in the box represents the median; the box represents the IQR; and whiskers indicate minimum and maximum values.



Lea Tuzovic, MD. Utility of Fetal Cardiac Axis and Cardiac Position Assessment in Predicting Neonatal Respiratory Morbidity in Fetal Congenital Lung Lesions. J Ultrasound Med 2019; 00:1–12.

Eje y posición cardíaca

CERPO

Table 4. Sensitivity, specificity, PPV, and NPV of CA and/or CP and CVR at Two Cutoffs (0.5 and 0.8) in Predicting Any and Severe Respiratory Morbidity Before 24 Weeks

	Any Respiratory Morbidity				Severe Respiratory Morbidity			
Parameter	SEN	SPEC	PPV	NPV	SEN	SPEC	PPV	NPV
CA and/or CP, all lesions	0.67	0.61	0.33	0.86	0.80	0.58	0.17	0.97
CVR (>0.5), all lesions[a]	0.50	0.73	0.35	0.83	0.80	0.73	0.24	0.97
CVR (>0.8), all lesions[b]	0.42	0.85	0.45	0.83	0.80	0.85	0.36	0.97
CA and/or CP, left-sided lesions	0.86	0.46	0.28	0.93	1.00	0.56	0.18	1.00
CA and/or CP, right-sided lesions	0.40	0.92	0.66	0.80	0.50	0.80	0.30	0.93

SEN indicates sensitivity; and SPEC, specificity.
[a]McNemar test (CA and/or CP versus CVR 0.5), $P < .05$.
[b]McNemar test (CA and/or CP versus CVR 0.8), $P < .05$.

Table 5. Sensitivity, Specificity, PPV, and NPV of CA and/or CP and CVR at Two Cutoffs (0.5 and 0.8) in Predicting Any and Severe Respiratory Morbidity Between 24 and 32 Weeks

	Any Respiratory Morbidity				Severe Respiratory Morbidity			
Parameter	SEN	SPEC	PPV	NPV	SEN	SPEC	PPV	NPV
CA and/or CP, all lesions	0.75	0.73	0.45	0.91	0.80	0.67	0.20	0.97
CVR (>0.5), all lesions[a]	0.58	0.87	0.58	0.87	0.8	0.82	0.33	0.97
CVR (>0.8), all lesions[b]	0.33	0.89	0.5	0.81	0.8	0.91	0.5	0.97
CA and/or CP, left-sided lesions	1.0	0.6	0.4	1.0	1.0	0.56	0.18	1.0
CA and/or CP, right-sided lesions	0.4	0.9	0.66	1.0	0.5	0.9	0.3	0.9

SEN indicates sensitivity; and SPEC, specificity.
[a]McNemar test (CA and/or CP versus CVR 0.5), $P < .05$.
[b]McNemar test (CA and/or CP versus CVR 0.8), $P < .05$.

Lea Tuzovic, MD. Utility of Fetal Cardiac Axis and Cardiac Position Assessment in Predicting Neonatal Respiratory Morbidity in Fetal Congenital Lung Lesions. J Ultrasound Med 2019; 00:1–12.

Ultrasonografía 3D

- Utilidad en displasias esqueléticas para determinar Volumen pulmonar fetal y predecir hipoplasia pulmonar letal. (k=0,714; p<0,001)
- Realización entre las 20 y 32 semanas.
- Letalidad parece depender del tipo de displasia esquelética

Table 2. Distribution of the types of bone dysplasia type according to postnatal diagnosis.

	Lethal dysplasia *N* (%)	Non-lethal dysplasia *N* (%)
Thanatophoric dysplasia	3 (16.5%)	0
Campomelic dysplasia	2 (11.1%)	0
Osteogenesis imperfect type I	0	1 (16.6%)
Osteogenesis imperfect type II	4 (22.2%)	0
Osteogenesis imperfecta type III	0	2 (33.3%)
Achondroplasia	0	1 (16.6%)
Diastrophic dysplasia	0	1 (16.6%)
Unclassified	9 (50%)	1 (16.6%)
Total	18 (100%)	6 (100%)

Table 4. Diagnostic accuracy of lethal pulmonary hypoplasia by 2D and 3D parameters.

	Sensitivity	Specificity	PPV	NPV
Total lung volume	83.3%	100%	100%	66.7%
TC	72%	83%	92%	50%
TC/AC	66%	75%	92%	33%
TA/HA	29%	80%	83%	25%
FL/AC	72%	80%	92%	44%

PPV, positive predictive value; NPV, negative predictive value; TC, thoracic circumference; AC, abdominal circumference; TA, thoracic area; HA, cardiac area; FL, femur length.

