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RESEARCH ARTICLE

Hemodynamic phenotypes in congenital diaphragmatic hernia and their association with morbidity and mortality

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Abstract

Background: *Congenital diaphragmatic hernia (CDH) is a severe condition associated with high morbidity and mortality. Its severity correlates with the degree of pulmonary hypoplasia. Recent literature has emphasized the importance of identifying distinct hemodynamic phenotypes (HP) to guide physiology-based management.* **Method:** *We included all CDH patients evaluated by targeted neonatal echocardiography from January 2017 to April 2022. HPs were classified into three groups: HP1 (mild pulmonary hypertension [PH] without ventricular dysfunction), HP2 (pre-capillary PH), and HP3 (post-capillary PH). We compared differences between survivors and non-survivors using the Mann–Whitney U-test, analyzed baseline and pre/post-surgical echocardiographic parameters using the Wilcoxon test, estimated survival curves using Kaplan–Meier analysis, and compared length of stay using the Kruskal–Wallis test.* **Results:** *Among 28 included neonates, 24 survived (86%). HP distribution was: HP1 9 patients (32%), HP2 8 patients (29%), and HP3 11 patients (39%). Four patients died, two post-surgery and two without surgical intervention. Mortality-associated factors included higher pCO_2, lower left ventricular (LV) output, decreased LV compliance, and elevated pulmonary vascular resistance (PVR). Survival analysis revealed a non-significant trend toward higher mortality in HP2 (one death) and HP3 (three deaths). Follow-up demonstrated progressive increases in biventricular output, PVR reduction, and compensatory cerebral vasodilation.* **Conclusion:** *HP correlated with patient mortality, particularly in cases with greater pulmonary hypoplasia (higher CO_2) and compromised ventricular performance. Echocardiographic monitoring revealed improvements in biventricular performance, decreased PVR facilitating surgical intervention, and cerebral perfusion adaptation.*

Keywords: *Congenital diaphragmatic hernia. Echocardiography. Mortality. Hemodynamics. Hemodynamic monitoring. Phenotype.*

Fenotipos hemodinámicos en hernia diafragmática congénita y su asociación con morbilidad y mortalidad

Resumen

Introducción: *La hernia diafragmática congénita (HDC) es una patología grave y de alta morbimortalidad. Su gravedad está relacionada con el grado de hipoplasia pulmonar; Recientemente, se ha descrito la importancia de reconocer diferentes fenotipos hemodinámicos (FH) para el manejo fisiopatológico.* **Método:** *Se incluyeron pacientes con HDC evaluados mediante*

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ecocardiografía funcional desde enero 2017 hasta abril 2022. Los FH se clasificaron en 3: FH1: Hipertensión pulmonar (HP) leve sin disfunción ventricular; FH2: HP precapilar; y FH3: HP postcapilar. Diferencias entre sobrevivientes y no sobrevivientes se compararon con U Man Whitney; parámetros ecocardiográficos basales, pre y post quirúrgicos con Wilcoxon. Las curvas de supervivencia se estimaron con Kaplan-Meier y la duración de la estancia hospitalaria se comparó con Kruskal Wallis. **Resultados:** *Se incluyeron 28 neonatos, 24 supervivientes (86%). Los FH encontrados fueron: 9 FH1 (32%), 8 FH2 (29%) y 11 FH3 (39%). Dos murieron tras cirugía y dos sin cirugía. Factores asociados a mortalidad fueron mayor pCO2, menor gasto cardiaco y distensibilidad del ventrículo izquierdo, y mayores resistencias vasculares pulmonares (RVP). Las curvas de supervivencia mostraron una tendencia no significativa hacia una mayor mortalidad en el FH2 y FH3. En seguimiento, se observó un aumento gradual del gasto biventricular, disminución de la RVP y vasodilatación cerebral compensatoria.* **Conclusión:** *Los FH se relacionaron con la mortalidad de los pacientes con mayor hipoplasia pulmonar y rendimiento ventricular subóptimo. El seguimiento ecocardiográfico mostró un aumento del gasto biventricular, una disminución de la RVP que permitió la cirugía y una adaptación de la perfusión cerebral.*

Palabras clave: *Hernia diafragmática congénita. Ecocardiografía. Mortalidad. Hemodinamia. Monitoreo hemodinámico. Fenotipo.*

Introduction

Congenital diaphragmatic hernia (CDH) is a developmental defect of the diaphragm, usually posterolateral, through which abdominal viscera migrate into the chest during fetal life, causing compression and hypoplasia with mainly ipsilateral lung involvement, but also contralateral damage. The herniation of abdominal viscera yields a complex pathophysiology (two-hit theory) characterized by pulmonary hypoplasia (arrest of both lungs) and compression (abnormal pulmonary parenchymal and vascular development); this generates aberrant pulmonary vasoreactivity and pulmonary hypertension (PH), and ventricular dysfunction (right ventricular [RV] hypertrophy and dilatation and different spectrum of left ventricular [LV] hypoplasia), which can lead to pulmonary venous hypertension.

