

CERPO

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



Seminario

Ventriculomegalia

Ximena Marques J.

**Programa de especialización
Medicina Materno Fetal**

Definición



- La evaluación de los atrios de los ventrículos laterales forma parte de la ecografía de screening
- Diámetro estable entre las 15-40 semanas
- Diámetro atrial mayor o igual a 10 mm en el 2do y 3er trimestre.
- ~1% de los fetos en el 2do trimestre de la gestación.

Categorización

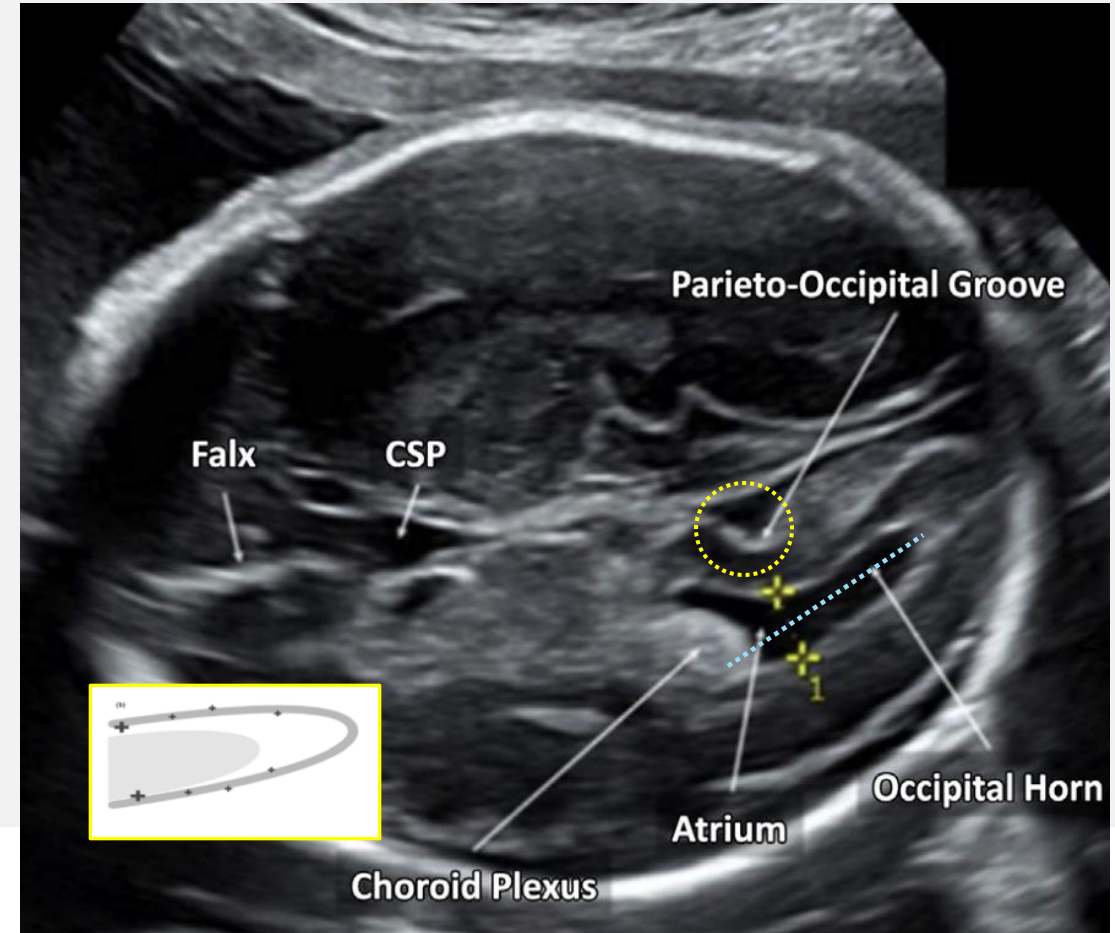
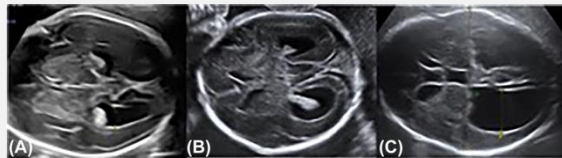
Leve 10-12 mm

