HIPERTENSIÓN PULMONAR EN PEDIATRÍA

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DEFINICIÓN de HIPERTENSIÓN PULMONAR

- PAPm 14+-3 mmhg.
- PAPm >20 mmhg
- Hipertensión arterial pulmonar es una enfermedad crónica y progresiva de los vasos pulmonares que da lugar a elevación de resistencias pulmonares con consiguiente remodelado, cambio de estructura y de función del VD—Marca pronóstico de la enfermedad

RECOMMENDATIONS FROM THE SIXTH WORLD SYMPOSIUM ON PULMONARY HYPERTENSION (2018)

Pediatric Pulmonary Hypertension
Guidelines From the American Heart Association and American Thoracic Society

Hipertensión Pulmonar en la Edad Pediátrica

- SIMILITUDES y DIFERENCIAS con el adulto.
  - Definición: Igual
    - Diferencia primera etapa de la vida:
      - In útero : P sistémicas= P pulmonar
      - 2-3 meses deben ser como las del adulto.

Hemodynamic profiles of pulmonary hypertensio.

Classification	Mean pulmonary artery pressure	Pulmonary capillary wedge pressure	Pulmonary vascular resistance
Isolated pre-capillary PH	>20 mm Hg	<15 mm Hg	>3 WU
Combined pre- and post-capillary PH		>15 mm Hg	>3 WU
Isolated post-capillary PH		>15 mm Hg	<3 WU

The 6th World Symposium on Pulmonary Hypertension defined three hemodynamic profiles of pulmonary hypertension (PH): isolated pre-capillary PH, combined pre- and post-capillary PH, and isolated post-capillary PH. WU, Wood units.

1. Pulmonary arterial hypertension

- 1.1 Idiopathic
- 1.2 Heritable
  - 1.2.1 BMPR2 mutation
  - 1.2.2 Other mutations
- 1.3 Drugs and toxins induced
- 1.4 Associated with:
  - 1.4.1 Connective tissue disease
  - 1.4.2 Human immunodeficiency virus (HIV) infection
  - 1.4.3 Portal hypertension
  - 1.4.4 Congenital heart disease (Table 6)
  - 1.4.5 Schistosomiasis

1'. Pulmonary veno-occlusive disease and/or pulmonary capillary haemangiomatosis

- 1'.1 Idiopathic
- 1'.2 Heritable
  - 1'.2.1 EIF2AK4 mutation
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1''. Persistent pulmonary hypertension of the newborn

2. Pulmonary hypertension due to left heart disease

- 2.1 Left ventricular systolic dysfunction
- 2.2 Left ventricular diastolic dysfunction
- 2.3 Valvular disease
- 2.4 Congenital / acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies
- 2.5 Congenital /acquired pulmonary veins stenosis

3. Pulmonary hypertension due to lung diseases and/or hypoxia

- 3.1 Chronic obstructive pulmonary disease
- 3.2 Interstitial lung disease
- 3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
- 3.4 Sleep-disordered breathing
- 3.5 Alveolar hypoventilation disorders
- 3.6 Chronic exposure to high altitude
- 3.7 Developmental lung diseases (Web Table III)

4. Chronic thromboembolic pulmonary hypertension and other pulmonary artery obstructions

- 4.1 Chronic thromboembolic pulmonary hypertension
- 4.2 Other pulmonary artery obstructions
  - 4.2.1 Angiosarcoma
  - 4.2.2 Other intravascular tumors
  - 4.2.3 Arteritis
  - 4.2.4 Congenital pulmonary arteries stenoses
  - 4.2.5 Parasites (hydatidosis)

5. Pulmonary hypertension with unclear and/or multifactorial mechanisms

- 5.1 Haematological disorders: chronic haemolytic anaemia, myeloproliferative disorders, splenectomy
- 5.2 Systemic disorders, sarcoidosis, pulmonary histiocytosis, lymphangioleiomyomatosis
- 5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
- 5.4 Others: pulmonary tumoral thrombotic microangiopathy, fibrosing mediastinitis, chronic renal failure (with/without dialysis), segmental pulmonary hypertension

Clasificación

WHO classification

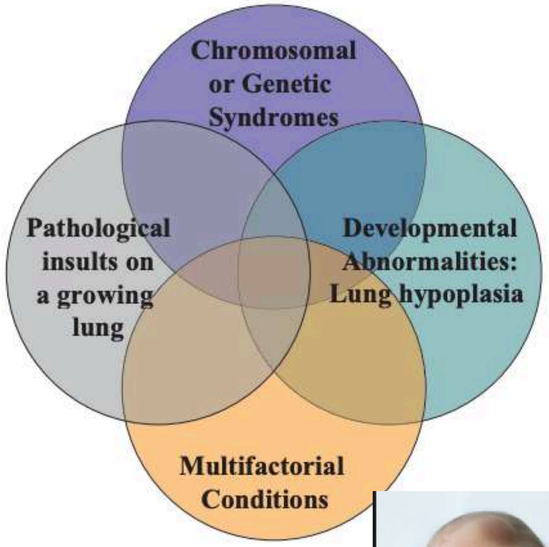
5 Categorías o grupos :

- presentación clínica
- hallazgos patológicos
- hallazgos hemodinámicos
- posibilidades terapéuticas

Agreed on by the ESC in 2016 and the Sixth World Symposium 2018

Hipertensión Pulmonar en la Edad Pediátrica

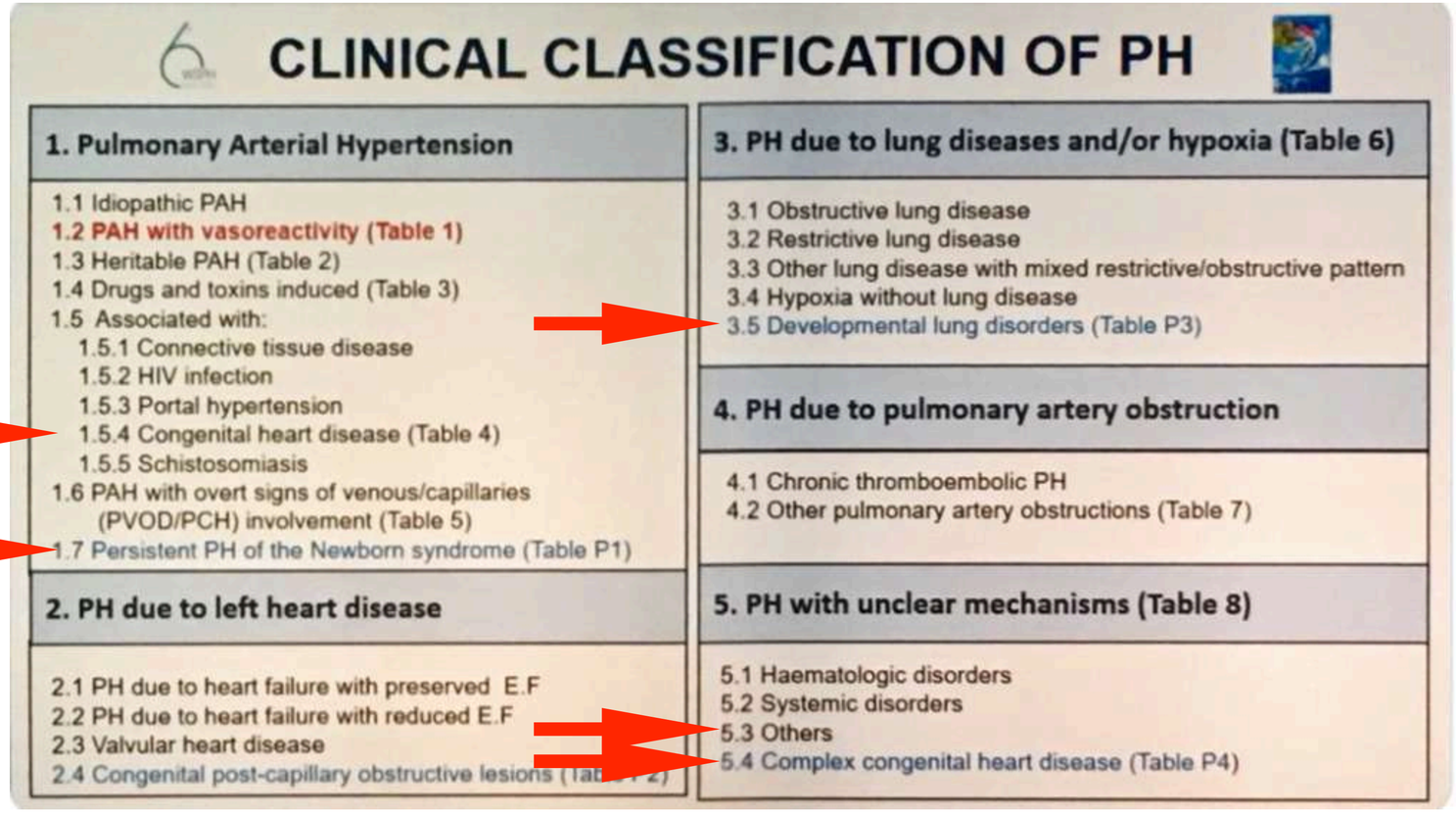
- Espectro VARIADO Y COMPLEJO.
- Etiología muy HETEROGÉNEA. Co-morbilidades.
  - Enf cardiaca, pulmonar , hepática…
  - Sd polimarformativos, cromosomopatías
- Rango de edad : 0-18 años.
- Poco frecuente. Desconocida. Poco estudiada en pacientes pediátricos. Escaso nº de pacientes por centro.
  - Asociada a otras patologías frecuentes: DBP, CC…
  - Aumento de nº hospitalizaciones en relación HP.
  - Aumento de diagnostico, adecuado screening.



Hipertensión Pulmonar en la Edad Pediátrica

- ~~SIMILITUDES con el adulto.~~ Ttnos específicos y/o únicos pediátricos.