It represents a serious pathology with high morbidity and mortality. Population-based studies have reported that the prevalence of CDH is between 1 in 2500 and 1 in 3000 live births. Approximately 80% of CDH cases are left-sided, 15% are right-sided, and < 5% are bilateral[1].

Despite advances in neonatal resuscitation and intensive care, newborns with CDH continue to have high mortality, with increasing recognition that cardiac dysfunction plays an important role. Current survival rates in population-based studies are around 55% to 80%. Highly specialized centers report up to 90% survival but rule out hidden mortality, mainly in the prenatal period[2].

Targeted neonatal echocardiography (TnECHO) programs have been established in several Neonatal Intensive Care Units (NICUs) with comprehensive guidelines, a training framework, and robust clinical governance processes[3]. This modern hemodynamic monitoring method includes anatomical assessment for congenital heart disease, PH assessment, and ventricular size and function evaluation, including shunts across the patent ductus arteriosus (PDA) and *foramen ovale* (PFO). Systolic and diastolic dysfunction have been described, correlating with mortality and the need for extracorporeal membrane oxygenation (ECMO)[4-9].

Recently, three main hemodynamic phenotypes (HPs) have been described[1,10,11]: 1. Mild or no PH with normal cardiac function; 2. Pulmonary arterial hypertension (pre-capillary PH) with either no cardiac dysfunction or primary RV dysfunction; and 3. Pulmonary venous hypertension (post-capillary PH) with primary LV dysfunction with or without RV dysfunction.

Method

The study was conducted in a Pediatric Tertiary Level Referral NICU with a Hemodynamic Consultation (HC) team in Mexico City. All patients with CDH consulted from January 2017 to April 2022 were included in the study. The Institutional Research Ethics Committee approved this retrospective study, and the requirement for informed consent was waived. All patients had a basal TnECHO study performed within 8 h of admission. Irrespective of the number of patients' studies, the closest pre-surgical TnECHO was considered; post-surgical TnECHO was taken after post-surgical stability was obtained. TnECHO and middle cerebral artery (MCA) Doppler were performed with the available equipment using a standardized imaging protocol based on the American Society of Echocardiography guidelines[12]: Acuson ×300™ (Siemens Healthcare, Munich, Germany; LU with a 9 MHz phased array transducer) during 2018-2019 and Vivid E90™ (GE Medical Systems, Milwaukee, WI, USA; with a 7-12 MHz phased

array transducer) during 2020-2022. After a comprehensive Hemodynamic Consultation (HC), a physiology-based recommendation was formulated; the attending team ultimately decided on the patient's treatment.

Vital signs were obtained from the cardiorespiratory monitor at the time of HC. The highest CO_2 in the first 72 h was recorded.

The study analyzed cardiac images using apical, subcostal, short axis, and RV 3-chamber (RV-3C) projections with M-mode, color Doppler, pulsed wave Doppler, and continuous wave Doppler. It evaluated pulmonary artery pressure, right and LV function, pulmonary vascular resistance (PVR), and cerebral circulation, with PH classified into three phenotypes.

For pulmonary artery pressure, right ventricular systolic pressure was determined by identifying regurgitant flow with color Doppler and applying the Bernoulli equation. The interventricular septum's motion, specifically its curvature during systole and diastole, was assessed at the papillary muscle level.

PVR was evaluated through pulmonary artery acceleration time (PAAT), right ventricular ejection time (RVET), and the velocity time integral (VTI) of the pulmonary Doppler profile[13]. Right ventricular function included right ventricular output (RVO), tricuspid annular plane systolic excursion (TAPSE), and fractional area change (FAC). RVO was calculated as the product of VTI, heart rate, and half the cross-sectional area of the pulmonary artery squared[14,15].