Moderada 13-15 mm

Severa > 15 mm

Unilateral 50-60%

Bilateral 40-50%

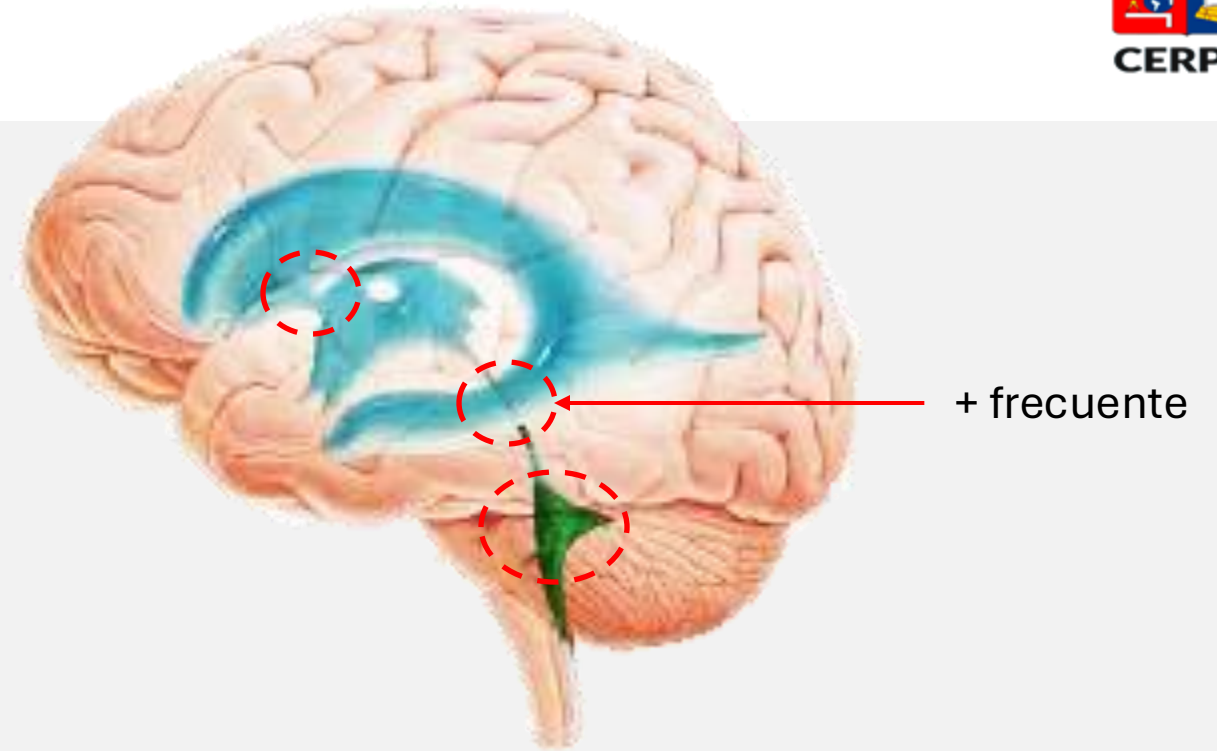


Definición



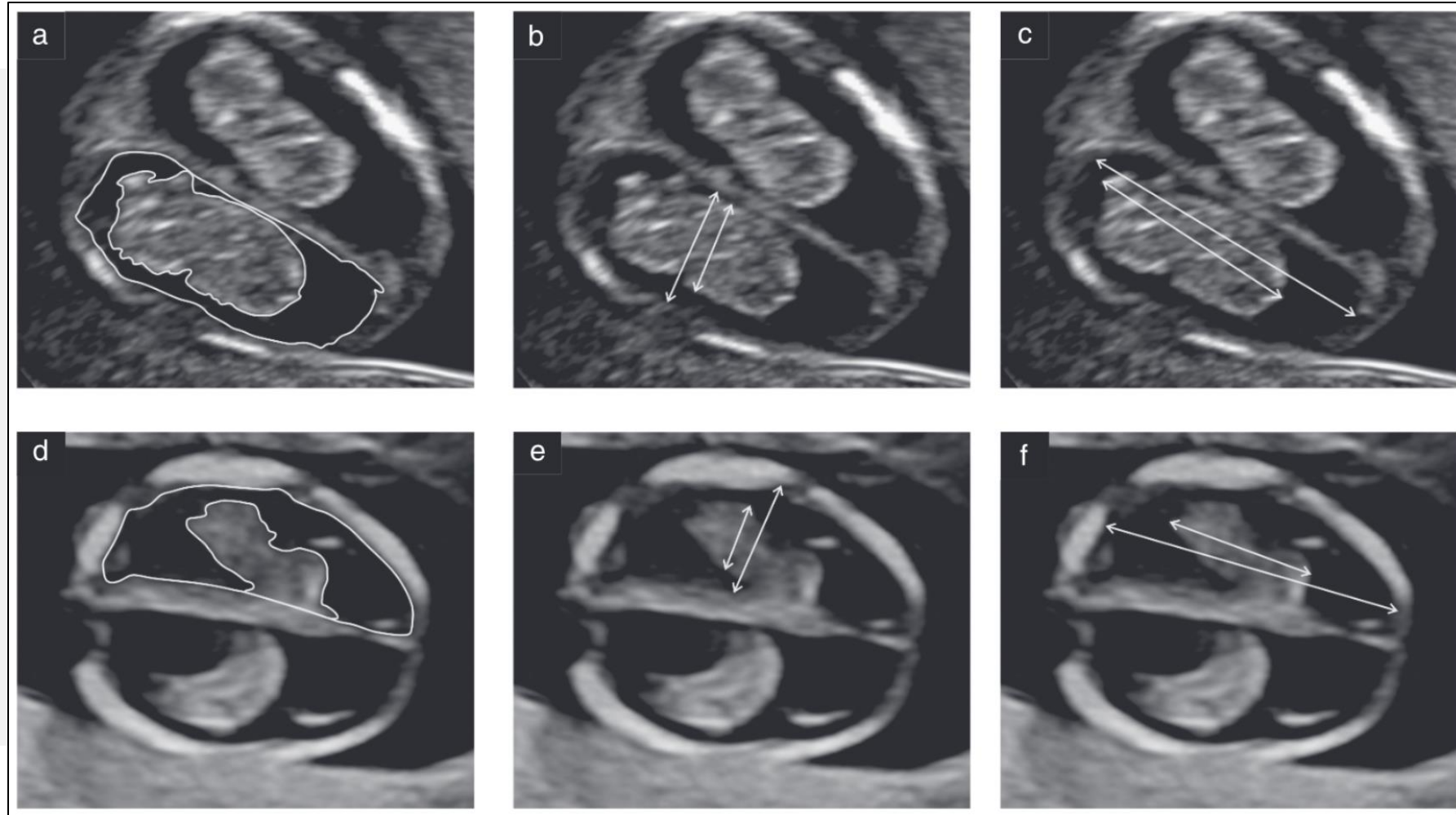
Clasificación Ventriculomegalia Severa

- Hidrocefalia Obstructiva.
Comunicante – No comunicante
- Ventriculomegalia severa asociada con otras malformaciones intra o extracraneales



La incidencia de Hidrocefalia varía entre 0,3 a 1,5 por
1000 RNV

Primer Trimestre



First-trimester choroid-plexus-to-lateral-ventricle disproportion and prediction of subsequent ventriculomegaly

S. PRASAD^{1,2} , C. DI FABRIZIO^{1,2}, N. ELTAWHEEL³ , E. KALAFAT^{4,5}  and A. KHALIL^{1,2} 

¹Fetal Medicine Unit, St George's University Hospitals NHS Foundation Trust, University of London, London, UK; ²Vascular Biology Research Centre, Molecular and Clinical Sciences Research Institute, St George's University of London, London, UK; ³Department of Obstetrics and Gynaecology, University Hospital of Coventry and Warwickshire, Coventry, UK; ⁴Department of Obstetrics and Gynecology, School of Medicine, Koc University, Istanbul, Turkey; ⁵Department of Statistics, Faculty of Arts and Sciences, Middle East Technical University, Ankara, Turkey

Estudio de casos y controles.

683 embarazos únicos.

102 fetos con VM / 86 L-M 16 S diagnosticada después de las 16 semanas

Table 1 Baseline characteristics and ultrasound measurements of cases with ventriculomegaly, according to severity (mild vs severe), compared with controls

Variable	Control (n = 581)	Mild ventriculomegaly (n = 86)	Severe ventriculomegaly (n = 16)	P*
PL (mm)	13.5 (12.4–14.6)	12.4 (10.8–13.6)	11.5 (10.7–12.6)	< 0.001
VL (mm)	17.6 (16.1–19.7)	18.0 (16.6–20.1)	19.4 (18.1–20.4)	0.051
PA (mm ²)	67.0 (57.3–77.3)	60.9 (50.0–67.8)	58.1 (42.0–70.5)	< 0.001
VA (mm ²)	102.3 (88.9–121.4)	113.0 (93.0–137.3)	130.8 (112.7–153.8)	< 0.001
PD (mm)	5.6 (5.1–6.1)	5.5 (4.9–6.0)	5.6 (5.3–6.1)	0.825
VD (mm)	7.3 (6.6–8.0)	8.0 (7.1–9.0)	8.1 (7.3–9.1)	< 0.001
PL/VL ratio	0.77 (0.72–0.81)	0.67 (0.60–0.74)	0.63 (0.57–0.68)	< 0.001
PA/VA ratio	0.66 (0.58–0.74)	0.53 (0.46–0.60)	0.47 (0.41–0.56)	< 0.001
PD/VD ratio	0.77 (0.72–0.82)	0.69 (0.64–0.73)	0.70 (0.66–0.76)	< 0.001
PA/BPD ratio	3.15 (2.81–3.50)	2.73 (2.45–2.97)	2.62 (2.20–2.94)	< 0.001

Table 3 Predictive accuracy of first-trimester ultrasound parameters for subsequent development of ventriculomegaly at their Youden index cut-offs

	Mild ventriculomegaly	Severe ventriculomegaly
PA/BPD ratio		
Sensitivity	0.76 (0.73–0.80)	0.67 (0.63–0.71)
Specificity	0.73 (0.62–0.82)	0.81 (0.54–0.96)
NPV	0.95 (0.92–0.96)	0.99 (0.98–1.00)
PPV	0.31 (0.25–0.38)	0.06 (0.03–0.11)
LR+	2.87 (2.02–4.09)	3.60 (1.29–9.99)
LR–	0.31 (0.25–0.38)	0.40 (0.31–0.52)
PA/VA ratio		
Sensitivity	0.80 (0.77–0.83)	0.81 (0.77–0.84)
Specificity	0.68 (0.57–0.78)	0.87 (0.62–0.98)
NPV	0.94 (0.92–0.96)	0.99 (0.98–1.00)
PPV	0.34 (0.27–0.42)	0.11 (0.06–0.18)
LR+	2.57 (1.87–3.52)	6.45 (1.76–23.62)
LR–	0.28 (0.22–0.35)	0.22 (0.17–0.28)
PL/VL ratio		
Sensitivity	0.76 (0.72–0.79)	0.75 (0.71–0.78)
Specificity	0.77 (0.67–0.86)	0.87 (0.62–0.98)
NPV	0.95 (0.93–0.97)	1.00 (0.98–1.00)
PPV	0.32 (0.26–0.39)	0.09 (0.05–0.14)
LR+	3.44 (2.30–5.13)	5.96 (1.63–21.80)
LR–	0.30 (0.25–0.36)	0.29 (0.23–0.38)
PD/VD ratio		
Sensitivity	0.76 (0.73–0.80)	0.40 (0.36–0.44)
Specificity	0.73 (0.62–0.82)	0.87 (0.62–0.98)
NPV	0.95 (0.92–0.96)	0.99 (0.97–1.00)
PPV	0.31 (0.25–0.38)	0.04 (0.02–0.06)
LR+	2.87 (2.02–4.09)	3.19 (0.87–11.69)
LR–	0.31 (0.25–0.38)	0.69 (0.56–0.84)

Values in parentheses are 95% CI. BPD, biparietal diameter; LR–, negative likelihood ratio; LR+, positive likelihood ratio; NPV, negative predictive value; PA, choroid plexus area; PD, choroid plexus diameter; PL, choroid plexus length; PPV, positive predictive value; VA, lateral ventricular area; VD, lateral ventricular diameter; VL, lateral ventricular length.