Carolina Amorim Barros. Prediction of lethal pulmonary hypoplasia by means fetal lung volumen in skeletal dysplasias: a three-dimensional ultrasound assessment. J Matern Fetal Neonatal Med, Early Online: 1–6. July 2015.

Ultrasonografía 3D

- En fetos de alto riesgo de desarrollar hipoplasia pulmonar, específicamente anomalías renales

- Sensibilidad 94%, Especificidad 82%, VPP 83%, VPN 93%

Carolina Amorim Barros. Prediction of lethal pulmonary hypoplasia by means fetal lung volumen in skeletal dysplasias: a three-dimensional ultrasound assessment. J Matern Fetal Neonatal Med, Early Online: 1–6. July 2015.

RM

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- Validada desde las 22 semanas
- Permite cálculo de volumen pulmonar con mayor precisión que la ultrasonografía.
- Tablas de VPT (TLV) según edad gestacional (Osada: V=2,41*GA-37,6)

- Comparación del Observado vs. Esperado (Gorincour et al) (O/E TLV)
- Su precisión puede mejorar al ajustar a volumen corporal fetal.

- O/E <15% se asocia a 100% de letalidad (Anomalía congénita de mal pronóstico vital)

- La displasia acinar con mayor proporción de tejido cartilaginoso y menor tejido alveolar y vascular, se manifiesta con un aumento de la intensidad de la señal en comparación al hígado.

Reuven Achiron. Primary Fetal Lung Hypoplasia (PFLH): Imaging and Clinical Characteristics. Ultraschall in Med 2017; 38: 301–309.

RM

- O/E Total fetal lung volumen (TFLV), Variación de O/E TFLV, % hernia hepática (LiTR), Variación TFLV/semanal
- Outcomes primarios: sobrevida, ECMO, PAH

ΔTFLV (Growth rate) = (TFLV2 – TFLV1)/study interval,
Δo/e TFLV: o/e TFLV2 – o/e TFLV1.

- Promedio de edad gestacional en RM 2do trimestre 23,6+/-2,3 sem, para 3er trimestre 33,2+/-1,7sem. Promedio de 9,95+/-4,3sem entre dos imágenes.

- Sobrevida 79%, PAH severa 68% con requerimiento de NO y 40% requirió ECMO
- PAH persistente hasta el año 26%
- Promedio de días de intubación 18
- Promedio de duración de estadía 52 días

Candace C. Style. Timing of Prenatal Magnetic Resonance Imaging in the Assessment of Congenital Diaphragmatic Hernia. Fetal Diagnosis and Therapy. August 2019.

Table 2. Predictor variables of PAH, ECMO, and survival

Predictor variables	Severe PAH (68%, $n = 39$)	Mild/no PAH ($n = 18$)	p value
O/e TFLV 2nd trimester, %	32±11.7	39.4±14	0.060
O/e TFLV 3rd trimester, %	30±9.9	35±13.2	0.118
ΔO/e TFLV	6.63±6.3	10.3±8.2	0.115
ΔTFLV: growth rate/week, mL	1.23±0.6	1.87±1.1	**0.009**
%LH 2nd trimester, %	20.3±12.5	25±11	0.238
%LH 3rd trimester, %	25±15.9	24.3±14	0.904
	Persistent PAH ($n = 15$)	Resolution of PAH ($n = 35$)	p value
O/e TFLV 2nd trimester, %	25.7±9.1	38.3±13.1	**0.002**
O/e TFLV 3rd trimester, %	25.6±13.1	34.4±10.7	**0.031**
ΔO/e TFLV	9.4±8.8	6.91±6.21	0.275
ΔTFLV: growth rate/week, mL	1.33±1.2	1.46±0.77	0.667
%LH 2nd trimester, %	27.9±12.5	12.6±12.1	**0.001**
%LH 3rd trimester, %	25.4±18.2	14.9±13.8	0.099
	ECMO ($n = 23$)	No ECMO ($n = 34$)	p value
O/e TFLV 2nd trimester, %	25.9±10	39.17±11.9	**<0.001**
O/e TFLV 3rd trimester, %	24.6±9.2	36±9.4	**<0.001**
ΔO/e TFLV	7.92±8.0	7.84±6.56	0.414
ΔTFLV: growth rate/week, mL	1.08±0.93	1.65±0.76	**0.021**
%LH 2nd trimester, %	23.9±11.4	20.9±12.6	0.462
%LH 3rd trimester, %	27.9±12.1	23.1±16.1	0.351
	Non-survival ($n = 12$)	Survival ($n = 45$)	p value
O/e TFLV 2nd trimester, %	24.6±6.3	36.1±13.1	**<0.001**
O/e TFLV 3rd trimester, %	26±12.2	32.4±11.2	0.12
ΔO/e TFLV	7.75±7.79	7.8±6.92	0.98
ΔTFLV: growth rate/week, mL	1.5±1.4	1.34±0.77	0.73
%LH 2nd trimester, %	24.3±13.5	21.6±12.1	0.719
%LH 3rd trimester, %	26.7±14.5	24.3±15.2	0.732