For LV systolic function, left ventricular output (LVO) was calculated similarly to RVO using aortic valve measurements. The Simpson's biplane method was applied to calculate the LV ejection fraction using two orthogonal imaging planes. LV diastolic performance involved calculating the E/A ratio of mitral valve flow and assessing pulmonary venous return at the pulmonary vein confluence using pulsed Doppler in the four-chamber view[16].

MCA Doppler was performed through the trans-temporal window.

HPs were classified into three groups (Fig. 1):

- HP1: Mild PH without ventricular dysfunction; PDA and PFO shunt predominantly left to right.
- HP2 (Pre-capillary PH phenotype): Moderate-to-severe PH with right ventricular dysfunction; PDA and FO shunt right to left.
- HP3 (Post-capillary PH phenotype): Moderate-to-severe PH with LV dysfunction/biventricular dysfunction; PDA shunt right to left, FO shunt left to right.

The differences between survivors and non-survivors were compared using the Mann–Whitney U-test. Baseline, pre-surgical, and post-surgical echocardiographic parameters were analyzed using the Wilcoxon test. Survival analysis was performed, and Kaplan–Meier survival curves were plotted. Length of stay was compared using the Kruskal–Wallis test.

Results

A total of 28 neonates were included, with 24 survivors (86%). The median maternal age was 24 years, with a low rate of prenatal diagnosis (25%). Only one patient had fetal surgery (survivor). Six patients (21%) were inborn with prenatal diagnosis included as a program to avoid postnatal transport (5 survivors and one death). From the overall population, 57% were intubated at birth, and only one patient required chest compressions and adrenaline at birth (out born, deceased). A left anatomical defect was found in 22 patients (78.5%), one left eventration (3.5%); four patients showed right-sided hernias (14.5%), and in one patient, the defect was bilateral (3.5%). Demographics are depicted in table 1.

At the time of HC, 20 patients were assessed on conventional mechanical ventilation and 8 (29%) under high-frequency oscillatory ventilation (HFOV). The HP encountered were 9 HP1 (32%), 8 HP2 (29%), and 11 HP3 (39%). Treatment recommendations were made according to the physiology found (Fig. 2).

Mild or no PH with normal cardiac function usually responded to appropriate ventilatory settings, lung recruitment, early switch to HFOV, and adequate sedation. TnECHO showed predominantly left-to-right flow through the PDA and PFO. In pre-capillary PH with either no cardiac dysfunction or primary RV dysfunction, management focused on reducing PVR with adequate ventilation, sedation, and pulmonary vasodilators (iNO and/or milrinone). TnECHO showed right-to-left flow through the PDA and PFO. In the third HP showing post-capillary PH with primary LV dysfunction, treatment was directed toward improving LV function (iNO could lead to clinical deterioration). TnECHO showed right-to-left flow through the PDA and left-to-right flow through the PFO.

When systemic vasoconstrictors were needed, norepinephrine was used; in the setting of high FiO_2, vasopressin was preferred for its theoretical benefit of reducing PVR[17] (norepinephrine was not recommended as it might increase PVR)[18]. In cases of right or biventricular dysfunction with a restrictive PDA, Prostaglandin