  - Clasificación:



CLINICAL CLASSIFICATION OF PH

1. Pulmonary Arterial Hypertension

1.1 Idiopathic PAH
1.2 PAH with vasoreactivity (Table 1)
1.3 Heritable PAH (Table 2)
1.4 Drugs and toxins induced (Table 3)
1.5 Associated with:
- 1.5.1 Connective tissue disease
- 1.5.2 HIV infection
- 1.5.3 Portal hypertension
- 1.5.4 Congenital heart disease (Table 4)
- 1.5.5 Schistosomiasis

1.6 PAH with overt signs of venous/capillaries (PVOD/PCH) involvement (Table 5)
1.7 Persistent PH of the Newborn syndrome (Table P1)

2. PH due to left heart disease

2.1 PH due to heart failure with preserved E.F
2.2 PH due to heart failure with reduced E.F
2.3 Valvular heart disease
2.4 Congenital post-capillary obstructive lesions (Tab... 2)

3. PH due to lung diseases and/or hypoxia (Table 6)

3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders (Table P3)

4. PH due to pulmonary artery obstruction

4.1 Chronic thromboembolic PH
4.2 Other pulmonary artery obstructions (Table 7)

5. PH with unclear mechanisms (Table 8)

5.1 Haematologic disorders
5.2 Systemic disorders
5.3 Others
5.4 Complex congenital heart disease (Table P4)

Hipertensión Pulmonar en la Edad Pediátrica

- Clasificación: Panamá 2011

A consensus approach to the classification of pediatric pulmonary hypertensive vascular disease: Report from the PVRI Pediatric Taskforce, Panama 2011

Pulmonary Circulation | April-June 2011 | Vol 1 | No 2

Table 1: The broad schema of 10 basic categories of Pediatric Pulmonary Hypertensive Vascular Disease

Category	Description
1	Prenatal or developmental pulmonary hypertensive vascular disease
2	Perinatal pulmonary vascular maladaptation
3	Pediatric cardiovascular disease
4	Bronchopulmonary dysplasia
5	Isolated pediatric pulmonary hypertensive vascular disease (isolated pediatric PAH)
6	Multifactorial pulmonary hypertensive vascular disease in congenital malformation syndromes
7	Pediatric lung disease
8	Pediatric thromboembolic disease
9	Pediatric hypobaric hypoxic exposure
10	Pediatric pulmonary vascular disease associated with other system disorders

1. Enfermedad Vascular Hipertensiva Pulmonar (EVHP) PRENATAL.

1.1. Asociada con Anomalías Maternas or Placentarias: corioamnionitis, preeclampsia,...

1.2. Asociada con Anomalías en el Desarrollo del Pulmón Fetal: displasia alveolo-capilar, hipoplasia pulmonar, hernia diafragmática congénita, ..

1.3. Asociada con Anomalías en el Desarrollo del Corazón Fetal: cierre prematuro intraútero del ductus o el foramen ovale, drenaje venoso pulmonar anómalo obstructivo,...

2. Hipertensión Pulmonar persistente del recién nacido (HPPRN) (Maladaptación vascular pulmonar perinatal)

2.1. HPPRN Idiopática.

2.2. Asociada a o desencadenada por: sepsis, aspiración meconial, Cardiopatía congénita, hernia diafragmática, trisomías, fármacos (diazoxido).,..

3. Enfermedad Cardiaca Pediátrica

3.1. Shunts sistémico – Pulmonares

3.2. EVHP tras reparación de cardiopatía congénita: shunts, D-TGA, Fallot, obstrucción corazón izquierdo...

3.3. EVHP tras la paliación de cardiopatías con fisiología Univentricular (Glenn, Fontan,...)

3.4. EVHP asociada con Anomalías Congénitas de las Arterias o Venas Pulmonares

3.5. Hipertensión Pulmonar Venosa (secundaria a enfermedad del corazón izquierdo)

4. Displasia Broncopulmonar

4.1. Asociada con Hipoplasia Vascular Pulmonar

4.2. Asociada conEstenosis de Venas Pulmonares

4.3. Asociada con Disfunción diastólica del ventrículo izquierdo

4.4. Asociada con shunts sistémico- pulmonares (ductus, CIA, CIV, colaterales aorto-pulmonares

4.5. Asociada con hipercabia y/o hipoxia significativas

5. Enfermedad Vascular Hipertensiva Pulmonar Aislada

5.1. Idiopática

5.2. Hereditaria

5.3. Fármacos y toxinas

5.4. Enfermedad Veno-oclusiva Pulmonar y Hemangiomatosis Capilar Pulmonar

6. EVHP Multifactorial en Síndromes Polimalformativos

6.1. Con Cardiopatía Congénita asociada

6.2. in Cardiopatía Congénita asociada

7. Enfermedad Pulmonar Pediátrica:

Fibrosis quística, neumopatías interstitiales, síndromes de apnea obstructiva del sueño (SAOS), neumopatías restrictivas, anomalías de la caja torácica, enfermedad pulmonar obstructiva crónica...

8. Enfermedad Tromboembólica Pediátrica causante de EVHP:

Tromboembolismo asociado a catéres venosos centrales, cables de marcapasos endovenosos, enfermedad de células falciformes, fobroelastosis endocárdica primaria, acidemia metilmalónica y homocistinuria, tumores (Tumor de Wilms, osteosarcoma),postesplenectomía,...

9. Exposición a Hipoxia Hipobárica en Edad pediátrica:

Forma infantil del edema pulmonar de grandes alturas, forma subaguda de la enfermedad de montaña, exposición a hipoxia hipobárica asociada a HPPRN, cardiopatía congénita, ...

10. Enfermedad Vascular Hipertensiva Pulmonar Asociada con Trastornos de otros órganos o sistemas:

10.1. Hipertensión portal pediátrica (shunt portocava congénitos, cirrosis hepàtica)

10.2. Enfermedades hematológicas

10.3. Enfermedades oncológicas

10.4. Enfermedades metabólicas o endocrinológicas

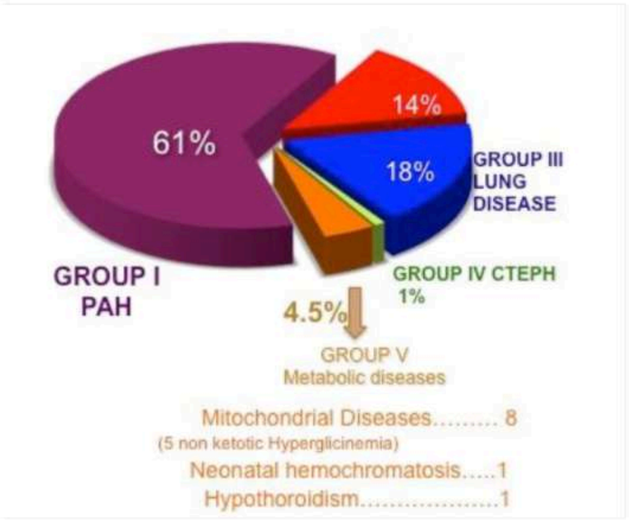
10.5. Enfermedades autoinmunes o inflamatorias pediátricas

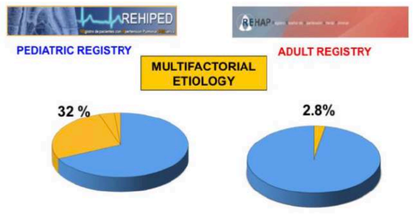
10.6. Enfermedades infecciosas pediátricas

10.7. Insuficiencia renal crónica pediátrica

Hipertensión Pulmonar en la Edad Pediátrica

- **EPIDEMIOLOGÍA:**
  - IPAH: 0.7/ 1.000.000
  - Asociada a CC: 2.2/1.000.000
  - Grupo 1 : 66%
  - GRUPO 2 : 14%
  - GRUPO 3 18%
  - GRUPO 4 : <1%
  - GRUPO 5 : 4,5 %
  - 31% varias etiología a la vez.





- **DIAGNÓSTICO**
  - Retraso. Caso clínico.
    Equipo multidisciplinar
    Centro Referencia
    Múltiples P.C
    Cateterismo
    Genética

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Clasificación

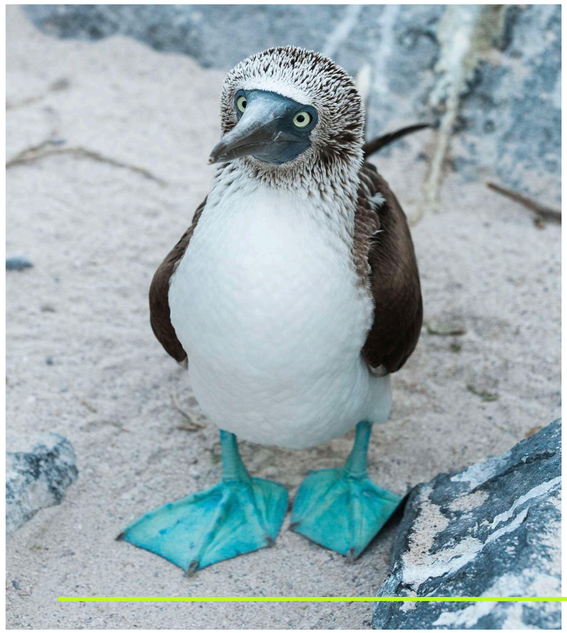
WHO classification

Grupo 1 : HIPERTENSIÓN ARTERIAL PULMONAR

- HAPI: idiopática
- Heredable: BMPR2 80%, otros (TGF-B, ALK -1, ENG, CAv-1…)
- Inducida por DROGAS: Benfluorex, Interferon (aumenta resistencias vasculares pulmonares) Sd aceite de colza.
- HAPA: Asociada a :
  - Asociada a enf de tej conectivo: ESCLERODERMIA 7-12 % prevalencia
  - VIH: 0,5 % prevalencia
  - Hipertensión portal
  - Cardiopatías congénitas (Shunt)
  - Esquistosomiasis

Grupo 1: HIPERTENSIÓN ARTERIAL PULMONAR

Asociada a CC



- CIA, CIV, Canal AV, DAP… (shunt, hiperaflujo pulmonar)
- 10% de los adultos con CC tienen HTP (irán disminuyendo conforme se reparen más tempranamente)
- Determinante pronóstico y de calidad de vida
- Shunt :difícil manejo, supone un dilema de manejo terapéutico, el cierre puede curar al paciente o transformar en peor pco.