Analysis with independent t test. p value <0.05 considered significant. Bold values indicate statistical significance between groups. Values presented as mean ± SD. O/e TFLV, observed to expected total fetal lung volume; TFLV, total fetal lung volume; %LH, liver herniation; PAH, pulmonary hypertension; ECMO, extracorporeal membrane oxygenation.

Candace C. Style. Timing of Prenatal Magnetic Resonance Imaging in the Assessment of Congenital Diaphragmatic Hernia. Fetal Diagnosis and Therapy. August 2019.

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Table 3. Fetal lung volume predictor variable by logistic regression

Predictor variables	OR	*p* value	Upper bound (95% CI)	Lower bound (95% CI)
Severe PAH (68%, *n* = 39)				
O/e TFLV 2nd trimester	0.950	**0.037**	0.905	0.997
O/e TFLV 3nd trimester	0.953	0.088	0.901	1.007
ΔO/e TFLV	0.259	0.595	0.001	66.57
ΔTFLV: growth rate/week	0.361	**0.019**	0.155	0.843
Persistent PAH (26%, *n* = 15)				
O/e TFLV 2nd trimester	0.895	**0.006**	0.827	0.968
O/e TFLV 3rd trimester	0.911	**0.009**	0.850	0.977
ΔO/e TFLV	3.995	0.217	0.096	3.785
ΔTFLV: growth rate/week	0.864	0.661	0.450	1.659
ECMO (40%, *n* = 23)				
O/e TFLV 2nd trimester	0.878	**0.001**	0.811	0.950
O/e TFLV 3rd trimester	0.872	**0.001**	0.807	0.942
ΔO/e TFLV	1.603	0.905	0.001	3,569.1
ΔTFLV: growth rate/week	0.545	0.082	0.275	1.080
Death (21%, *n* = 12)				
O/e TFLV 2nd trimester	0.890	**0.009**	0.815	0.972
O/e TFLV 3nd trimester	0.933	0.049	0.875	1.000
ΔO/e TFLV	0.910	0.984	0.001	8,674.3
ΔTFLV: growth rate/week	1.185	0.617	0.610	2.302

p value <0.05 considered significant. Bold values indicate statistical significance on logistic regression. O/e TFLV, observed to expected total fetal lung volume; TFLV, total fetal lung volume; PAH, pulmonary hypertension; ECMO, extracorporeal membrane oxygenation.

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Table 4. ROC analysis of predictor variables for survival, ECMO and PAH

	Predictor variables	AUC	*p* value	Cut-off, %	Sensitivity, %	Specificity, %
Survival	O/e TFLV 2nd trimester	0.72	0.021	25	82	50
	O/e TFLV 3rd trimester	0.78	0.004	26	77	50
ECMO	Growth rate/week	0.72	0.005	0.98	85	52
	O/e TFLV 3rd trimester	0.79	0.001	26.5	82	57
Severe PAH	Growth rate/week	0.69	0.025	1.14	78	56
	O/e TFLV 2nd trimester	0.7	0.015	31	78	65
Persistent PAH	O/e TFLV 2nd trimester	0.78	0.002	26.7	80	57
	O/e TFLV 3rd trimester	0.75	0.006	26.5	80	67
	Growth rate/week	0.7	0.028	1.06	80	60

p value <0.05 considered significant.

O/e TFLV, observed to expected total fetal lung volume; TFLV, total fetal lung volume; PAH, pulmonary hypertension; ECMO, extracorporeal membrane oxygenation; ROC, receiver operator characteristic.

Candace C. Style. Timing of Prenatal Magnetic Resonance Imaging in the Assessment of Congenital Diaphragmatic Hernia. Fetal Diagnosis and Therapy. August 2019.