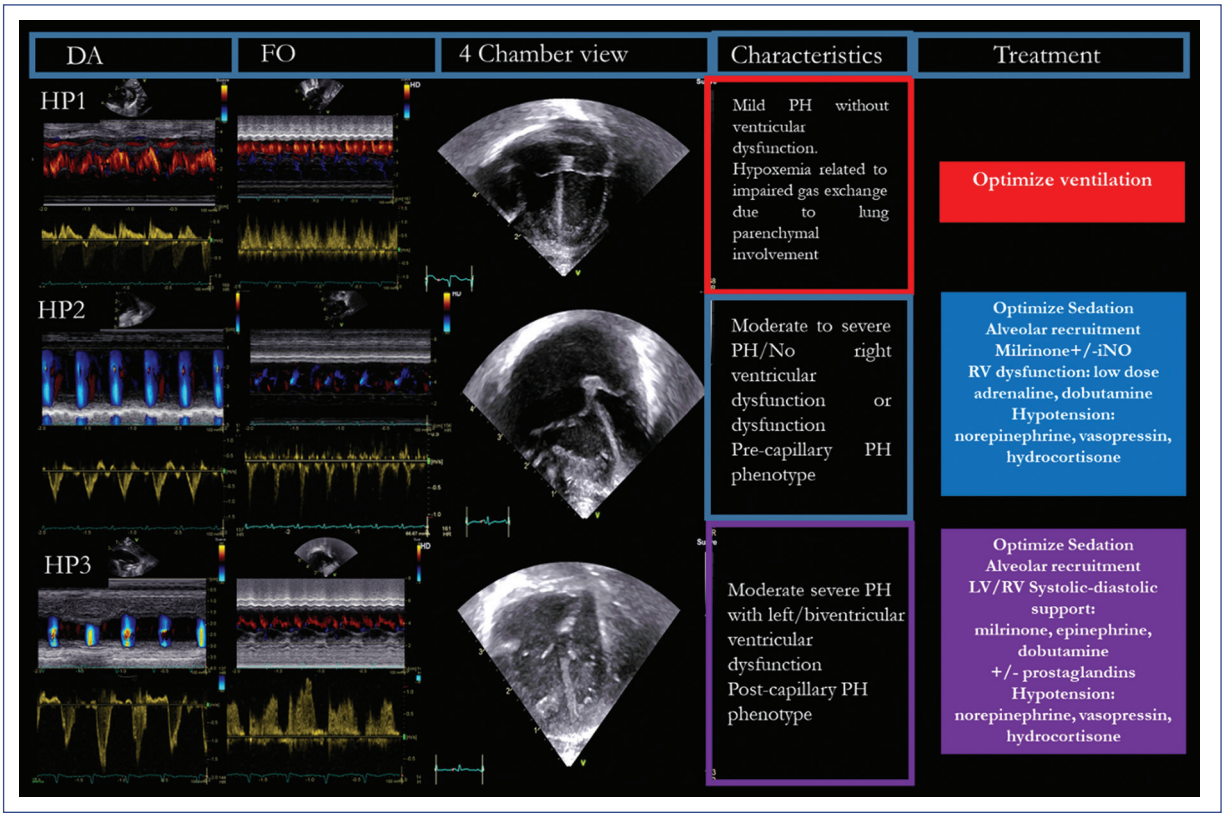

Figure 1. Hemodynamic phenotypes and standardized clinical management. DA: ductus arteriosus; FO: foramen ovale; HP: hemodynamic phenotype; PH: pulmonary hypertension; iNO: inhaled nitric oxide.

E1 (PGE1) was prescribed as a potent pulmonary vasodilator and acted as a "pop-off" valve for RV dysfunction[19]. Low-dose epinephrine infusion was indicated in six patients with HP3 (54%) and three patients with HP2 (37%). Hydrocortisone was used in six cases (two survivors and four non-survivors).

Two patients died after surgery, and two without surgery. Surgery occurred at a median of 6 (3, 7) days after hemodynamic stability was obtained. All patients with HP1 underwent thoracoscopic intervention. Clinical and hemodynamic differences between survivors and non-survivors were compared. Gestational age and birth weight between groups were similar. RVSP [available in 13 patients (46%)] showed no difference between groups. Factors associated with mortality were higher pCO_2, lower LVO, less compliant left ventricle depicted by the E/A ratio, and higher PVR demonstrated by the PAAT/RVET ratio (Table 2).

Survival curves were computed, finding a non-significant trend toward higher mortality in HP2 (one death) and HP3 (three deaths) (Fig. 3). HP2, followed by HP3, showed longer length of stay ($p < 0.05$) (Fig. 4).

At follow-up, a gradual increase in biventricular output, a decrease in PVR, and compensatory cerebral vasodilation were observed ($p < 0.05$) (Table 3).

Discussion

As described in the literature, CDH newborns with mild/no PH (HP1) tend to maintain stability without worsening of PH severity and have a good prognosis. In our cohort, all patients underwent thoracoscopic surgery, experienced no mortality, and had a reduced length of stay. Patients with severe PH at any point have a significantly higher risk for ECMO and mortality[20]. Patients who died were classified as HP2 and HP3 and had higher mortality and longer length of stay.