- No incluyen :
  - Patología cardiaca postcapilar : GRUPO 2.
  - Presencia de HTP en algún lóbulo aislado, tras reparación de CC, grupo 5
  - HT asociada a TGV sin shunt SP. Mecanismo fisiopatológico no claro.

Hipertensión Pulmonar en la Edad Pediátrica

- **PPHN: Hipertensión Pulmonar persistente del RN.**
- Causa más frecuente de Hipertensión pulmonar transitoria.
- FR Preeclampsia, coriamnionitis
- 30 casos /millon. En aumento. Mayor riesgo en menor edad gestacional.
  - 18,5 % EG 22-24 sem
  - 4,4 % EG 27 sem
- Dco: clínico y ecocardiográfico (Shunt, RVP/RVS >0.5)
- 11% mortalidad.
- Riesgo futuro de desarrollo de HTP.
- Tratamiento:
  - Indice oxigenación >25: iNO
  - Milrinona

  - Milrinona
  - Sildanafilo, bosentan, prostaciclinas.
  - ECMO
  - Displasia alveolo- capilar o enfermedad surfactante.

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Clasificación

- Grupo 2:
  - Asociada a enfermedad corazón izquierdo, POSTCAPILAR:
    - Estenosis de venas pulmonares
    - Estenosis mitral
    - Disfunción diastólica y/o sistólica del VI.
    - Estenosis Ao
    - Coartación AO.

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Clasificación

GRUPO 3

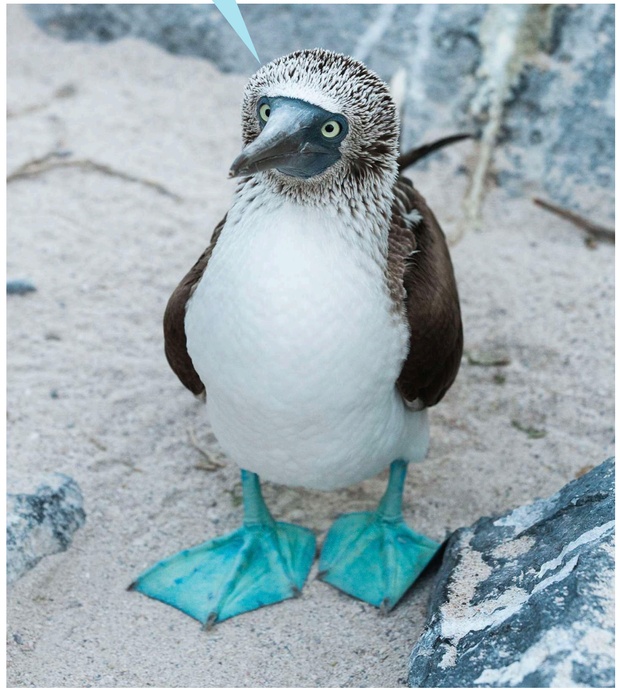
DEBEN REALIZARSE ECOCARDIOGRAFÍA DE SCREENING PARA DESCARTAR EXISTENCIA DE HTP (SOBRE TODO FASES AVANZADAS DE LA ENFERMEDAD)

- Secundaria a enfermedad respiratoria

  - Apneas obstructivas

  - Patología crónica difusa respiratoria, enfermedad intersticial 32-39% prevalencia, sobre todo con fibrosis y enfisema.

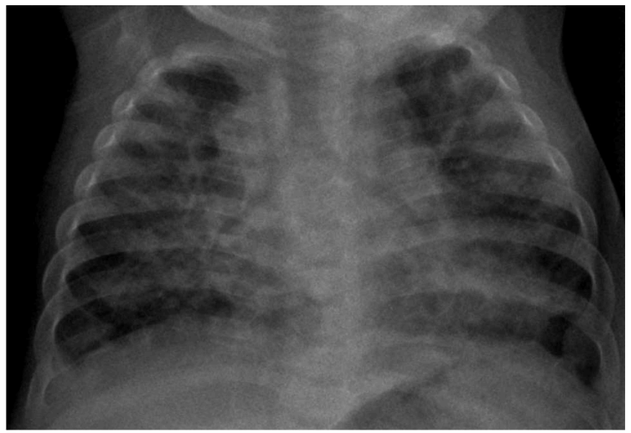
    - ReHiPed Grupo 3: 82 pacientes
      - 52% DBP (infraestimado)
      - 33% Otros trastornos del desarrollo pulmonar
        - Hernia diafragmática congénita
        - Displasia alveolo-capilar
        - Sd Genéticos: Sd Down
      - 7% Ttnos obstructivos crónicos.



Hipertensión Pulmonar en la Edad Pediátrica

Displasia broncopulmonar

- Es una enfermedad pulmonar crónica asociada con un nacimiento prematuro como consecuencia del impacto de diferentes factores de riesgo en el pulmón neonatal subdesarrollado.
- Cada vez más numeroso en Pediatría:
- Aumento de RN pretérminos y supervivencia de EG cada vez menores. Aumento de screening para su diagnóstico.
- Definición DBP: Necesidad de O2 suplementario a las 36 sem de edad post-concepcional en RN <32 sem de EG.



- 40% (EG< 28 sem)
- HTP :
  - 6% DBP leve,
  - 12% DBP moderada,
  - 39% DBP severa (rango 15-64%).
  - Empeora drásticamente el pco de la enfermedad pulmonar. tasas de supervivencia a los 3 años del 52%-66%

Hipertensión Pulmonar en la Edad Pediátrica

- **DBP: Displasia Broncopulmonar**

- SCREENING : con ECOCARDIOGRAFÍA: a pie de cama del neonato.
  - Hipoxia severa con enfermedad parenquimatosa mínima
  - >7 días con soporte respiratorio
  - Al dco de DBP sobre todo si es moderada/severa.

- BIOMARCADORES: PRO-BNP-NT, BNP: REL PMPa.
- Malformaciones asociadas (Shunt, venas pulmonares)

- CATETERISMO:
- Recomendable previo a inicio de terapia vasodilatadora.
- Descartar colaterales S-P, Estenosis de VVPP, HTP postcapilar…
- Riesgo alto en paciente crítico

- PRONÓSTICO
  - Benigno en principio, con desaparición de la HTP.
  - Riesgo recurrencia con infecciones respiratorias
  - Riesgo tardío de desarrollo de HTP (con el ejercicio)
  - Función pulmonar y de Vd disminuidas

Table 1 – Infant characteristics associated with the presence of pulmonary hypertension.

Characteristic	Infants with or without BPD RR(CI)	Infants with BPD RR(CI)
Male sex	1.1 (0.9, 1.3)	0.9 (0.7, 1.2)
SGA	1.8 (1.2, 2.)	0.5 (0.1, 1.8)
BPD	1.3 (1.1, 1.5)	NA
Severe BPD	2.7 (1.7, 4.2)	NA
NEC	1.8 (0.9, 3.9)	3.4 (1.1, 10.2)
PDA	1.3 (1.2, 1.5)	1.2 (1.0, 1.5)
PDA ligation	1.8 (1.3, 2.4)	NA
Severe IVH	1.7 (0.8, 3.4)	NA
ROP	1.9 (1.3, 2.7)	1.2 (0.8, 1.9)

BPD, bronchopulmonary dysplasia; RR, risk ratio; CI, confidence interval; NA, data not available;
SGA, small for gestational age; ROP, retinopathy of prematurity; NEC, necrotizing enterocolitis; PDA,
patent ductus arteriosus. Adapted from reference (9).

Hipertensión Pulmonar en la Edad Pediátrica

- Tto DBP
  - Equipo multidisplinar
  - Descartar malformaciones asociadas y cc.
  - Determinación seriada de Probnp.
  - Casos selecionados : cateterismo.
  - INO para crisis de HTp.
  - O2 : para sat O2 92-95% (Class I, level B)
  - Terapia específica con vasodilatadores (Class I , level B)

Table IV. Pharmacotherapy of pulmonary hypertension in BPD

Names	Dose/titration	Side effects	Comments
Sildenafil phiosphodiesterase-5 inhibitor	PO: 1 mg/kg 6-8 h; start with low dose (0.3-0.5 mg/kg/dose) and increase gradually to 1 mg/kg/dose as tolerated; slower as outpatient. Maximal dose of 10 mg q 8 h per EMA guidelines for infants. Intravenous:0.25-0.5 mg/kg/dose q 6-8 h (titrate slowly and administer over 60 min.	Hypotension, GER, irritability (headache), bronchospasm, nasal stuffiness, fever, rarely priapism	Monitor for adverse effects, lower the dose or switch to alternate therapy if not tolerated
Bosentan (Endothelin receptor antagonist)	1 mg/kg PO q 12 h as starting dose; may increase to 2 mg/kg BID in 2-4 wk, if tolerated and liver enzymes stable.	Liver dysfunction especially during viral infections, VQ mismatch, hypotension, anemia (edema and airway issues rare in infants)	Monitor LFTs monthly (earlier with respiratory infections); monitor CBC quarterly. Teratogenicity precautions for caregivers
Inhaled Iloprost	2.5-5 mcg every 2-4 h. Can be given as continuous inhalation during mechanical ventilation. Can titrate dose from 1-5 mcg and frequency from every 4 h to continuous.	Bronchospasm, hypotension, ventilator tube crystallization and clogging, pulmonary hemorrhage, prostanoid side effects (GI disturbances), may be teratogenic to caregivers	Need close monitoring for clogged tubing, may need further dilution. May need bronchodilators or inhaled steroid pretreatment with bronchospasm.
Intravenous Epoprostenol (Flolan)	Start at 1-2 ng/kg/min, titrate up slowly every 4-6 h to 20 ng/kg/min; need to increase dose at regular intervals because of tachyphylaxis. Further increases as guided by clinical targets and avoiding adverse effects.	Hypotension, VQ mismatch, GI disturbances. Needs dedicated line, very short half-life with high risk for rebound PH with brief interruption of therapy; line related complications include infection, clogging, breaks in line, thrombosis, arrhythmia)	Monitor closely if added to other vasodilator therapies, such as milrinone; careful attention to line care is essential.
Treprostinil (Remodulin) IV or Subcutaneous	Start at 2 ng/kg/min and titrate every 4-6 h up to 20 ng/kg/min, then slow increase dose as tolerated (dose often 1.5-2 times greater than equivalent epoprostenol dose, if switching medications)	SQ: local site pain; IV: similar risks as with epoprostenol, but treprostinil has a longer half- life, which reduces risk for severe PH with interruption of infusion	Site pain managed with local and systemic measures
Milrinone (IV) (phosphodiesterase-3 inhibitor)	0.15-0.5 mcg/kg/min –lower dosage range when used with other vasodilators	Arrhythmogenic; systemic hypotension and high risk for decreased myocardial perfusion; caution with renal dysfunction	May need to add a pressor, such as vasopressin, to mitigate effects of decrease in systemic pressures.