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Table 1. Clinical characteristics of the study population ($n = 12$)

Characteristics	Values
GA at prenatal MRI (weeks)[a]	31.1 (22.4–37.3)
GA at delivery (weeks)[a]	37.6 (32.7–38.4)
Male sex[b]	9 (75%)
Left-sided CDH[b]	12 (100%)
Median O:E LHR	38 (29–51)
Median prenatal total lung volume (TLV in mL)	23.7 (11.2–48.5)
Median prenatal percent predicted lung volume (PPLV)	23.3 (16.9–36)
Mild CDH[b]	1 (8.3%)
Moderate CDH[b]	11 (91.7%)
Severe CDH[b]	0 (0%)
Day of life at diaphragm repair[a]	7.5 (3–40)
Interval between diaphragm repair and postnatal MRI (weeks)[a]	3.2 (1.0–4.6)
Interval between 2 imaging studies (weeks)[a]	10.4 (5.4–20.1)
Day of life at postnatal MRI[a]	30.5 (13-56)
Corrected GA at postnatal MRI (weeks)[a]	41.3 (38.1–45.7)
Respiratory support at postnatal MRI[b]	
Ventilator, MAP at the time of MRI	1 (8%), MAP 9.0
CPAP	2 (17%)
NC	3 (25%)
RA	6 (50%)

CDH congenital diaphragmatic hernia, *CPAP* continuous positive airway pressure, *GA* gestational age, *MAP* mean airway pressure, *MRI* magnetic resonance imaging, *NC* nasal cannula, *O:E LHR* observed-to-expected lung area-to-head circumference ratio, *RA* room air

[a]Expressed as median (range)

[b]Expressed as *N* (% of total)

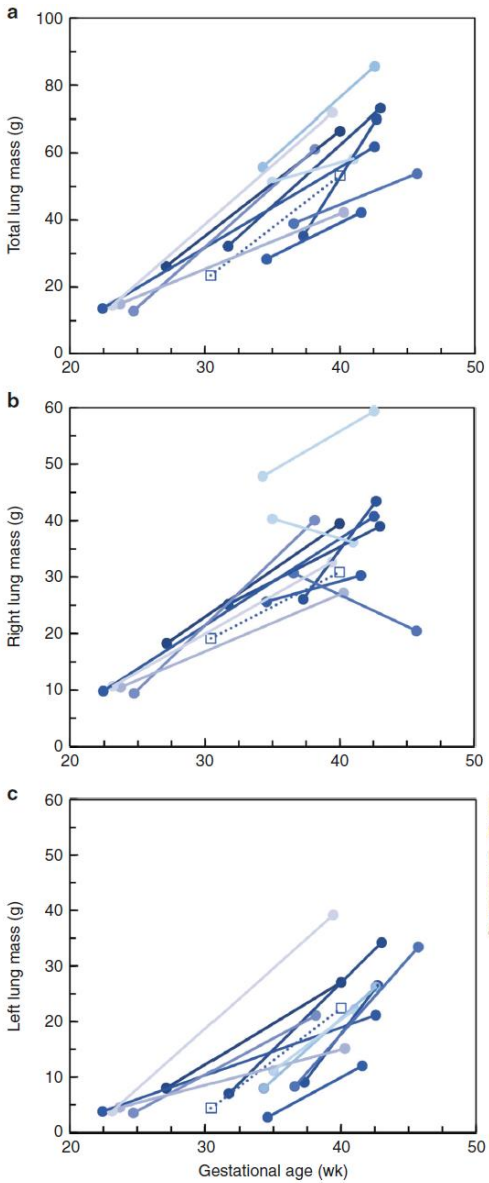

Fig. 1 Prenatal and post-repair magnetic resonance imaging lung mass measurements in infants with mild (empty squares) and moderate (filled circles) congenital diaphragmatic hernia. Lung masses were calculated for the total lung (**a**), right lung (**b**), and left lung (**c**). Total lung mass significantly increased in all infants with an average increase of 3.0 ± 1.3 g/week ($p < 0.001$) (Total). The average increase in contralateral (right) lung mass was 1.1 ± 1.1 g/week ($p = 0.003$), and the average increase in ipsilateral (left) lung mass was 1.8 ± 0.7 g/week ($p < 0.001$)