Of the seven patients with prenatal diagnosis in our study, only one patient with severe pulmonary hypoplasia (defined as liver herniation and observed/expected lung-to-head circumference ratio below 26%) underwent fetal surgery (survivor). In our population, it has been demonstrated that temporary endotracheal

Table 1. Demographic characteristics (n = 28)

Birth history	n = 28	
Maternal age (years), median (IQR)	24 (21, 30)	
Prenatal diagnosis, n (%)	7 (25)	
Fetal surgery, n (%)	1 (3.5)	
Female, n (%)	11 (39)	
Gestational age (weeks), median (IQR)	38.5 (37.8, 39)	
Inborn, n (%)	6 (21)	
Vaginal delivery, n (%)	11 (39)	
5-minute Apgar score, median (IQR)	8 (7, 9)	
Birthweight, median (IQR)	3022 (2897, 3200)	
Intubated at birth, n (%)	16 (57)	
Chest compressions, n (%)	1 (3.5)	
Associated malformations	7 (25)	
Anatomical defect, n (%)	Left: 22 (78.5) Left eventration 1 (3.5) Right: 4 (14.5) Bilateral: 1 (3.5)	Defect size: A: 7 (28) B: 10 (40) C: 7 (28) D: 1 (4)
Liver herniation, n (%)	10 (35)	
Hernia sac, n (%)	10 (35)	
Days of conventional mechanical ventilation, median (IQR)	7 (5, 12)	
HFOV, n (%)	8 (29%)	
Days of HFOV, median (IQR)	3 (1, 5)	
Days of iNO, median (IQR)	3 (2, 7)	
Days of life at surgery, median (IQR)	6 (3, 7)	
Thoracoscopic repair, n (%)	17 (61)	
Thoracoscopic converted to open, n (%)	2 (7)	
Open repair, n (%)	7 (25)	
No surgery, n (%)	2 (7)	
Patch repair, n (%)	8 (28)	
Survivors' length of stay, median (IQR)	21 (16, 30)	
Non survivors' length of stay, median (IQR)	4 (1, 7)	

IQR: interquartile range; CMV: mechanical ventilation; HFOV: high frequency oscillatory ventilation; iNO: inhaled nitric oxide.

occlusion of the fetus prevents the leakage of lung fluid, favoring its growth and improving survival by 32%[21].

Most protocols recommend immediate intubation at birth with gentle ventilation, avoiding mask ventilation to minimize air entry into the stomach, as well as gastric tube decompression. Recently, the consensus has suggested allowing spontaneous breathing of low-risk patients (mild CDH)[22]. In our study, 57% required advanced neonatal resuscitation, including intubation at birth (100% of inborn and 45% of outborn) and chest compressions in one patient (outborn, deceased). Inborn babies had moderate and severe CDH, so spontaneous breathing was not attempted with inborn babies had moderate and severe CDH, so spontaneous breathing was not attempted.

In the present study, we found that 80% of the neonates had left diaphragmatic hernia. As reported in a study by Kotecha et al., of the total number of CDH, about 90% correspond to hernias affecting the left side, and only 10% occur on the right side[23]. Poor prognostic factors have been described, including prematurity and low birth weight[24]. In our study, most of our patients were full-term (38.5 [37.8-39 weeks), with only one being a late-preterm at 35 weeks of gestation (survivor).

CDH is a condition that, despite advances in its diagnosis and management, has high mortality rates due to PH secondary to pulmonary hypoplasia. Among the biochemical variables that allow monitoring of pulmonary hypoplasia are the pCO_2 values in the first 72 h. Permissive hypercarbia is recommended[25]. Salas et al. found that $pCO_2 \geq 80$ mmHg in the first arterial blood gas and/or before ECMO may indicate severe pulmonary hypoplasia[26]. In addition, it has been reported that $PaCO_2 \geq 60$ mmHg in the first 24 h of life is associated with higher mortality[27]. Our study also found a significant association between increased pCO_2 values and mortality (66 [51,71] vs. 120 [85,182]).

As there are no randomized trials regarding optimal cardiovascular management, the correct diagnosis and effective management of PH and cardiac dysfunction are necessary for optimizing outcomes. HC with TnECHO is fundamental in delineating the pathophysiology-targeted treatment of CDH[28]. In our study, treatment recommendations were made based on the physiology assessed by a trained neonatologist using TnECHO and Neonatal Hemodynamics[29].

Milrinone, a phosphodiesterase-3 inhibitor that leads to pulmonary and systemic vasodilation, providing positive inotropism and lusitropism, was the most common vasoactive drug used in our population (68%). Given elevated PVR and frequent ventricular dysfunction, it is