First-trimester choroid-plexus-to-lateral-ventricle disproportion and prediction of subsequent ventriculomegaly

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¹Fetal Medicine Unit, St George's University Hospitals NHS Foundation Trust, University of London, London, UK; ²Vascular Biology Research Centre, Molecular and Clinical Sciences Research Institute, St George's University of London, London, UK; ³Department of Obstetrics and Gynaecology, University Hospital of Coventry and Warwickshire, Coventry, UK; ⁴Department of Obstetrics and Gynaecology, School of Medicine, Koc University, Istanbul, Turkey; ⁵Department of Statistics, Faculty of Arts and Sciences, Middle East Technical University, Ankara, Turkey

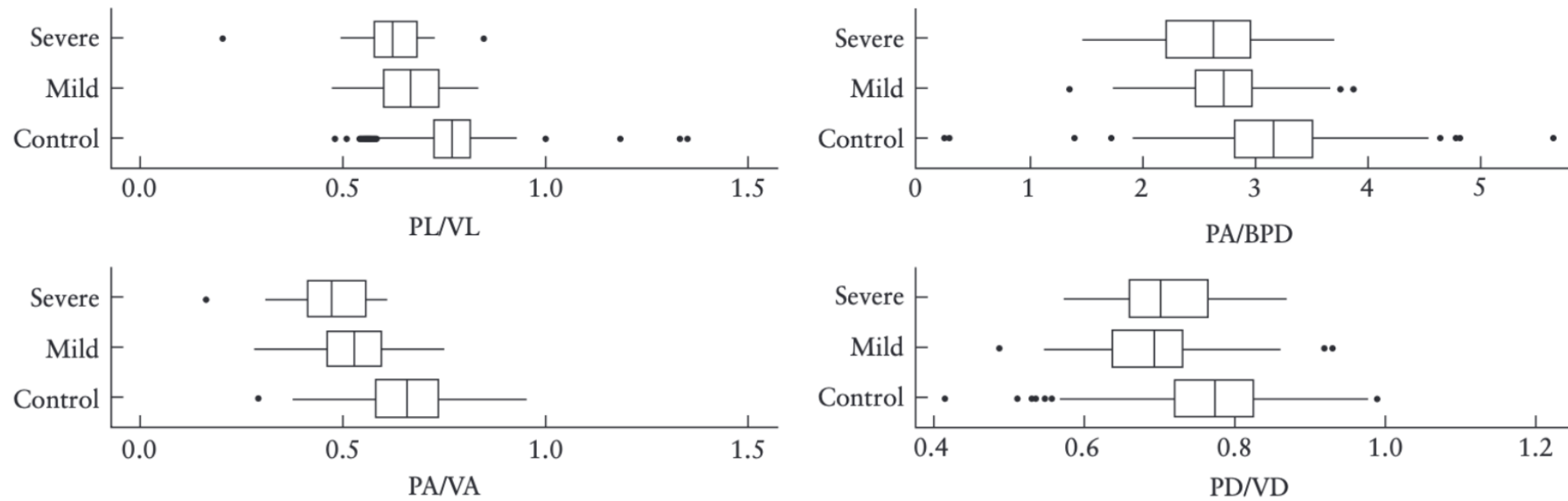


Figure 2 Box-and-whiskers plots of ratios of choroid plexus to lateral ventricle or head of fetuses subsequently diagnosed with severe or mild ventriculomegaly compared with controls. BPD, biparietal diameter; PA, choroid plexus area; PD, choroid plexus diameter; PL, choroid plexus length; VA, lateral ventricular area; VD, lateral ventricular diameter; VL, lateral ventricular length.

Etiología



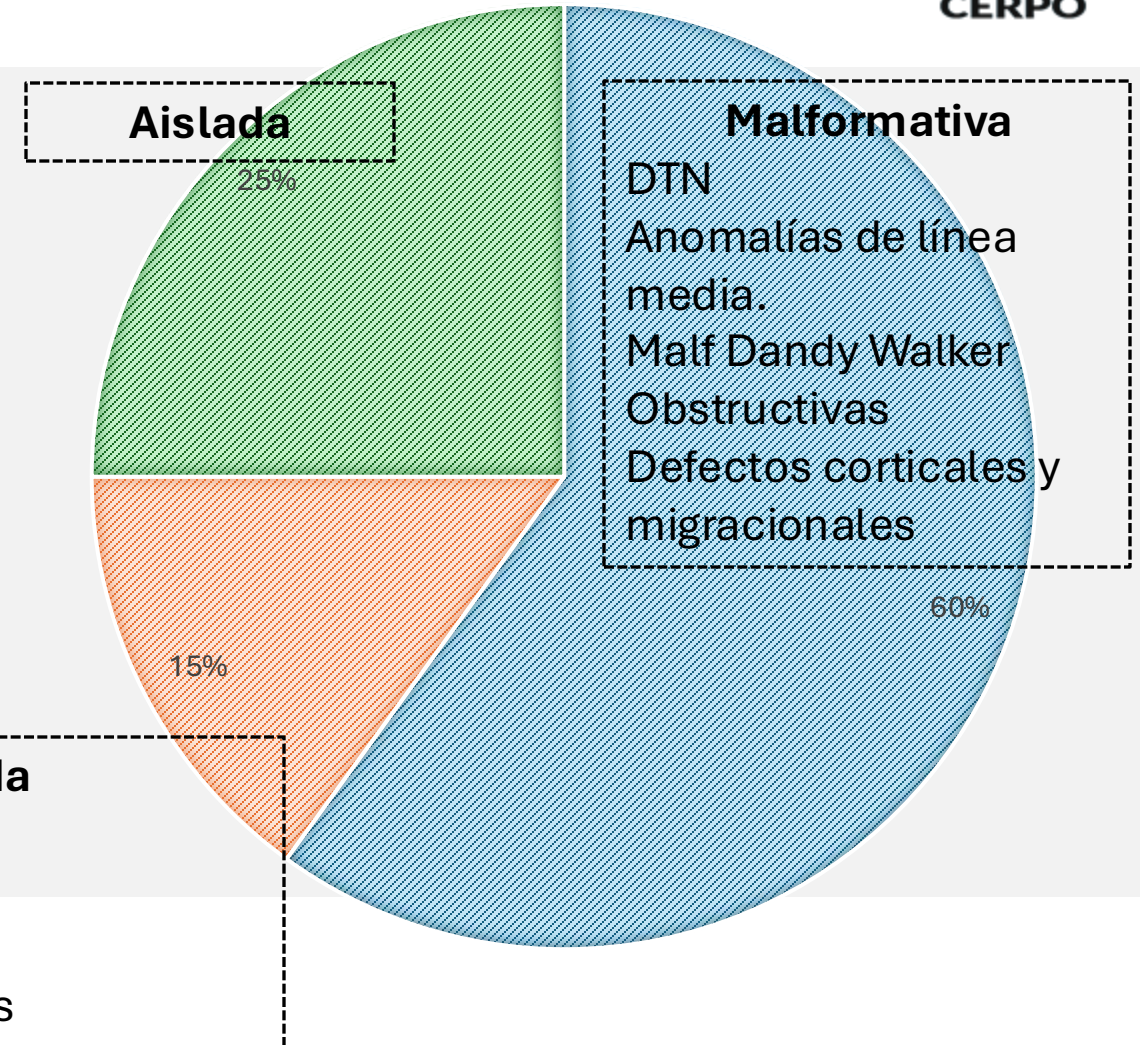
No es un diagnóstico, es un signo

Anomalia más frecuente del SNC (1-2/1000 gestaciones)

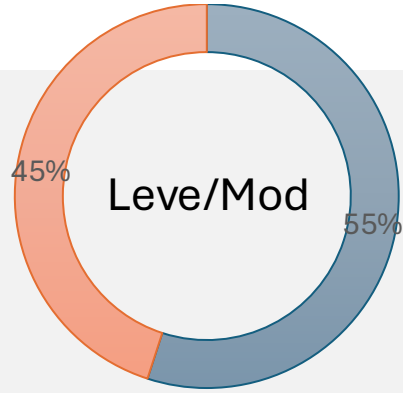
Marcador más sensible de anomalía del desarrollo del SNC

Espectro heterogéneo de condiciones – procesos patológicos asociados a alteraciones severas del neurodesarrollo a variantes de la normalidad.