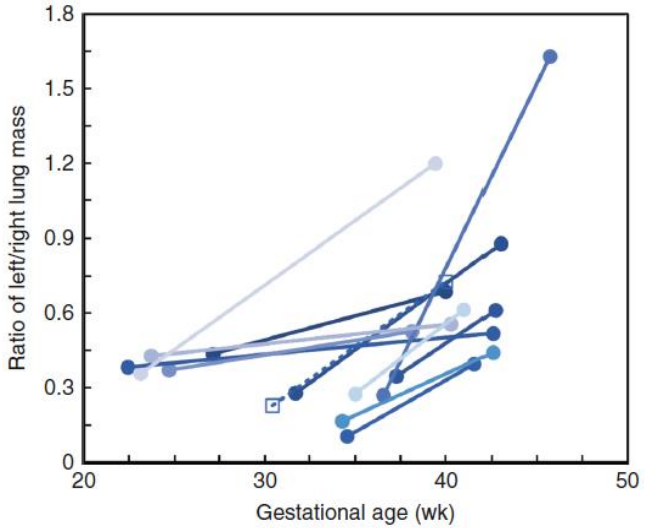

Fig. 2 Ratio of left (ipsilateral) lung mass to right (contralateral) lung mass at prenatal and post congenital diaphragmatic hernia (CDH) repair time points in infants with mild (empty squares) and moderate (filled circles) CDH. The ratio significantly increased in all infants with average prenatal and post-repair ratios of 0.30 ± 0.10 and 0.73 ± 0.34, respectively ($p = 0.002$)

Stephanie A. Adaikalam et al. Neonatal lung growth in congenital diaphragmatic hernia: evaluation of lung density and mass by pulmonary MRI. Pediatric Research, June 2019.

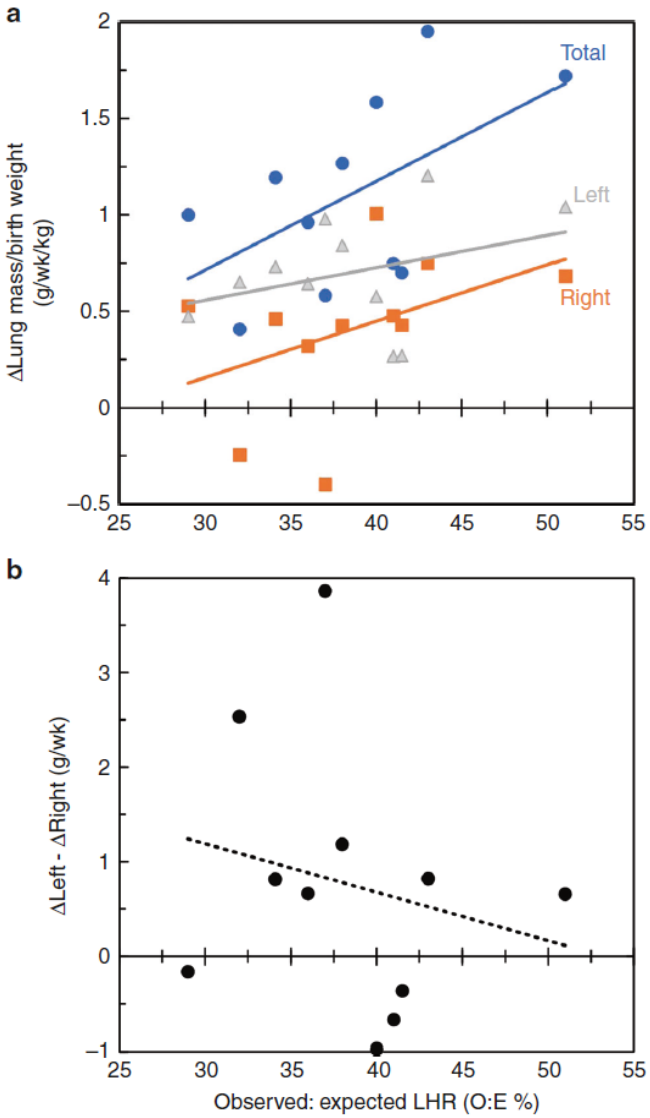

Fig. 3 **a** Correlation of severity (observed-to-expected lung area-to-head circumference ratio (O:E LHR)) and rate of growth of total (blue circles), right (orange squares), and left (gray triangles) lung mass (g/week/birth weight). The change in total lung mass normalized to birth weight was lower in the patients with a lower O:E LHR and more severe congenital diaphragmatic hernia (total lung mass, Pearson's $r = 0.554$, $p = 0.077$). **b** Comparison of severity (O:E LHR) and difference in mass growth rate of the ipsilateral (left) lung versus the contralateral lung (right)