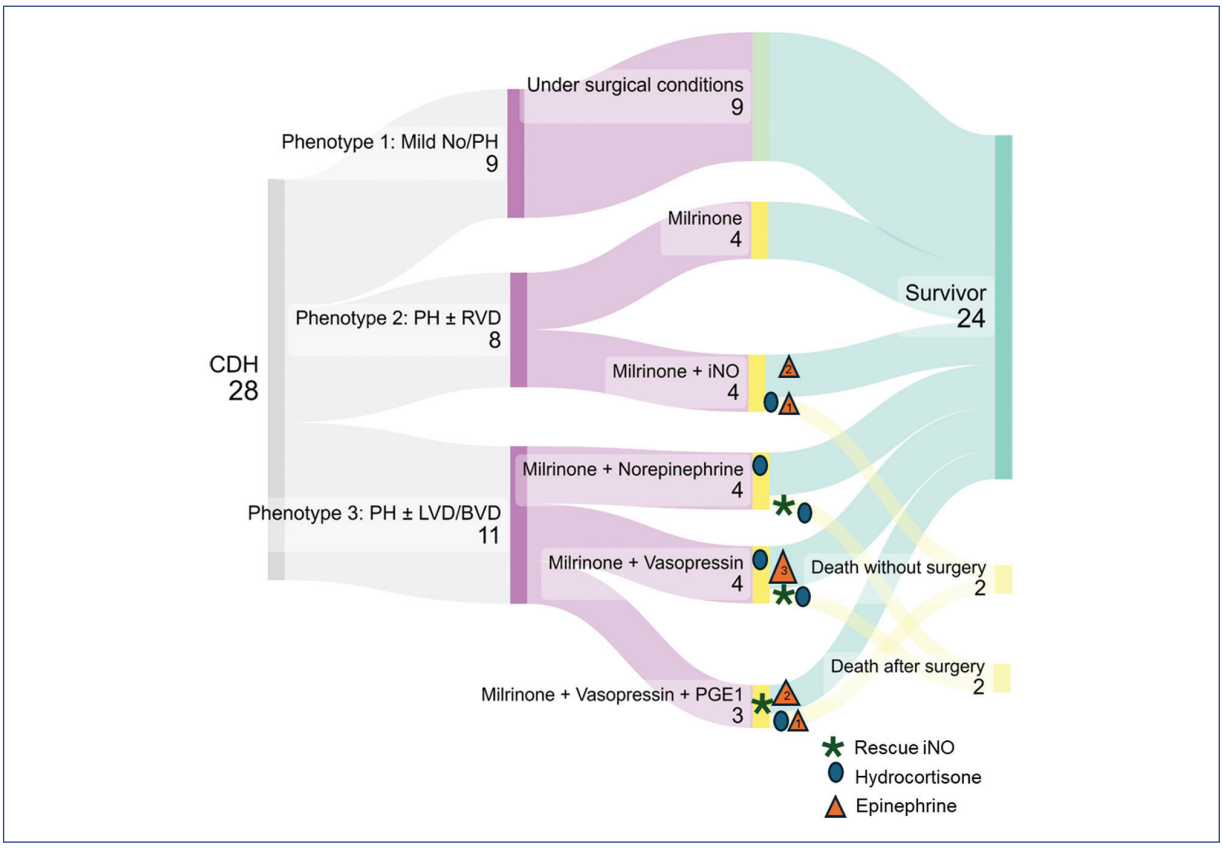

Figure 2. Sankey diagram depicting hemodynamic phenotypes, initial management, and survival.
*Rescue iNO. CDH: Congenital diaphragmatic hernia; PH: pulmonary hypertension; RVD: right ventricular dysfunction; LVD: left ventricular dysfunction; BVD: bi-ventricular dysfunction; iNO: inhaled nitric oxide; PGE_1: prostaglandin-E1.

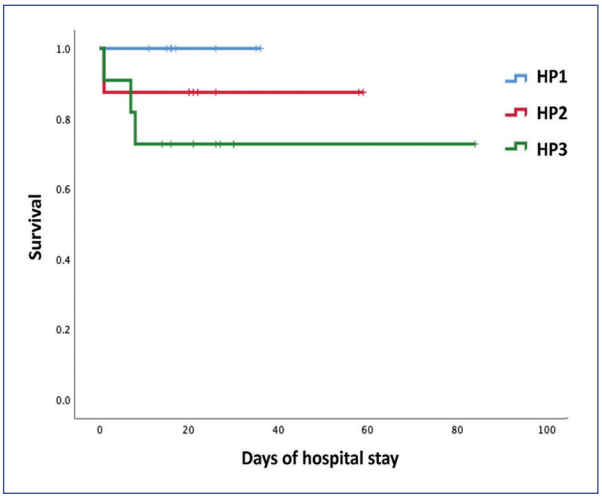

Figure 3. Kaplan–Meyer curves, survival probability according to hemodynamic phenotype.