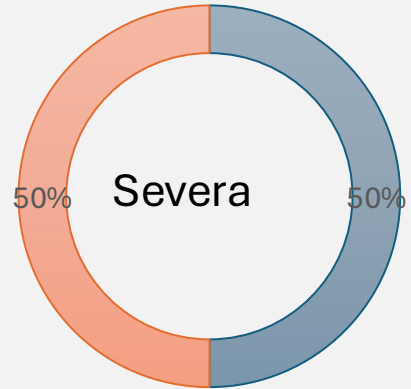
Factor pronóstico más importante es la asociación con otras anomalías y la progresión de la dilatación ventricular.



Anomalías Asociadas - Estructurales

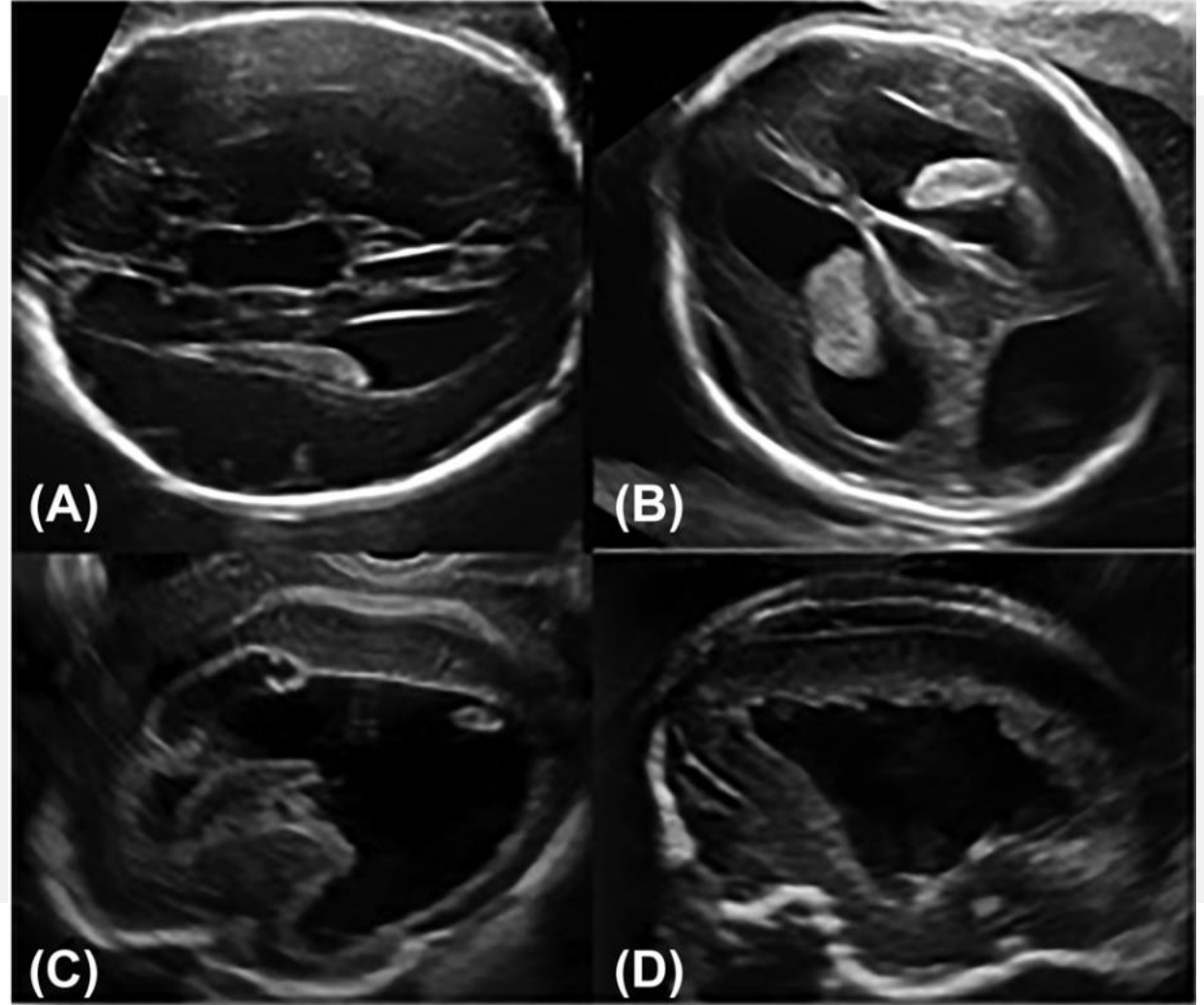


43%
SNC 32%
Extra SNC
CC 3,9
Urogenitales 2,3



50%
SNC 34%
Extra SNC
CC 6,4%
Cleft orofaciales 4,5%
Genotiuritarias 2,5%

**10–13% de las anomalías asociadas son reconocidas luego del nacimiento
Ecografía morfológica y Ecocardio**



Cuánto agrega el estudio con RMN?

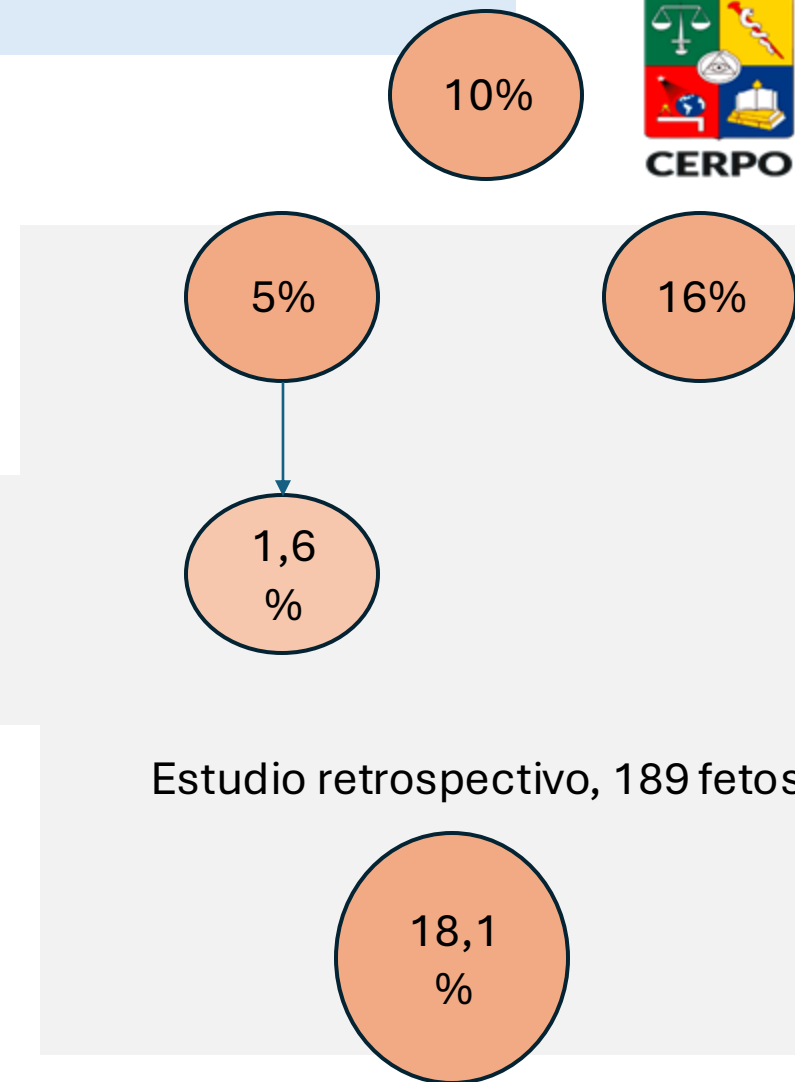
Role of magnetic resonance imaging in fetuses with mild or moderate ventriculomegaly in the era of fetal neurosonography: systematic review and meta-analysis