BID, twice a day; *CBC*, complete blood count; *EMA*, European Medicines Agency; *GER*, gastroesophageal reflux; *GI*, gastrointestinal; *IV*, intravenous; *kg*, kilogram; *LFT*, liver function tests; *mcg*, microgram; *ng*, nanogram; *PO*, oral; *SC*, subcutaneous; *SR*, sustained release; *VQ*, ventilation-perfusion.

Evaluation and Management of Pulmonary Hypertension in Children with Bronchopulmonary Dysplasia

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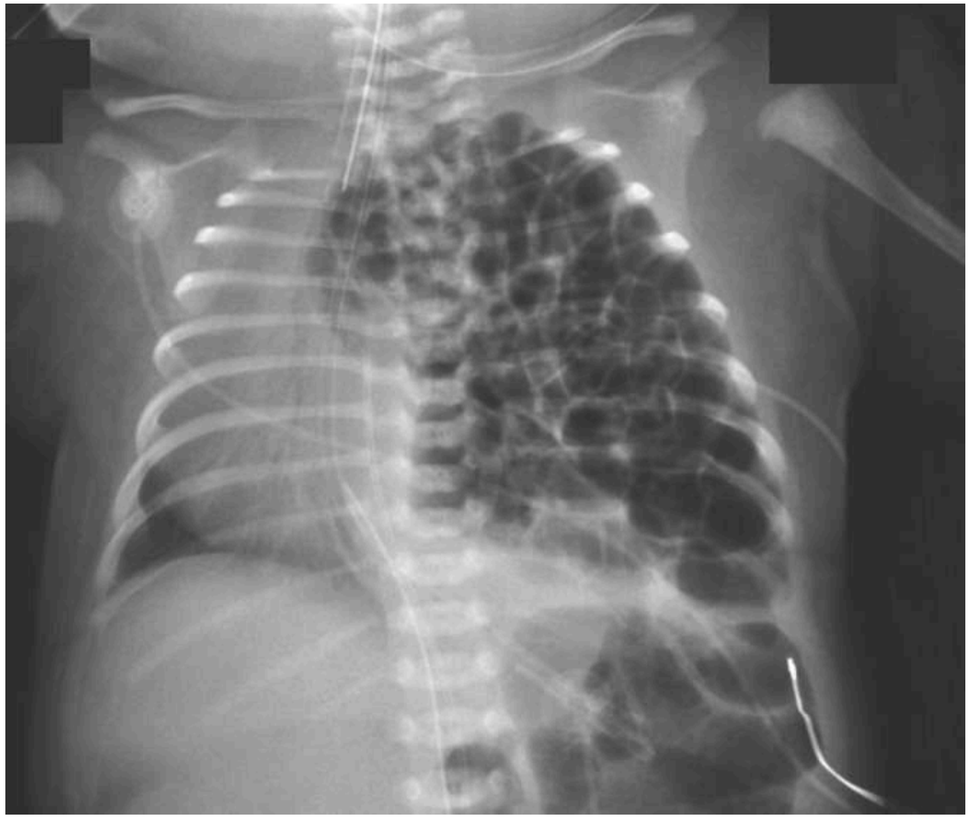
THE JOURNAL OF PEDIATRICS

Hipertensión Pulmonar en la Edad Pediátrica

- **Hernia diafragmática congénita.**
- 2/3 tienen presión sistólica pulmonar> 2/3 de las sistémicas
- Hipoplasia vascular. Pulmón contralateral.
- Aumento morbimortalidad:
  - PSP/SBP < 0.5 supervivencia 98%
  - PSP/SBP 0.5-0.67 : supervivencia 92%
  - PSP/SBP >0.67: supervivencia 43%



Clasificación

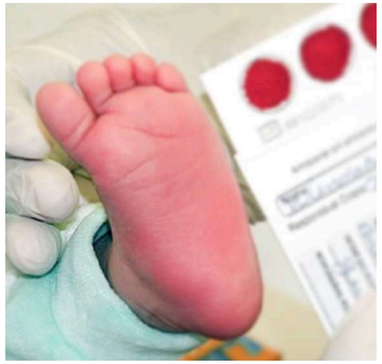
4. Chronic thromboembolic pulmonary hypertension and other pulmonary artery obstructions
4.1 Chronic thromboembolic pulmonary hypertension
4.2 Other pulmonary artery obstructions
4.2.1 Angiosarcoma
4.2.2 Other intravascular tumors
4.2.3 Arteritis
4.2.4 Congenital pulmonary arteries stenoses
4.2.5 Parasites (hydatidosis)
5. Pulmonary hypertension with unclear and/or multifactorial mechanisms
5.1 Haematological disorders: chronic haemolytic anaemia, myeloproliferative disorders, splenectomy
5.2 Systemic disorders, sarcoidosis, pulmonary histiocytosis, lymphangioleiomyomatosis
5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
5.4 Others: pulmonary tumoral thrombothic microangiopathy, fibrosing mediastinitis, chronic renal failure (with/without dialysis), segmental pulmonary hypertension

GRUPO 4: Tromboembólica crónica.

- GRUPO 5: Mecanismos fisiopatológicos inciertos:
  - E. hematológicas: hemoglobinopatías hemofílicas: anemia hemolítica crónica (prev: 3%, muy similar a a la HAPI, contraindicado sildenafilo, aumenta crisis agudas)
  - E. renales
  - E. sistémicas y metabólicos con síntomas cardiorrespiratorios, otros...

Hipertensión Pulmonar en la Edad Pediátrica

- **METABOLOPATÍAS:**
  - Trastornos del metabolismo de los aminoácidos
  - Hiperglicemia no cetósica, Mutacion gen NFU
  - Enfermedades mitocondriales.
  - Enfermedad Gaucher, Trastornos tiroides.
  - Debut HTP puede ser primario.
  - Muy mal pronóstico
  -



Diagnóstico clínico.

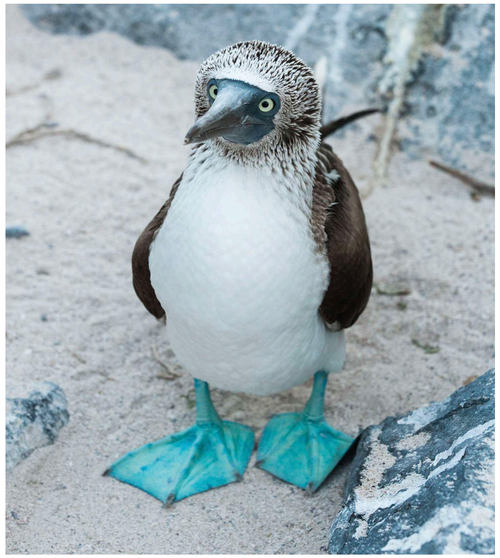
- Asintomático mientras el VD mantiene su función sistólica, hipertrofia , mecanismo de adaptación secundario al incremento de postcarga.
- Alteración de función sistólica y/o diastólica: signos de bajo gasto e insuficiencia cardiaca dcha.
- Sintomas: síncopes, disnea, deterioro funcional, intolerancia al ejercicio. Crisis. Decaimiento en lactantes. Palpitaciones. Dolor precordial.
- Debut: suele ser un diagnóstico tardío, cuando aparecen síntomas ya estamos en fase avanzada de la enfermedad.
- Sin tratamiento, supervivencia media de 2,8 años
- Screening en grupos de riesgo: ecocardiografía

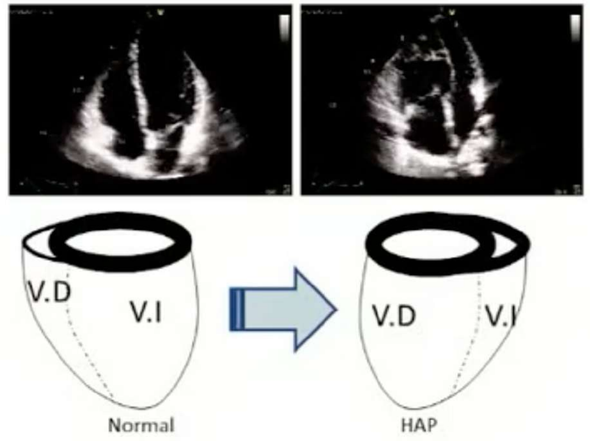
Diagnóstico ecocardiográfico

SCREENING

VD SE CONVIERTE EN PROTAGONISTA

- Herramienta diagnóstica, etiología, evaluación hemodinámica no invasiva, seguimiento y pronóstico.