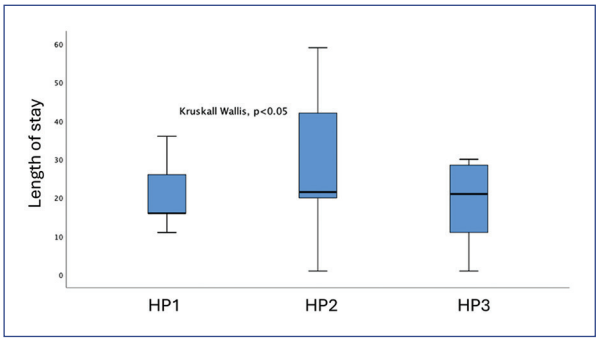

Figure 4. Length of stay between hemodynamic phenotypes.

a compelling agent for HP2 and HP3[30,31]. Nevertheless, it is still understudied in CDH. At present, there is an ongoing randomized phase 2 trial[32].

Hemodynamic variables associated with mortality were a lower LVO, less compliant left ventricle depicted by the E/A ratio, and higher PVR demonstrated by the PAAT/RVET ratio. Hemodynamically, prognostic markers of CDH have been described, including severe PH, LV dimensions, and dysfunction. In CDH patients, pulmonary vascular disease starts *in utero*, causing circulatory changes and LV hypoplasia that generates

Table 2. Clinical and hemodynamic differences between survivors and non-survivors

Clinical and echocardiographic parameters	Survivors		Non-survivors		p
	Median	P25-75	Median	P25-75	
Clinical parameters					
Gestational age (weeks)	39	38-40	38	37-39	0.4
Birth weight (g)	3020	2895-3203	3145	2755-3200	0.7
Maximum CO_2 (first 72 h)	66	51-71	120	85-182	0.01
Hemodynamic consultation					
SAP (mm Hg)	67	59-81	58	51-82	0.5
DAP (mm Hg)	43	38-47	49	26-53	0.7
HR (lpm)	138	125-152	136	126-160	1
RVO (mL/kg/min)	139	84-159	110	81-147	0.5
TAPSE (mm)	8.4	6.9-8.9	8.3	7.9-8.6	0.9
RV FAC (%)	42	38-44	37	25-41	0.1
RVSP (mm Hg)	62	43-66	67	64-70	0.4
RVET (ms)	192	171-207	186	120-197	0.4
PAAT (ms)	51	41-67	30	23-53	0.09
PAAT/RVET	0.29	0.24-0.33	0.19	0.16-0.26	0.04
PV S (cm/s)	39	33-50	37	25-48	0.5
PV D (cm/s)	55	42-71	47	36-57	0.4
E/A ratio	0.96	0.81-1.12	0.8	0.73-0.88	0.02
LVO (mL/kg/min)	139	108-160	73	48-79	0.001
Simpsons biplane EF (%)	64	57-70	56	54-66	0.3

SAP: systolic arterial pressure; DAP: diastolic arterial pressure; HR: heart rate; RVO: right ventricular output; TAPSE: tricuspid annular plane excursion; RV FAC: right ventricular fractional area change; RVPS: right ventricular systolic pressure; RVET: right ventricular ejection time; PAAT: pulmonary artery acceleration time; PV: pulmonary vein; LVO: left ventricular output; EF: ejection fraction.

Table 3. Baseline, pre-, and post-surgical echocardiographic assessment

Clinical and echocardiographic parameters	Baseline		Pre-surgical		Post-surgical		p
	Median	P25-P75	Median	P25-P75	Median	P25-P75	
SAP (mm Hg)	66	57-82	71	64-82	70	65-77	0.5
DAP (mm Hg)	43	37-49	43	37-52	43	34-51	0.6
HR (bpm)	137	126-152	146	130-158	147	139-163	0.03
RVO (ml/kg/min)	135	84-157	160	134-186	185	135-223	0.005
TAPSE (mm)	8.2	6.7-8.8	8.2	7.1-10.2	9.2	6.8-9.8	0.4
RV FAC (%)	41	38-44	39	37-42	46	39-51	0.2
RSVP (mmHg)	64	45-66	45	41-49	45	38-60	0.5
RVET (ms)	190	163-207	182	170-207	184	170-200	0.6
PAAT (ms)	50	40-64	51	43-64	58	45-73	0.5
PAAT/RVET	0.26	0.24-0.30	0.28	0.25-30	0.31	0.26-0.37	0.005
PV S (cm/s)	39	32-49	39	33-57	45	41-54	0.4
PV D (cm/s)	55	41-71	54	50-60	59	45-69	0.6
E/A ratio	0.82	0.69-1.07	0.88	0.73-1.04	0.96	0.68-1.15	0.6
LVO (ml/kg/min)	134	90-158	150	138-197	169	141-203	0.07
Simpsons biplane EF (%)	70	66-76	68	64-72	71	63-74	0.03
MCA PI	1.30	1.12-1.63	1.18	0.86-1.47	1.28	0.98-1.44	0.1
MCA RI	0.69	0.53-0.77	0.69	0.65-0.81	0.73	0.67-0.77	0.05