D. DI MASCIO¹, F. G. SILEO², A. KHALIL^{2,3}, G. RIZZO^{4,5}, N. PERSICO^{6,7}, R. BRUNELLI¹, A. GIANCOTTI¹, P. B. PANICI¹, G. ACHARYA^{8,9} and F. D'ANTONIO^{9,10}

Detección de anomalías del desarrollo cortical
Agenesia del cuerpo calloso

Role of prenatal magnetic resonance imaging in fetuses with isolated severe ventriculomegaly at neurosonography: A multicenter study

Daniele Di Mascio¹, Asma Khalil², Gianluigi Pilu³, Giuseppe Rizzo⁴, Massimo Caulo⁵,



Di Mascio D, Sileo FG, Khalil A, et al. Role of magnetic resonance imaging in fetuses with mild or moderate ventriculomegaly in the era of fetal neurosonography: systematic review and meta-analysis. *Ultrasound Obstet Gynecol.* 2019

Malinger G, Birnbam R, Haratz KK. Dedicated neurosonography for recognition of pathology associated with mild-to-moderate ventriculomegaly. *Ultrasound Obstet Gynecol.* 2020

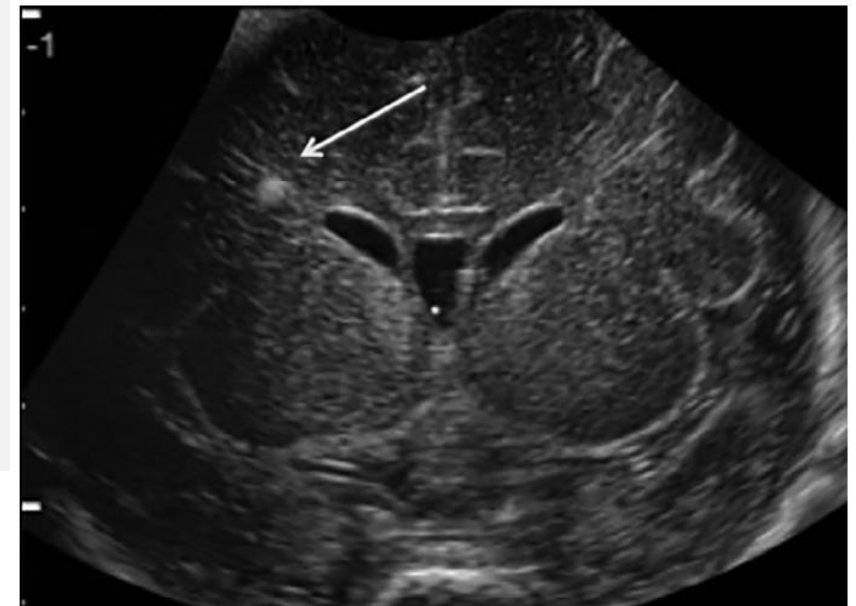
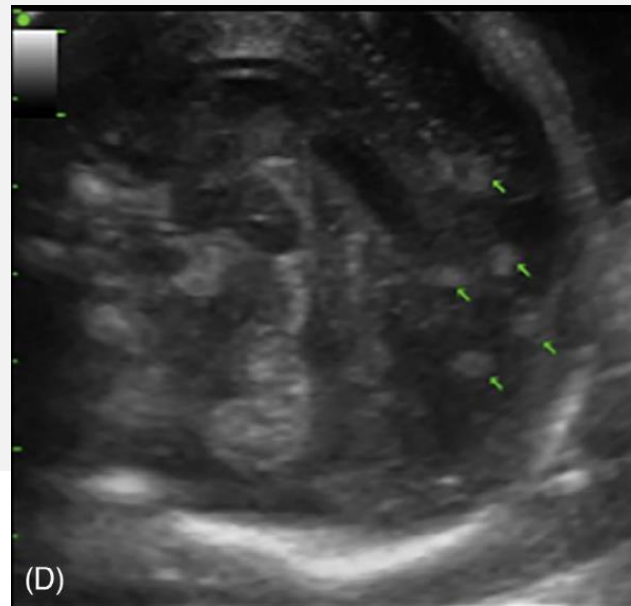
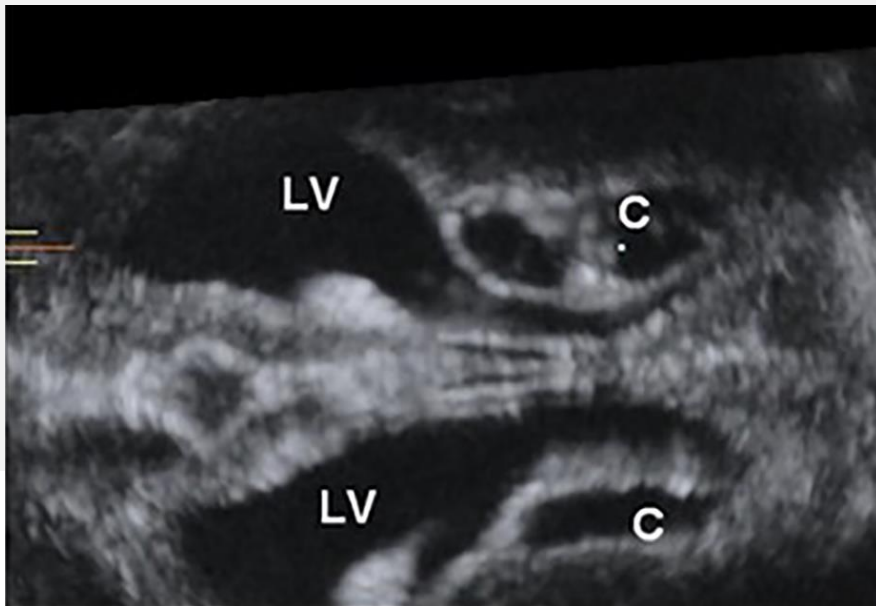
Di Mascio D, Khalil A, Pilu G, et al. Role of prenatal magnetic resonance imaging in fetuses with isolated severe ventriculomegaly at neurosonography: A multicenter study. *Eur J Obstet Gynecol Reprod Biol.* 2021

Infecciones congénitas



- La prevalencia de infecciones en fetos con ventriculomegalia es 2-5%
- Agentes más frecuentes: Citomegalovirus, Toxoplasma.
- Parvovirus B19, Zika y Herpes simplex.
- Más de la mitad de los casos presenta otros hallazgos US.

El estudio de infecciones congénitas debe ser ofrecido en todos los casos de ventriculomegalia aislada.



Anomalías Cromosómicas



Cariotipo anormal

2-15%

Trisomía 21, 18, 13
Monosomía X, triploidía.
Del, Dup , trisomía 9 en
mosaico, Dup 1q, Dup 7p,
Del 5p, Del 4p

Ventriculomegalia
moderada

Aislada
2.7-10%

No Aislada
11-14%

50%

T21

Ventriculomegalia
severa

3,2-8,3%

CNVs



- 5 y 10%
- Aislada 4–9.5%
- No aislada 6.6–37.9%
- Microdelección 22q11.2, Microdelección 15q11.2, Microdelección 16p13.11

Enfermedades Monogénicas

- Más de 100 genes asociados a VM fetal, sin embargo, en la mayoría de los casos se encuentra como parte de un síndrome genético bien definido.
- Genes únicos asociados a VM aislada: **L1CAM, AP1S2, MPDZ y CCDC88C.**
- L1CAM representa hasta un 10% de los hombres con hidrocefalia congénita aislada.