Diagnóstico ecocardiográfico

SCREENING

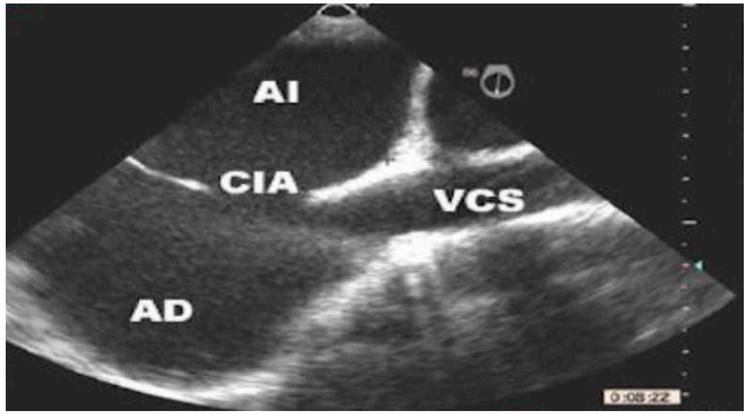
- Papel fundamental para detección de la HTP. Primer escalón en el dco.
- Screening población de riesgo:
  - Neumopatía instersticial crónica,
  - Esclerodermia
  - VIH,
  - Shunt S-P,
  - Síncopes de perfil cardiogénico.

Pediatric Pulmonary Hypertension
Guidelines From the American Heart Association and American Thoracic Society

Screening for PH by echocardiogram is recommended in infants with established BPD (*Class I; Level of Evidence B*).

Early evaluation for PH, including a Doppler echocardiogram, is reasonable for children with hemolytic hemoglobinopathies or hepatic, renal, or metabolic diseases who develop cardiorespiratory symptoms (*Class IIa; Level of Evidence C*).
In children with chronic hepatic disease, an echocardiogram should be performed to rule out portopulmonary hypertension (PPHTN) and pulmonary arteriovenous shunt before they are listed for liver transplantation (*Class I; Level of Evidence B*).
It is reasonable for children with SCD to undergo an echocardiogram to screen for PH and associated cardiac problems by 8 years of age or earlier in patients with frequent cardiorespiratory symptoms (*Class IIa; Level of Evidence C*).

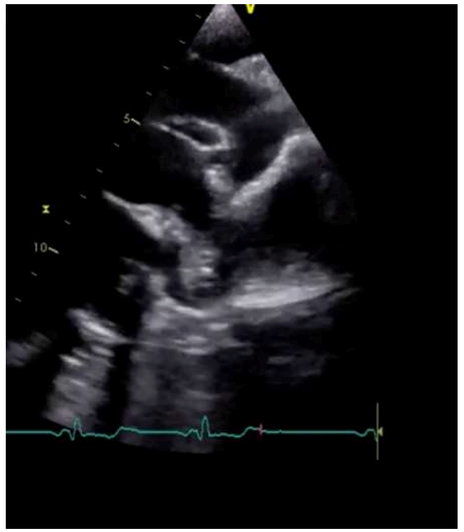
Echocardiography is recommended to assess PH and RV function in patients with severe obstructive sleep apnea (OSA) (*Class I; Level of Evidence B*).
For exercise-limited patients with advanced lung disease and evidence of PAH, the following are recommended:

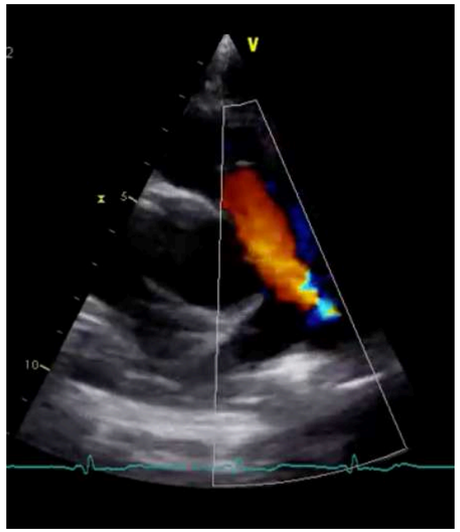


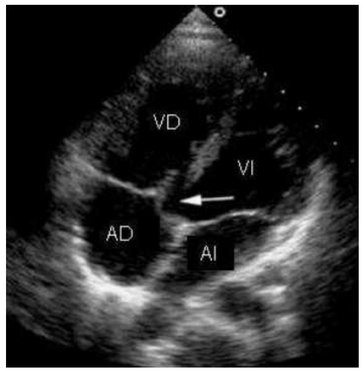
Ecocardiografía: Diagnóstico etiológico

- Diagnóstico de Shunt:
  - Intracardiacos: CIA, CIV …
  - Extracardiacos: DAP

- Diagnóstico diferencial de HT postcapilar.

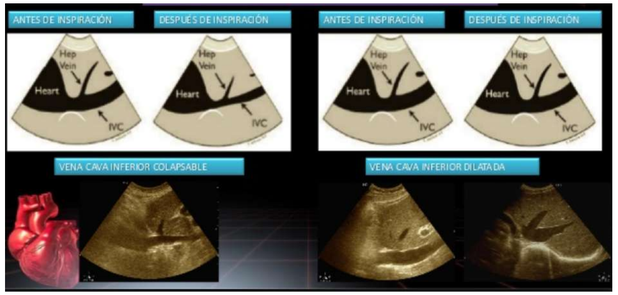






Ecocardiografía: valoración hemodinámica no invasiva, estimación de presiones.

- **1. PADm (presión AD)** :
  - Colapsabilidad de la VCI
  - Colapsabilidad >50%: buen predictor de PADm <10 mmhm (5 mmhg)
  - Si TiA abomba de D-I y suprahepáticas dilatadas : buen predictor de PADm > 10 mmhm (15 mmhg)

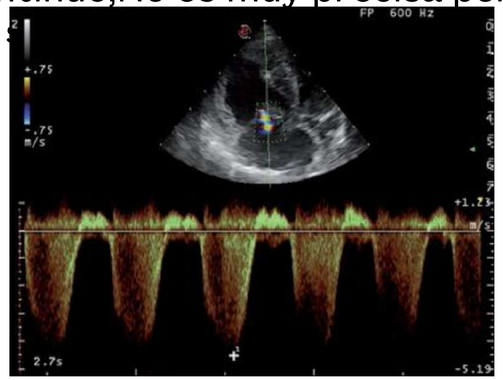


- **2. PSP (presión sistólica pulmonar):**
  - Estimación de la presión pulmonar sistólica pulmonar
    - Gradiente VD-AD (IT): doppler continuo,No es muy precisa pero es para estudio poblacionales y como

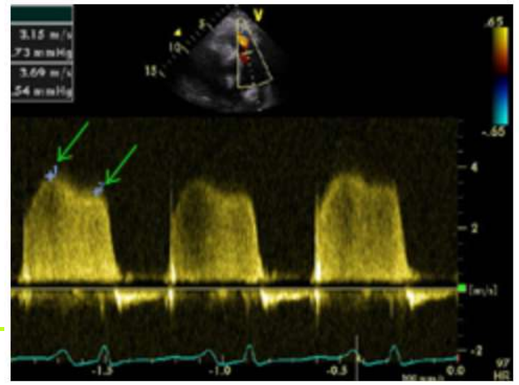
LEVE	MODERADA	GRAVE
36-45 mmHg	45-60 mmHg	>60 mmHg

Técnicas de imagen no invasivas en hipertensión pulmonar: ecocardiografía

3



- **3. PAPm (presión media pulmonar)**
  - Estimación de la presión pulmonar media pulmonar
  - Gradiente pico AP- VD en protodiástole (IP): doppler continuo,