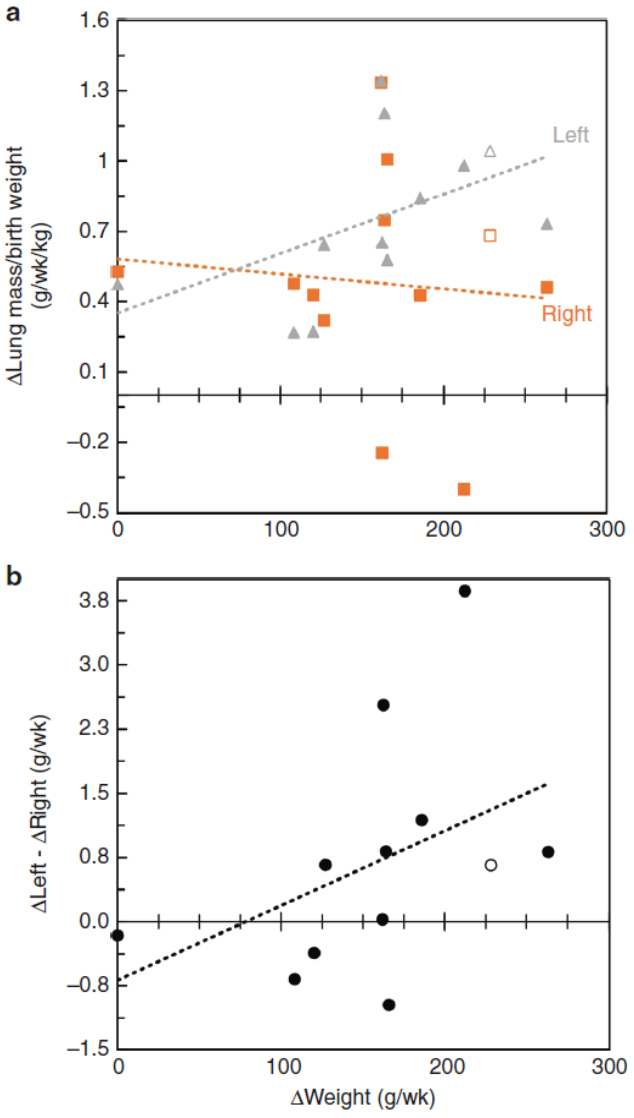

Fig. 4 **a** Correlation of infant weight gain (g/week) and rate of growth of right (orange circles) (Pearson's $r = 0.091$, $p = 0.778$) and left (gray squares) (Pearson's $r = 0.497$, $p = 0.100$) lung mass in infants with mild (empty markers) and moderate (filled markers) congenital diaphragmatic hernia (CDH). **b** Correlation of infant weight gain (g/week) and difference in mass growth rate of ipsilateral (left) and contralateral (right) lung (Pearson's $r = 0.428$, $p = 0.165$) in infants with mild (empty marker) and moderate (filled marker) CDH

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Estimación área bronquial

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Table 1 Results of comparison between DH and C

	DH ($n=12$)	Control ($n=5$)	p value
Total lung volume(ml)	133.3 ± 41.2	326 ± 22.5	0.0000001
Total lung area(cm^2)	78.8 ± 17.4	107.1 ± 10.3	0.006
Bronchial area(cm^2)	39.6 ± 11.9	52.2 ± 7.7	0.019
B/L ratio	0.45 ± 0.06	0.49 ± 0.05	0.28

*$p<0.05$ was considered to be statistically significant

Table 2 Spearman's correlation coefficient of each measured value

	Group DH ($n=12$)		Group C ($n=5$)	
	correlation coefficient** (95% confidence interval)	p value*	correlation coefficient (95% confidence interval)	p value
TLV and TLA	0.79 (0.71–0.85)	0.002	0.97 (0.96–0.98)	0.006
TLV and BA	0.73 (0.63–0.81)	0.007	0.67 (0.55–0.76)	0.2
TLV and B/L ratio	0.62 (0.49–0.72)	0.03	0.1 (– 0.08 to 0.28)	0.8

*$p<0.05$ considered to be statistically significant

**$r>0.3$ considered to be correlated

Takuya Kawaguchi. Original Article: A new approach using image analysis to assess pulmonary hypoplasia in the fetal lamb diaphragmatic hernia model. Pediatric Surgery International. August 2019. Springer-Verlag GmbH Germany, part of Springer Nature 2019.

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Diagnóstico de hipoplasia pulmonar

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