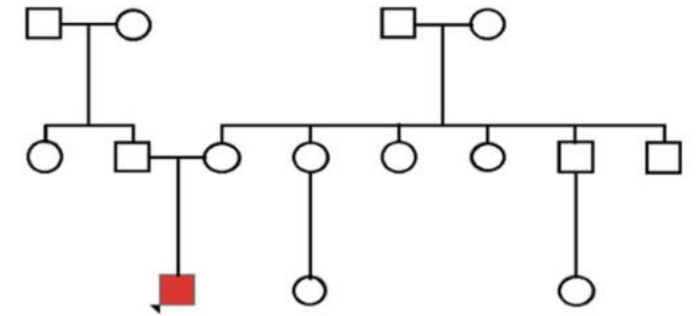
HC asociada a variantes L1CAM (HSAS)



L1CAM está ubicado en Xq28, y codifica para una molécula de adhesión celular

L1 Syndrome: Included Phenotypes ¹

- [X-linked](#) hydrocephalus with stenosis of the aqueduct of Sylvius (HSAS)
- MASA (*mental retardation, adducted thumbs, shuffling gait, aphasia*) syndrome, including SPG1 ([X-linked](#) complicated hereditary spastic paraplegia type 1)
- [X-linked](#) complicated corpus callosum agenesis



- Forma más común de VM heredable.
- Prevalencia 1:30.000 NV.
- 10% de los hombres con HC aislada idiopática.
- Pulgares aducidos se observan en el 50% de los casos

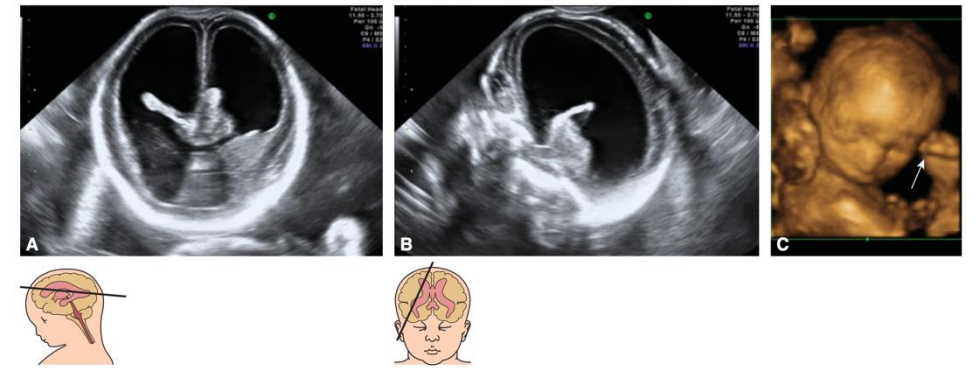


Figure 4-5. Severe ventriculomegaly in a fetus with X-linked hydrocephaly. (A) Axial plane. (B) Coronal plane. (C) Three-dimensional ultrasonography reconstruction of the body surface shows the adducted thumb (arrow).

Original Investigation | Genetics and Genomics

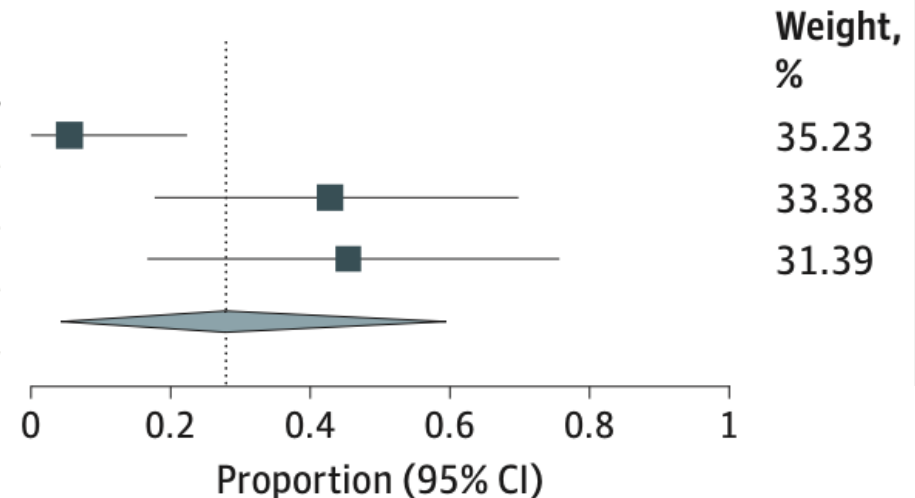
Molecular Diagnostic Yield of Exome Sequencing in Patients With Congenital Hydrocephalus A Systematic Review and Meta-Analysis

Ana B. W. Greenberg, BS; Neel H. Mehta, BA; Garrett Allington, PhD; Sheng Chih Jin, PhD; Andrés Moreno-De-Luca, MD; Kristopher T. Kahle, MD, PhD

C Individuals with only ventriculomegaly

Study	Events	Total	Proportion (95% CI)
Baptiste et al, ⁴⁰ 2022	1	18	0.056 (0-0.223)
Schindewolf et al, ³⁹ 2022	6	14	0.429 (0.177-0.699)
Yaron et al, ⁴⁴ 2022	5	11	0.455 (0.167-0.758)
Total (95% CI)	12	43	0.279 (0.044-0.594)

Heterogeneity: $\tau^2 = 8.72$; $\chi^2_2 = 8.72$; $P = .01$; $I^2 = 75.8\%$



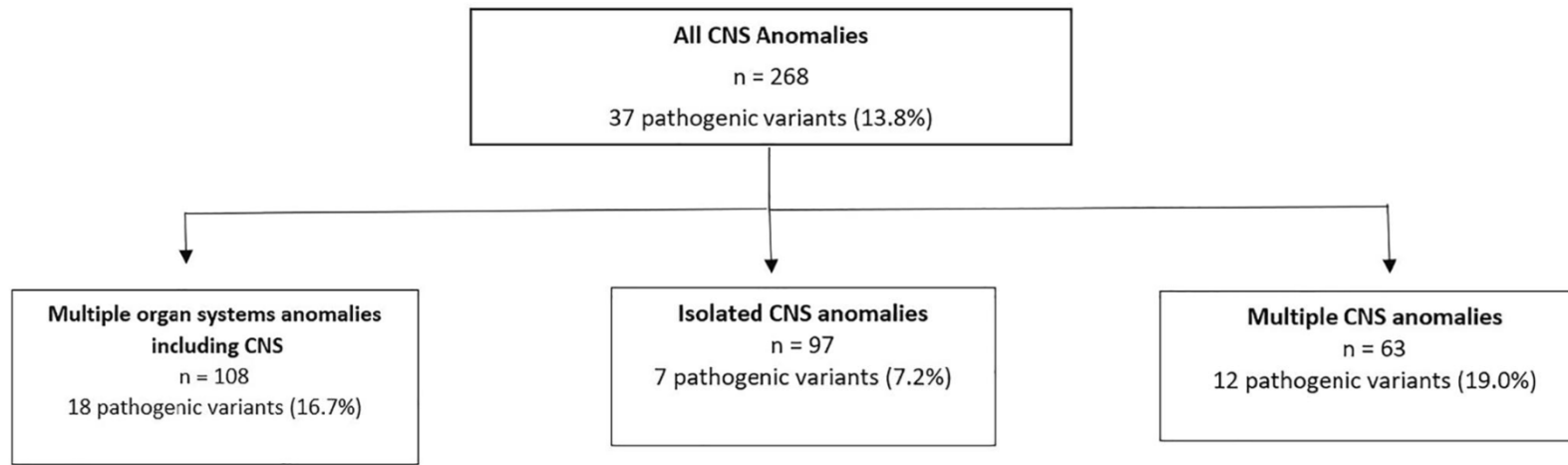


TABLE 1 Rates of likely pathogenic variants on exome sequencing (ES) in fetuses with central nervous system (CNS) anomalies and the genes involved