SAP: systolic arterial pressure; DAP: diastolic arterial pressure; HR: heart rate; RVO: right ventricular output; TAPSE: tricuspid annular plane excursion; RV FAC: right ventricular fractional area change; RVPS: right ventricular systolic pressure; RVET: right ventricular ejection time; PAAT: pulmonary artery acceleration time; PV: pulmonary vein; LVO: left ventricular output; EF: ejection fraction; MCA: medium cerebral artery; PI: pulsatility index; RI: resistive index.

systolic and diastolic dysfunction after birth[33]. In the largest randomized, double-masked, controlled multicenter study that compared the use of iNO in CDH, there was no difference in the combined endpoint of death/ECMO between patients treated with iNO and controls. ECMO use was higher in the iNO group (80% vs. 54%)[34]. It is possible that patients with HP3 had pulmonary venous hypertension secondary to LV diastolic dysfunction increasing wedge pressure and worsening pulmonary edema. In a recent large single-center cohort, Fraga et al. demonstrated that patients with CDH with LV dysfunction and left heart hypoplasia had the highest risk of ECMO use and death[35].

Based on this, the HC team did not recommend iNO in HP3 in our population. Although it was not part of the HC recommendation, rescue iNO was used in five patients prescribed by the attending team. It has been demonstrated in a large multicenter study that included 1777 CDH infants (863 with early iNO treatment) that iNO in the first 72 h of life was associated with significantly increased mortality and ECMO use. Stratification by HP and defect size did not uncover a subgroup that benefited from early iNO[36].

In three patients with right/biventricular dysfunction with a restrictive PDA, PGE1 was prescribed as a potent pulmonary vasodilator and a "pop-off" valve (2 survivors). It has been shown that PGE1 treatment improves oxygenation and hemodynamics[19,37].

Adrenal insufficiency is prevalent among patients with CDH[38]. Hydrocortisone was used in six cases (two survivors and all four non-survivors). As reported in the literature, steroid use was found in sicker newborns with increased mortality; currently, there are no proper guidelines to identify patients that might benefit, as prolonged steroid use might increase sepsis and mortality. In addition, 9 patients (28%) in HP2 and HP3 received a low-dose epinephrine infusion indicated by the attending team.

Recently, Le et al. reported an association between early systolic dysfunction of any ventricle and the need for ECMO. Failure to normalize biventricular function was associated with adverse outcomes. LV function normalized quicker and consistently with a milrinone infusion universally indicated by guidelines[39]. In our survival follow-up, a gradual increase in biventricular output, a decrease in PVR, and compensatory cerebral vasodilation were observed. Serial TnECHO might help identify cardiac dysfunction, recognizing that early treatment might improve prognosis. A protocolized approach recognizing different HP, assessing ventricular function, and atrial and ductal shunts enhances the understanding of CDH postnatal hemodynamics, allowing pathophysiology-based management[40].

Our study has several limitations. Only the patients with HC were included in the study. Only 21% had a prenatal diagnosis and were inborn. Outborn patients were filtered by time and survival to transport, leading to occult mortality. The strength is that it represents a case series in a middle-income country without ECMO that highlights the importance of hemodynamic phenotyping and depicts clinical and hemodynamic variables related to mortality.

Conclusion

HPs were related to patient mortality, which was higher in those with greater pulmonary hypoplasia (higher CO_2) and suboptimal ventricular performance. The post-capillary PH phenotype had higher mortality. Patients were treated according to pathophysiology; nevertheless, despite recent evidence discouraging its early use, rescue iNO was indicated in severe cases. Echocardiographic follow-up showed an increase in biventricular performance, a decrease in PVR that allows the repair of the defect, and an adaptation of cerebral perfusion.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's

confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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