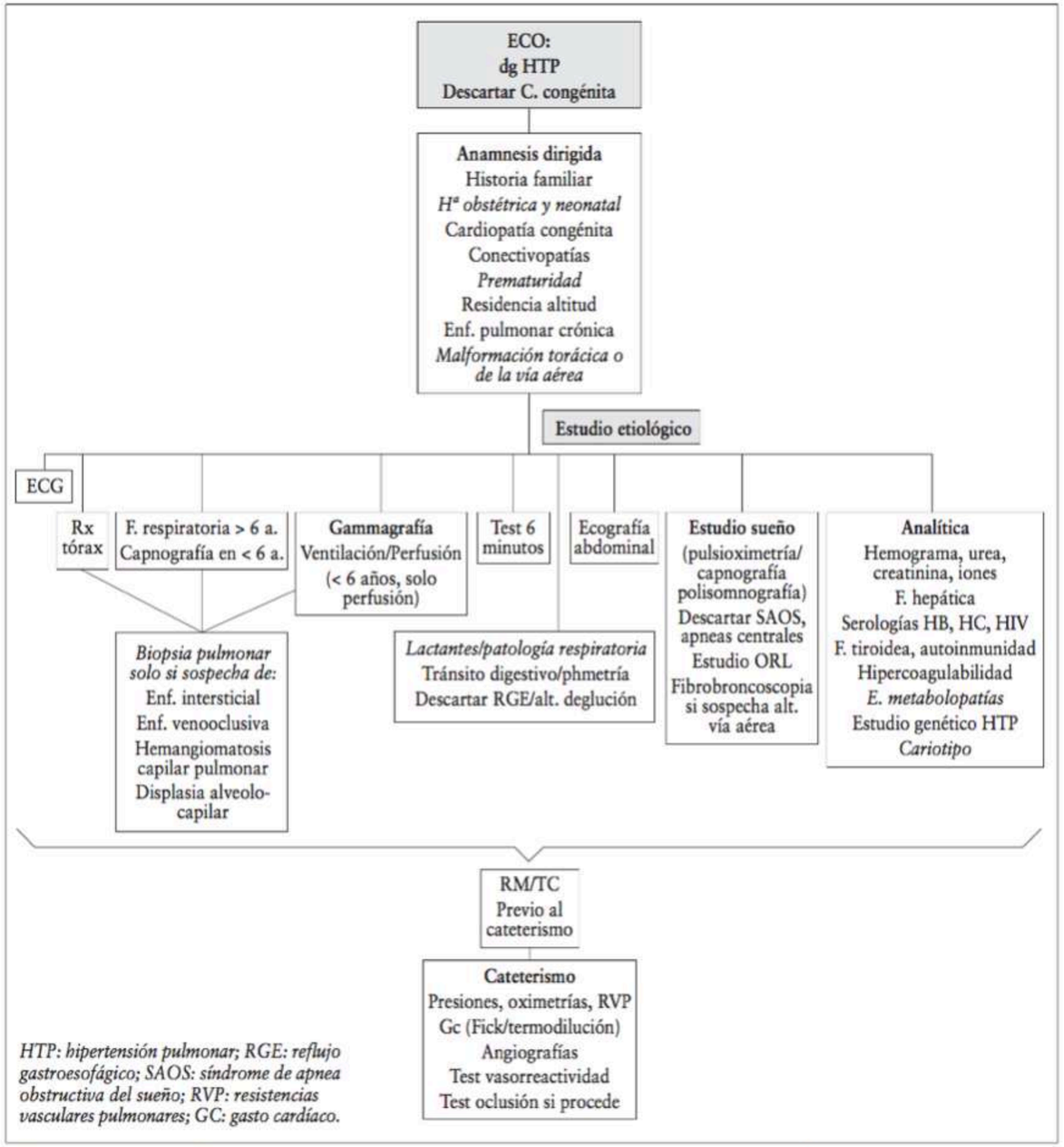


FIGURA 1. Algoritmo diagnóstico para la hipertensión pulmonar pediátrica. *(Modificado de: Mullen P. Crit Care Med 2010;11(suppl): S22-S26).*

Pediatric Pulmonary Hypertension

Guidelines From the American Heart Association and American Thoracic Society

At the time of initial PH diagnosis, a comprehensive history and physical examination, combined with diagnostic testing for assessment of PH pathogenesis/classification and formal assessment of cardiac function, should be performed before the initiation of therapy at an experienced center *(Class I; Level of Evidence B)*.

Analítica

- Serologías HB, HC, VIH.
- TSH.
- Función hepática y renal
- Autoinmunidad
- Hipercoagubilidad
- Enfermedades metabólicas: descartar errores congénitos del metabolismo: aa sangre, orina, LCR
- Genética (H la Paz)
- Cariotipo
- NT- porBNP. marcador pronóstico

- Lactantes: RGE, alteraciones deglución, cursa con aspiraciones, muy frecuentes en prematuros, polimarfomados, patología pulmonar.
- Estudio del sueño: pulsioximetría, capnografía, polisomnografía,ORL.

The recommendations for a sleep study are the following:

a. A sleep study should be part of the diagnostic evaluation of patients with PH at risk for sleep-disordered breathing (*Class I; Level of Evidence B*).

b. A sleep study is indicated in the evaluation of patients with poor responsiveness to PAH-targeted therapies (*Class I; Level of Evidence B*).

PPCC MEJOR ANTES DEL CATETERISMO

CATETERISMO CARDIACO

- GOLD STANDARD, necesario por definición para el diagnóstico.
- Debe realizarse al diagnóstico siempre, exceptuando pacientes gravemente enfermos. Repetir tras 3-12 meses de tto.
- Medida directa de PAPm
- Severidad
- Vasorreactividad
- Respuesta a agentes terapéuticos
- Causa: Shunt, postcapilar

Hipertensión pulmonar:

PAPm> ó = 20 mmhg

RVP >3 UW

Precapilar: PCP<ó = 15 mmhg;

Poscapilar PCP >15 mmhg

Pediatric Pulmonary Hypertension

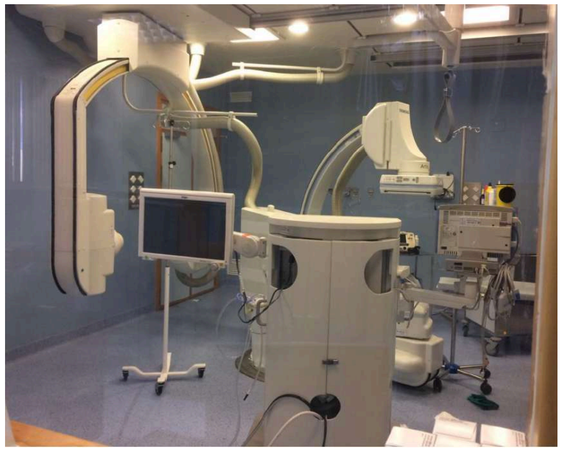
Guidelines From the American Heart Association and American Thoracic Society

Serial cardiac catheterizations with AVT are recommended as follows:

a. Serial cardiac catheterizations should be done during follow-up to assess prognosis and potential changes in therapy (*Class I; Level of Evidence B*)

b. Intervals for repeat catheterizations should be based on clinical judgment but include worsening clinical course or failure to improve during treatment (*Class I; Level of Evidence B*).

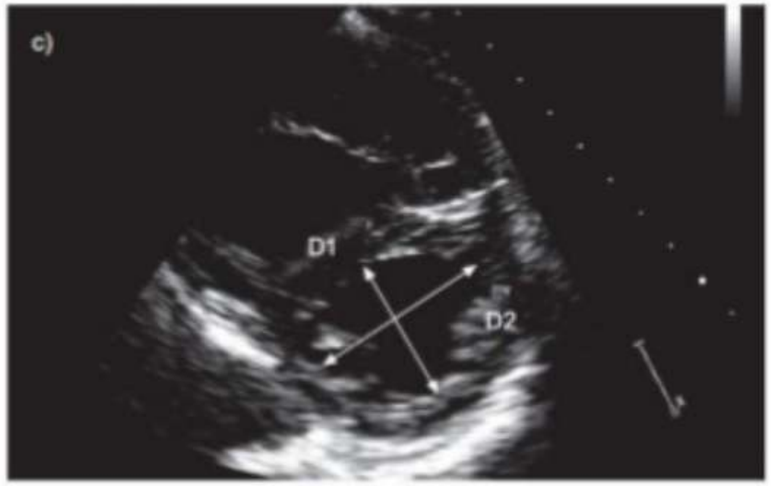
Hipertensión Pulmonar en la Edad Pediátrica

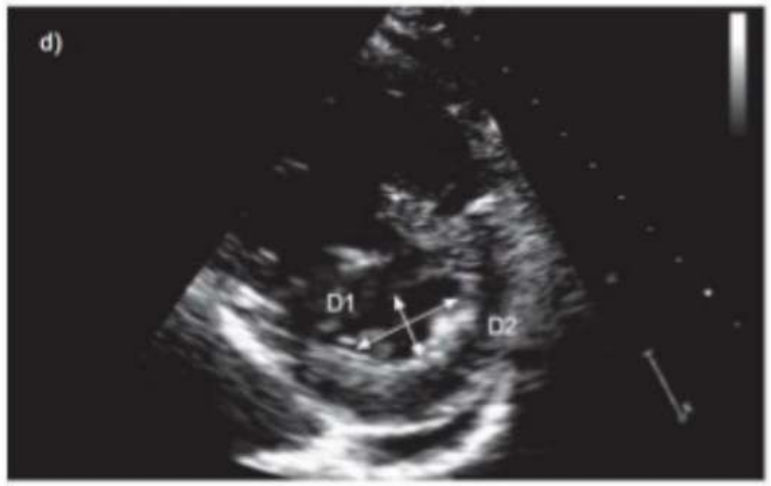


- **CATETERISMO:**
- Unidad dco de referencia.
- Dosis de radiación.
- Anestesia general. Riesgo elevado.
- Frecuencia menor de lo recomendado en Guías.
- Vía femoral. Presión simultánea sistémica. Cálculo de resistencias, presiones y GC.
- Realización arteriografía pulmonar. Vascularización pulmonar.
- Descartar anomalías cardiacas y/ó vasculares.
- Intervencionismo: Cierre de DAP, fístulas, etc…
- Test Vasorreactividad con Óxido Nítrico y Oxígeno.
- Interpretación de resultados.
  - Debe realizarse:
    - Al diagnóstico
    - Efecto del tratamiento
    - Ante deterioro clínico

Ecocardiografía: Seguimiento, parámetros pronósticos

- Parámetros de Interdependencia ventricular. Tamaño, función, forma, distensibilidad de uno afecta al otro.
- El Vd desplaza y comprime el izdo, en una cavidad limitada, bajo gasto.
- SIV Tipo I, II,III.
- Rel D/I: diastólico. Mayor valor peor.
- Índice de excentricidad:
  - Rel entre los dos ejes (paralelo y perpendicular al septo)
  - Sistólico y diastólico.
  - Normal = 1





RMN

- Valoración de Vd: morfológica, funcional, del lecho vascular pulmonar.
- Fe del VD predictor más fuerte de mortalidad (si es menor de 35% después de 6 meses de tto)
- Valor diagnóstico y pronóstico.
- QP/QS
- Volúmenes indexados: telediastólico y telesistólico: valor pco independiente de mortalidad
- Presencia de realce tardío con gadolino, áreas miocárdicas fibróticas.