	N	LP/p finding on ES (%)	Genes involved
Isolated, single CNS anomaly	97	7 (7.2)	
Mild ventriculomegaly	23	3 (13.0)	CHD7 ^a , B3GLCT ^a , ARID1A
Moderate ventriculomegaly	15		
Severe ventriculomegaly	18	1 (5.6)	KIDINS220
Unknown severity of ventriculomegaly	8		
Agenesis of the corpus callosum	10	3 (30.0)	L1CAM ^a , SHH, PTCH1
Cerebellar hypoplasia	2		
Dandy walker	5		
Encephalocele	3		
Holoprosencephaly	6		
Parenchymal defect	1		
Intracranial hemorrhage	1		
Other	5		
Multiple CNS anomalies	63	12 (19.0)	FLNA ^a , C5ORF42, CHD7 ^a , GPSM2, TUBB3, ARMC9, RAC1, OCRL, TUBA1A, ASPM, TUBB ^a , PIK3R2
Anomalies in multiple organ systems including CNS	108	18 (16.7)	TSC2 ^a , TMEM67 ^a , SCN2A ^a , COL4A1 ^a , CE0, CC2D2A, FLVCR2 ^a , FGFR2, PORCN, CPT2, TCTN2 ^a , TMEM67 ^a , PEX1, ISPD, CHD7, CDKN1C ^a , RAB23 ^a , TCTN3

TABLE 3

Phenotypic expression of genetic variants in isolated single cases with only bilateral severe ventriculomegaly

Gene	Number of cases	Phenotype	Postnatal autopsy findings
<i>L1CAM</i>	3	Hydrocephalus; hydrocephalus due to aqueductal stenosis	1. Ventriculomegaly involving the lateral and third ventricles 2. Narrow aqueduct without signs of ischemic, hemorrhagic, or inflammatory lesions 3. Normal neocortex and absence of any migration anomaly
<i>ACTB</i>	1	Baraitser–Winter syndrome	N/A
<i>CCDC88C</i>	1	Hydrocephalus, nonsyndromic, autosomal recessive	N/A
<i>DNAH5</i>	1	Ciliary dyskinesia, primary 3, with or without situs inversus	N/A
<i>FOXP2</i>	1	Speech-language disorder-1	N/A
<i>HACE1</i>	1	Nonspecified (Lord et al, ¹² 2019)	N/A
<i>KIDINS220</i>	1	Nonspecified (Lord et al, ¹² 2019)	N/A
<i>MYH10</i>	1	Bilateral ventriculomegaly, aqueductal stenosis	N/A
<i>POMGNT1</i>	1	Walker–Warburg syndrome	N/A
<i>POMK</i>	1	MDDGA12 (congenital muscular dystrophy-dystroglycanopathy with brain and eye anomalies, type A12) syndrome	1. Slightly dilated lateral ventricles 2. Normal internal organs 3. Eye abnormalities were not reported 4. Because dystroglycanopathy was not yet considered as part of the differential diagnosis, muscle fibers were not tested.
<i>SLC12A7 (KCC4)</i>	1	Congenital hydrocephalus	N/A
<i>SPG11</i>	1	Spastic paraplegia 11, autosomal recessive	N/A
<i>ST3GAL5</i>	1	Salt and pepper developmental regression syndrome	N/A

Mustafa. Exome sequencing in severe bilateral ventriculomegaly. *Am J Obstet Gynecol MFM* 2023.



Diagnostic yield

Proportion % (95% CI)	I^2 (%)
0)	47
3)	2
7)	6
9)	0

Pronóstico



- Falsos negativos 10%.
- Falsos positivos 12-15%. Media 10.3 mm – confirmatorio 7,5.

Leve y Moderada

Sobrevida 97%–98%,
Neurodesarrollo normal 90%

Severa

Sobrevida 88%
Neurodesarrollo normal 42%

Metanálisis 2014

652 casos de VM aislada y seguimiento postnatal

Alt. Neurodesarrollo (67) 7.9% o 1/12 a los 30 meses.

*2 – 3% en población general

*Progresión

1. Giorgione V, Haratz KK, Constantini S, Birnbaum R, Malinger G. Fetal cerebral ventriculomegaly: What do we tell the prospective parents?. Prenat Diagn. 2022

2. Pagani G, Thilaganathan B, Prefumo F. Neurodevelopmental outcome in isolated mild fetal ventriculomegaly: systematic review and meta-analysis. Ultrasound Obstet Gynecol. 2014

3. Carta S, Kaelin Agten A, Belcaro C, Bhide A. Outcome of fetuses with prenatal diagnosis of isolated severe bilateral ventriculomegaly: systematic review and meta-analysis Ultrasound Obstet Gynecol. 2018

Manejo



Ecografía morfológica + ecocardiografía en todos los casos

Estudio de cariotipo en todos los casos

Serología materna en todos los casos

RMN en casos progresivos y severos 30 -32 semanas

Control US c/ 2-4 semanas

Postnatal

Eco cerebral – RMN en casos seleccionados

Seguimiento con neuropediatra con realización de escalas estándar (Bayley, Griffiths)

No existe indicación para cesárea electiva en todos los casos

Casos severos con macrocefalia

No hay indicación para finalización de la gestación en forma PT

Manejo



Cirugía Fetal?

Shunt ventriculoamniótico

- 10% de muerte fetal intra procedimiento.
- 66% de discapacidad moderada a severa en los sobrevivientes.

Estudio Retrospectivo

44 casos

Ventriculomegalia severa bilateral

Shunt ventriculoamniótico

2010 y 2015

ORIGINAL RESEARCH ARTICLE

Ventriculo-amniotic shunting for severe fetal ventriculomegaly

Magdalena Litwinska¹  | Ewelina Litwinska²  | Marta Czaj¹ | Bartosz Polis³ |
Lech Polis³ | Krzysztof Szaflik¹

Criterios para la terapia fetal: presencia de ventriculomegalia severa con un diámetro ventricular lateral de >20 mm, ausencia de otras anomalías mayores, cariotipo normal y resultado negativo de infección materna

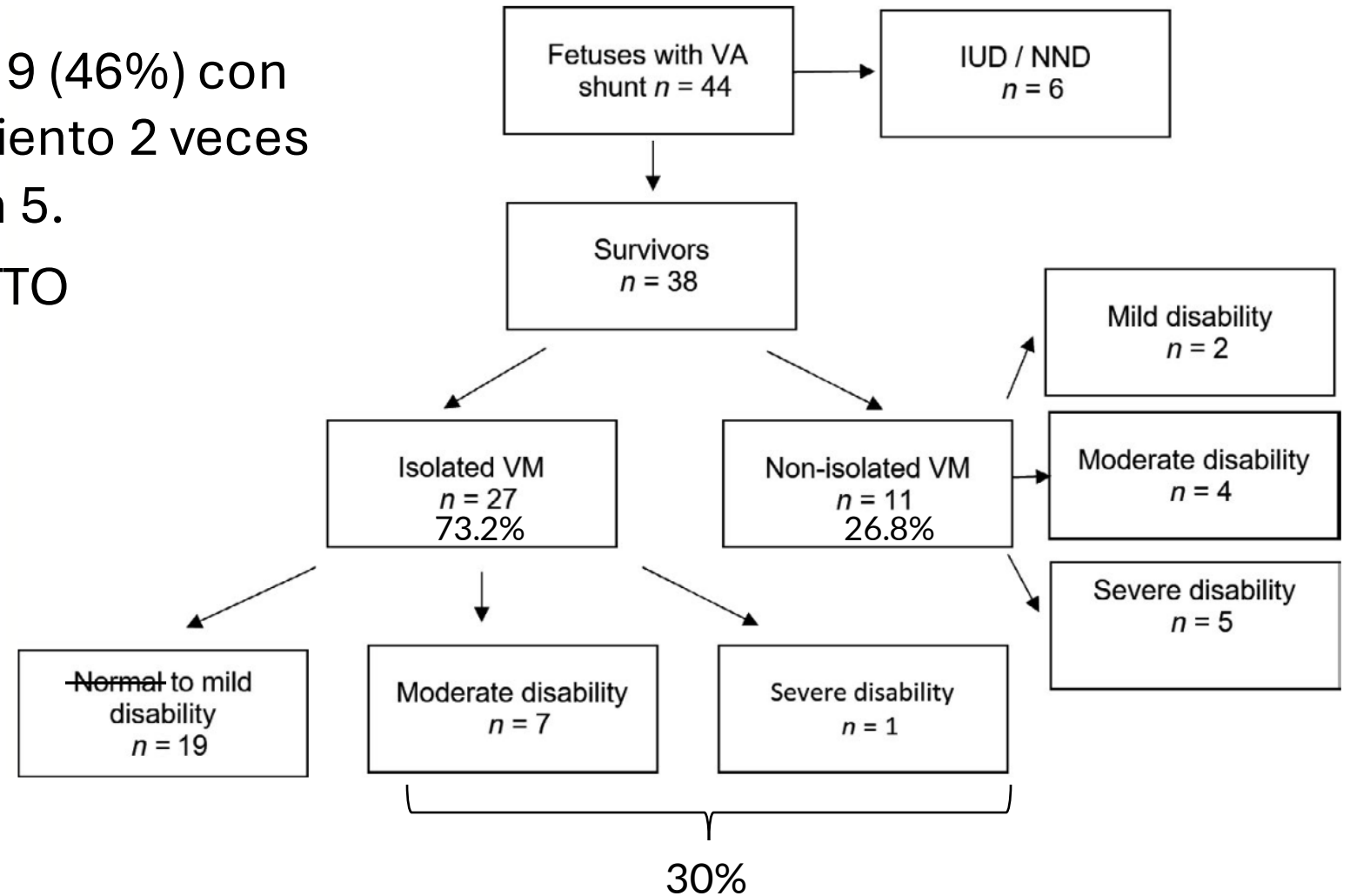
25 semanas (20-33 semanas)

VM 26 mm (20-50 mm)

¿Cirugía Fetal?



- Migración del shunt en 19 (46%) con repetición del procedimiento 2 veces en 14 casos y 3 veces en 5.
- 28 (73,7%) requirieron TTO quirúrgico postnatal.



Momento de la Interrupción?



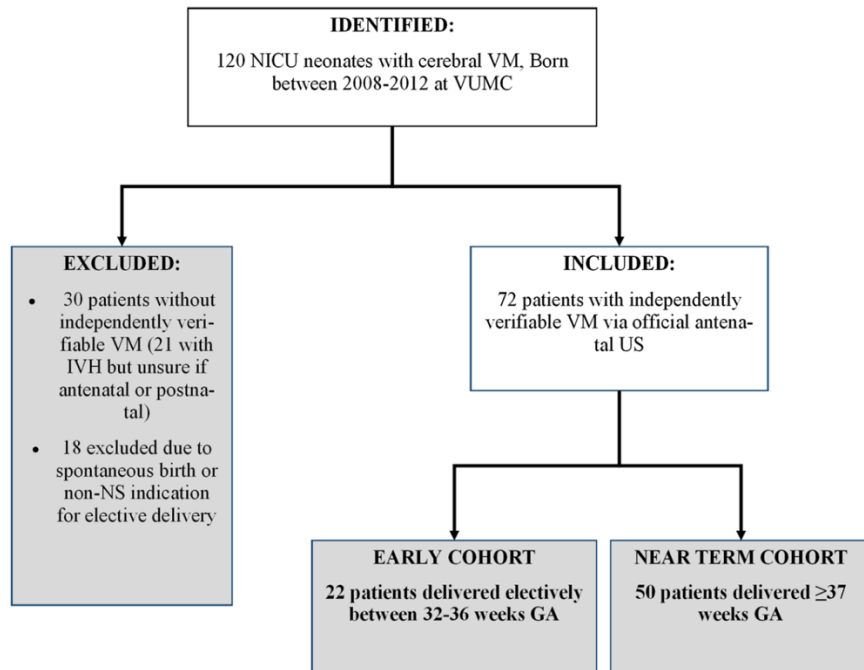
Child's Nervous System
<https://doi.org/10.1007/s00381-017-3662-0>

ORIGINAL PAPER



Early elective delivery for fetal ventriculomegaly: are neurosurgical and medical complications mitigated by this practice?

Clinton D. Morgan^{1,2,3} • Travis R. Ladner^{1,3} • George L. Yang^{1,3} • Marjorie N. Moore¹ • Russell D. Parks^{1,3} • William F. Walsh⁴ • John C. Wellons^{1,3} • Chevis N. Shannon^{1,3}



	Early, <i>N</i> = 22	Near term, <i>N</i> = 50	<i>p</i> value
EGA at delivery (weeks)	35 (33–36)	38 (37–40)	< 0.0001
Birthweight (g)	2975 (2080–3980)	3470 (2580–4600)	< 0.0001
Maternal age (years)	26 (19–37)	26 (15–40)	0.980
Antenatal ventricle width (mm)	39 (21–81)	20 (12–68)	< 0.0001
APGAR 1-minute	7 (5–8)	8 (7–8)	0.02
APGAR 5-minute	8 (2–9)	9 (2–9)	0.002
No. with IVH	2 (9%)	6 (12%)	> 0.999
Myelomeningocele	10 (45%)	30 (60%)	0.253
Follow-up (years)	4.3 (2.6–6.1)	5.4 (4.0–6.2)	0.195

EGA estimated gestational age, IVH intraventricular hemorrhage

Data given are median (25 to 75% interquartile range) and number (percentage)



	Early, N = 22 (%)	Near term, N = 50 (%)	p value
Neurosurgical procedures^a			
Time to initial VPS (days)	4 (1–8)	8 (6–11)	0.014
Neurosurgical procedures per patient	3 (1–5)	2 (1–3)	0.175
VPS revisions per patient	0 (0–1)	0 (0–1)	0.342
VPS re-insertions per patient	1 (1–2)	0.5 (0–1)	0.0009
Re-insertions for infected VPS per patient	0 (0–1)	0 (0–0)	0.014
No neurosurgical procedures	3 (14%)	9 (18%)	0.744
Myelomeningocele repair only	0 (0%)	2 (4%)	>0.999
VPS only (no MMC repair)	10 (45%)	11 (22%)	0.054
Myelomeningocele repair + VPS	9 (41%)	28 (56%)	0.308
Any VPS insertion	19 (86%)	39 (78%)	0.528
VPS revision ^b	12 (55%)	24 (48%)	0.798
VPS removal + re-insertion	10 (45%)	9 (22%)	0.021
VPS removal after VPS infection	9 (41%)	6 (12%)	0.010
Neurosurgical complications			
VPS infection, N (%)	9 (41%)	6 (12%)	0.010
Abdominal pseudocyst, N (%)	1 (5%)	2 (4%)	> 0.999
Shunt nephritis, N (%)	1 (5%)	3 (6%)	> 0.999
Hematoma at site of placement, N (%)	4 (18%)	4 (8%)	0.237
Proximal shunt obstruction, N (%)	8 (36%)	19 (38%)	0.895
Distal shunt obstruction, N (%)	5 (23%)	9 (18%)	0.641
Pleural effusion, N (%)	1 (5%)	0 (0%)	0.306
Distal shunt migration, N (%)	1 (5%)	1 (2%)	0.521

^a Median (IQR)

^b VPS revision includes proximal, valve, or distal VPS failure and conversions of distal site from VPS to VAS or from VAS to VPS

Mayor incidencia de insuficiencia respiratoria durante el primer año de vida en la cohorte de PT (32 vs. 6%, p = 0.037) que persiste hacia los 3 años de edad (32 vs. 10%, p = 0.037).

Conclusiones



- La ventriculomegalia es un hallazgo frecuente, que requiere de un estudio diagnóstico estandarizado
- Independiente de su grado de severidad debe realizarse una búsqueda exhaustiva de anomalías estructurales asociadas a nivel de SNC y extra SNC.
- La evaluación del cariotipo y el estudio de infecciones congénitas se recomienda en todos los casos.
- El consejo genético es altamente recomendable dentro de la consejería prenatal.
- Debe realizarse un seguimiento durante el embarazo para monitorizar la progresión y determinar el pronóstico