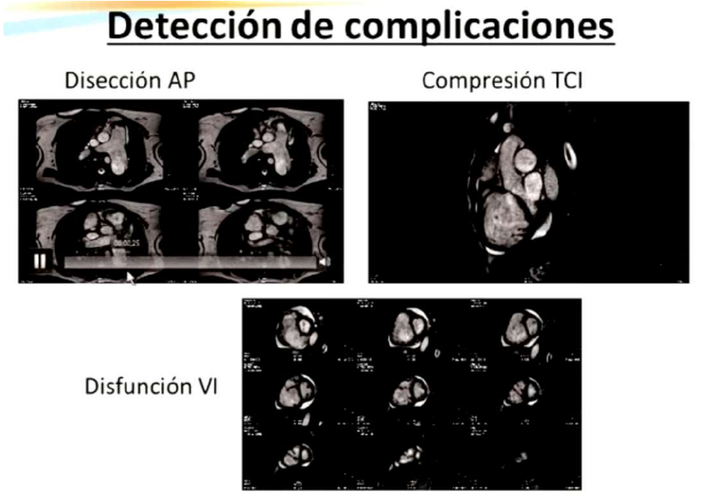


Tabla de riesgo pediátrico

2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension

Determinants of prognosis[a] (estimated 1-year mortality)	Low risk <5%	Intermediate risk 5–10%	High risk >10%
Clinical signs of right heart failure	Absent	Absent	Present
Progression of symptoms	No	Slow	Rapid
Syncope	No	Occasional syncope[b]	Repeated syncope[c]
WHO functional class	I, II	III	IV
6MWD	>440 m	165–440 m	<165 m
Cardiopulmonary exercise testing	Peak VO_2 >15 ml/min/kg (>65% pred.) VE/VCO_2 slope <36	Peak VO_2 11–15 ml/min/kg (35–65% pred.) VE/VCO_2 slope 36–44.9	Peak VO_2 <11 ml/min/kg (<35% pred.) VE/VCO_2 ≥45
NT-proBNP plasma levels	BNP <50 ng/l NT-proBNP <300 ng/ml	BNP 50–300 ng/l NT-proBNP 300–1400 ng/l	BNP >300 ng/l NT-proBNP >1400 ng/l
Imaging (echocardiography, CMR imaging)	RA area <18 cm^2 No pericardial effusion	RA area 18–26 cm^2 No or minimal, pericardial effusion	RA area >26 cm^2 Pericardial effusion
Haemodynamics	RAP <8 mmHg CI ≥2.5 l/min/m^2 SvO_2 >65%	RAP 8–14 mmHg CI 2.0–2.4 l/min/m^2 SvO_2 60–65%	RAP >14 mmHg CI <2.0 l/min/m^2 SvO_2 <60%

AHA/ATS Consensus Pediatric PAH: Disease Severity

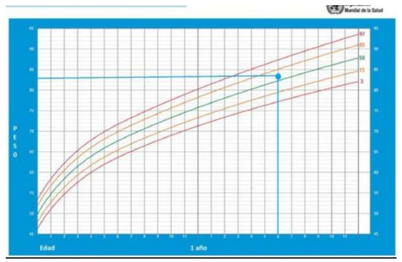
LOWER RISK	DETERMINANTS OF RISK	HIGHER RISK
No	Clinical evidence of RV failure	Yes
I,II	WHO class	III,IV
None	Syncope	Recurrent syncope
Minimal RV enlargement/dysfunction	Echocardiography	Significant RV enlargement/dysfunction Pericardial effusion
PVRI <10 WU•m^2 CI >3.0 L/min/m^2 PVR/SVR <0.5	Hemodynamics	PVRI >20 WU•m^2 CI <2.0 L/min/m^2 PVR/SVR >1.0
Minimally elevated	BNP / NTproBNP	Significantly elevated
Longer (>500 m)	6MWD	Shorter (<300 m)
Peak VO_2 >25 mL/kg/min	CPET	Peak VO_2 <15 mL/kg/min

- PRONÓSTICO
- 3a — 50%
- 1, 3, 5a ——-96%, 84% y 74%.
- FR independientes, según Rehiped:
  - Etiología
  - Edad <2a al dco.
  - Avanzada clase funcional
  - PAD muy elevada.

- SÍNCOPE : en niños + fc, < valor pco.
- Test 6 minutos
- Futuro: biomarcadores genéticos, proteómicos, epigenéticos.

Hipertensión Pulmonar en la Edad Pediátrica

- TRATAMIENTO:



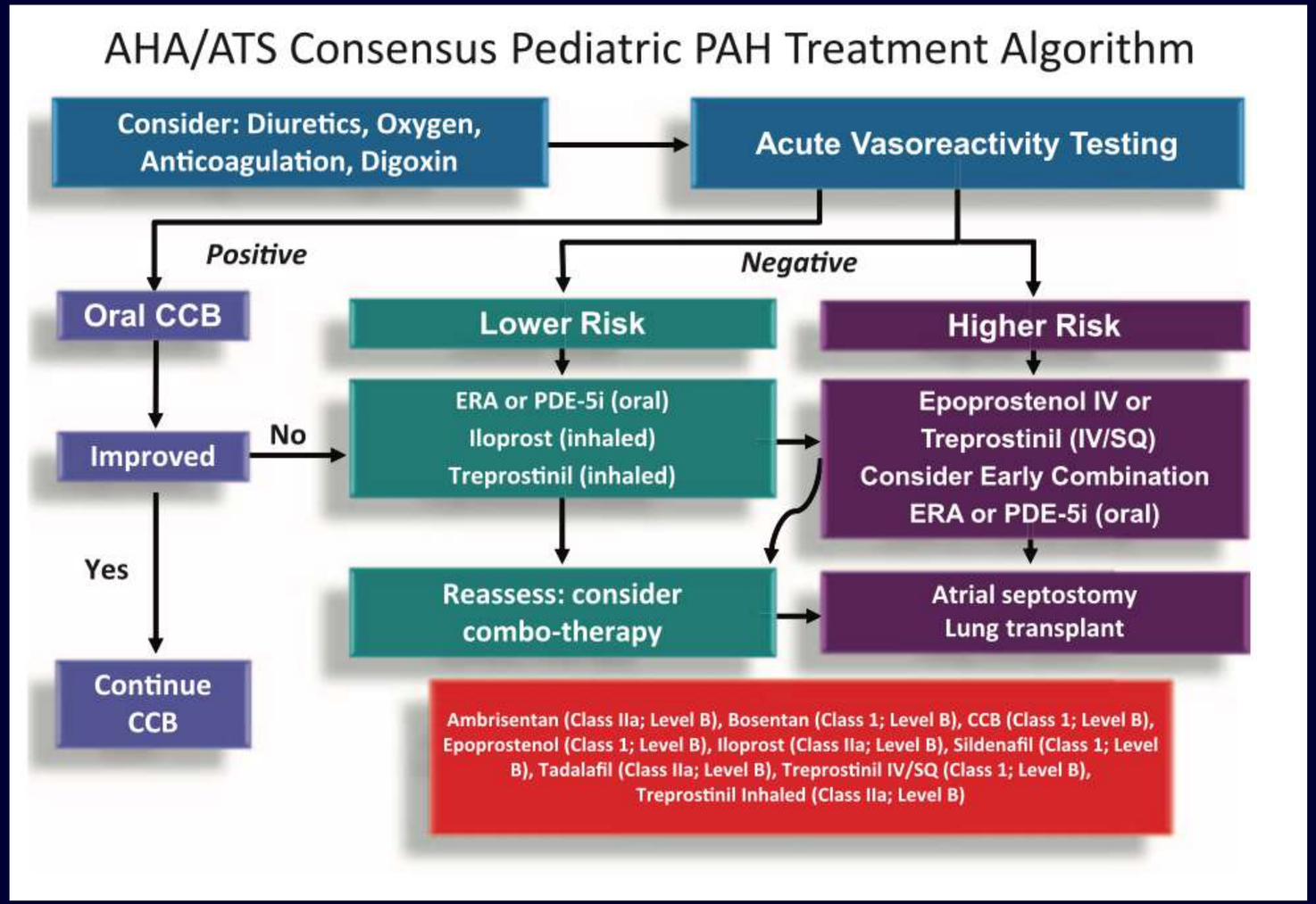
- No existen muchos ensayos clínicos en niños. Consenso expertos.
- RESPIRATORIO: terapia con oxígeno, tratamiento de procesos bronquiales, apneas del sueño, procesos alérgicos. Reconocimiento precoz y tratamiento de enfermedades intercurrentes

- DIGESTIVO/NUTRICIÓN: Monitorización de parámetros de crecimiento: percentiles de talla y peso.
  - Medidas generales: O2, anticoagulación.
    - Vacunas: VRS <2a, Gripe >6 m
    - Prevención de infecciones respiratorias
  - Diferencias en respuesta a fármacos:
    - sildenafil neonatos,
  - Diferente farmacocinética y farmacodinámica: prostaciclinas
  - Dificultad para admin de prostanoides.
  - Necesidad de persona responsable
- profilaxis endocarditis para pacientes con cianosis
- Intervenciones: H referencia, anestesistas experimentados.

- Alto riesgo ante enfermedad Covid 19
- Consejo genético, riesgo de embarazo, opciones de contracepción

- Limitación de ejercicio de alta intensidad o de competición (individualizar). Evitar ejercicio isométricos y poder autolimitarse.
- Viajes en avión: suplemento de O2.
- Soporte psicosocial
- Para fallo derecho: diuréticos (comenzar con

Algoritmo tratamiento



PDE5 inhibitor

Sildenafilo

Tadalafilo

CCB

Nifedipino

Amlodipino

Diltiazem

ERA

Bosentan

Ambrisentan

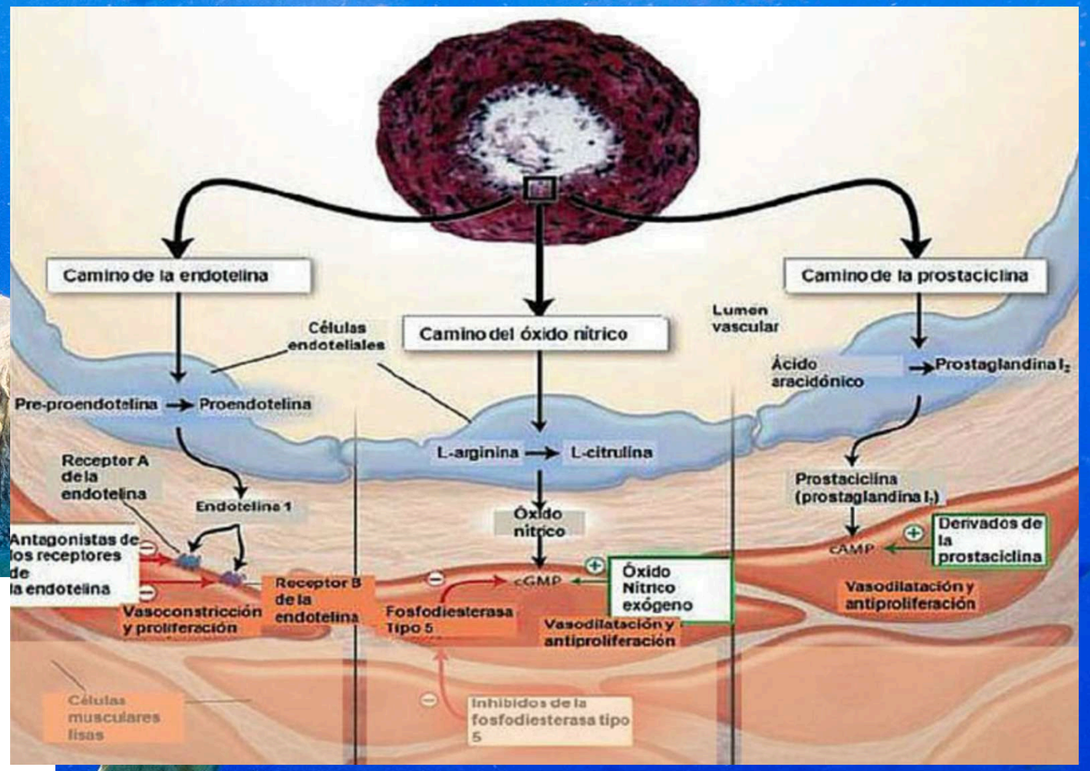
Macitentan

PROSTACYCLIN

Iloprost

Treprostinil

Epopostrenol



				state is reasonable
CCB	Nifedipine	Starting dose: 0.1–0.2 mg/kg orally 3 times daily Dose range: 2–3 mg·kg^{-1}·d^{-1} Maximum adult dose: 180 mg/d orally Always uptitrate from a lower dose If possible, use extended-release preparations	Bradycardia Decreased cardiac output Peripheral edema Rash Gum hyperplasia Constipation	COR I LOE B Duration of benefit may be limited even with initial favorable response; periodic repeat assessments for responsiveness are indicated
CCB	Diltiazem	Starting dose: 0.5 mg/kg orally 3 times daily Dose range: 3–5 mg·kg^{-1}·d^{-1} orally Maximum adult dose: 360 mg/d orally Always uptitrate from a lower dose If possible, use extended-release preparations	Bradycardia Decreased cardiac output Peripheral edema Rash Gum hyperplasia Constipation	COR I LOE B Duration of benefit may be limited even with initial favorable response; periodic repeat assessments for responsiveness are indicated May cause bradycardia more than other CCBs Suspension useful in younger children
CCB	Amlodipine	Starting dose: 0.1–0.3 mg·kg^{-1}·d^{-1} orally Dose range: 2.5–7.5 mg/d orally Maximum adult dose: 10 mg/d orally Always uptitrate from a lower dose	Bradycardia Decreased cardiac output Peripheral edema Rash Gum hyperplasia Constipation	COR I LOE B Duration of benefit may be limited even with initial favorable response

(*Continued*)

Drug Class	Agent	Dosing	Adverse Effects	COR/LOE Comments
PDE5 inhibitor	Sildenafil	Age <1 y: 0.5–1 mg/kg 3 times daily orally Weight <20 kg: 10 mg 3 times daily orally Weight >20 kg: 20 mg 3 times daily orally Delay use in extremely preterm infants until retinal vascularization is established	Headache Nasal congestion Flushing Agitation Hypotension Vision and hearing loss may be concerns Priapism Avoid nitrates	COR I LOE B Avoid higher dosing in children because a greater risk of mortality was noted in the STARTS-2 study in children with IPAH treated with high-dose sildenafil monotherapy Sildenafil approved in Europe and Canada FDA warning for use in children 1–17 y of age
PDE5 inhibitor	Tadalafil	Starting dose: 0.5–1 mg·kg^{-1}·d^{-1} Maximum dose: 40 mg orally daily Evaluated only in children >3 y of age	Headache Nasal congestion Flushing Agitation Hypotension Vision and hearing loss may be concerns Priapism Nosebleeds Avoid nitrates	COR IIa LOE B Once-daily dosing Safety and efficacy data in children are limited
ERA	Bosentan (dual ET_A and ET_B antagonist)	Starting dose is half the maintenance dose Maintenance dose: Weight <10 kg: 2 mg/kg twice daily orally Weight 10–20 kg: 31.25 mg twice daily Weight >20–40 kg: 62.5 mg twice daily Weight >40 kg: 125 mg twice daily	Monthly LFTs required due to risk for hepatotoxicity HCG and pregnancy test required monthly Incidence of AST/ALT elevation is less in children compared with adults Fluid retention Teratogenicity Male infertility May decrease sildenafil level	COR I LOE B Data have been published on efficacy in Eisenmenger PH 2 Forms of birth control required Drug interaction with sildenafil
ERA	Ambrisentan (a highly selective ET_A antagonist)	Dose range: 5–10 mg orally daily Use in pediatric patients <5 y of age is unstudied	Routine LFTs recommended HCT and pregnancy test required Incidence of AST/ALT elevation is less in children compared with adults Fluid retention Teratogenicity Male infertility	COR IIa LOE B Safety and efficacy data in children are limited Avoid use in neonates or infant because glucuronidation is not mature

				Male infertility
Prostacyclin	Epoprostenol (Flolan), Veletri (thermostable)	Continuous intravenous infusion Drug interaction with sildenafil Starting dose: 1–2 ng·kg^{-1}·min^{-1} IV without a known maximum In pediatric patients, a stable dose is usually between 50 and 80 ng·kg^{-1}·min^{-1} IV Doses >150 ng·kg^{-1}·min^{-1} IV have been used Dose increases are required High-output syndrome at high doses can occur	Flushing, jaw, foot and bone pain, headaches, and diarrhea Systemic hypotension is possible Half-life is short (2–5 min), so PH crises occur rapidly if the infusion is stopped Icepack cooling and remixing every 24 h needed Central line complications occur	COR I LOE B Standard therapy for severe PH A temperature-stable formulation is available
Prostacyclin	Treprostinil (Remodulin)	Intravenous or subcutaneous: 2 Starting dose: 2 ng·kg^{-1}·min^{-1} without a known maximum In pediatric patients, a stable dose is usually between 50 and 80 ng·kg^{-1}·min^{-1} IV or SC Dose increases are required	Flushing, muscle pain, headaches, and diarrhea are common side effects Frequency and severity of side effects are less than with epoprostenol Elimination half-life is 4.5 h The drug is stable at room temperature Central line complications can occur, including Gram-negative infections with intravenous route Subcutaneous injection site pain may limit this route	For intravenous and subcutaneous: COR I LOE B
		Inhaled: 1–9 patient-activated breaths every 6 h Oral: dosing not fully evaluated in children	Inhaled drug can worsen reactive airway symptoms GI side effects may be greater than with intravenous, subcutaneous, or inhaled	For inhalation: COR IIa LOE B The nebulizer requires patient activation and controlled inhalation limited by age and development

American Heart Association.
Circulation

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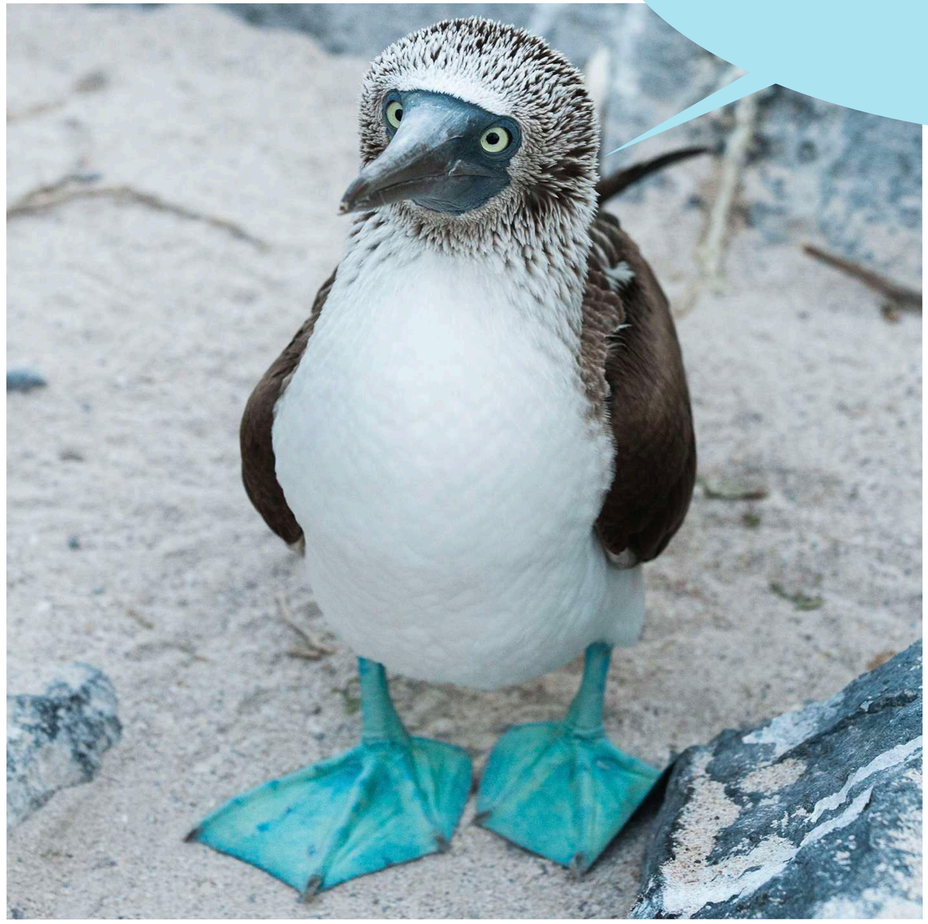

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