PORTUGUESE JOURNAL OF PEDIATRICS

PERMANYER

Check for updates

NARRATIVE REVIEW

Congenital diaphragmatic hernia: a neonatologist's perspective. A narrative review

Gustavo Rocha

Department of Neonatology, Centro Hospitalar Universitário de São João, Porto, Portugal

Abstract

Congenital diaphragmatic hernia (CDH) is a complex anomaly characterized by a defect in the diaphragm that allows abdominal organs to herniate into the thoracic cavity, leading to pulmonary hypoplasia, pulmonary hypertension, and cardiac dysfunction. Emerging evidence suggests that cardiac dysfunction plays a key role in CDH pathophysiology. From a neonatologist's perspective, early recognition through prenatal imaging is essential for risk stratification and planning perinatal management. Prognostic indices, such as lung-to-head ratio, liver herniation, observed-to-expected total fetal lung volume, and stomach position, provide valuable information on severity and expected outcomes. In the delivery room, stabilization focuses on gentle ventilation strategies and preventing pulmonary barotrauma, with careful monitoring of oxygenation and hemodynamics. Postnatally, multidisciplinary care is crucial, encompassing respiratory support, pulmonary hypertension management, hemodynamic support, nutritional support, and timing surgical repair after clinical stabilization. Despite advances in prenatal diagnosis and neonatal intensive care, CDH remains associated with significant morbidity and mortality, underscoring the importance of ongoing research and individualized patient management.

Keywords: Congenital diaphragmatic hernia. Mechanical ventilation. Hemodynamic support. Prognostic indicators. Pulmonary hypertension.

Hérnia diafragmática congénita: a perspetiva do neonatologista. Revisão narrativa

Resumo

A hérnia diafragmática congénita (HDC) é uma anomalia complexa caracterizada por um defeito no diafragma que permite a herniação dos órgãos abdominais para a cavidade torácica, conduzindo a hipoplasia pulmonar, hipertensão pulmonar e disfunção cardíaca. Novas evidências indicam que a disfunção cardíaca tem um papel importante no desenvolvimento da fisiopatologia da HDC. Na perspetiva do neonatologista, o reconhecimento precoce através da imagiologia pré-natal é essencial para a estratificação do risco e planeamento da abordagem perinatal. Indices prognósticos, como a relação pulmão-cabeça, a herniação hepática, o volume pulmonar fetal total observado/esperado e a posição do estômago fornecem informação valiosa sobre a gravidade da HDC, bem como sobre os resultados esperados. Na sala de partos, a estabilização foca-se em estratégias de ventilação com prevenção do barotrauma pulmonar, monitorização cuidadosa da oxigenação e hemodinâmica. No período pós-natal, um tratamento multidisciplinar é crucial, abrangendo suporte respiratório, controlo da hipertensão pulmonar, suporte hemodinâmico, apoio nutricional e o momento adequado para a reparação cirúrgica após estabilização clínica.

Correspondence:
Gustavo Rocha
E-mail: gusrocha@sapo.pt

Received: 22-07-2025
Accepted: 30-03-2026
https://pjp.spp.pt

Available online: 24-07-2026
Port J Pediatr. 2026;57(3):162-180
DOI: 10.24875/PJP.25000053

Apesar dos avanços no diagnóstico pré-natal e nos cuidados intensivos neonatais, a HDC continua associada a morbilidade e mortalidade significativas, sublinhando a importância da investigação contínua e do tratamento individualizado dos doentes.

Palavras-chave: Hérnia diafragmática congénita. Ventilação mecânica. Suporte hemodinâmico. Indicadores prognósticos. Hipertensão pulmonar.

Keypoints

What is known
- Congenital diaphragmatic hernia (CDH) is a life-threatening anomaly.
- Pulmonary hypoplasia, pulmonary hypertension, and cardiac dysfunction are the main determinants of morbidity and mortality.
- The management of CDH remains challenging and there is no universally accepted treatment protocol.

What is added
- This article provides a concise overview of current international treatment guidelines for CDH.
- It summarizes the most relevant prenatal prognostic indices, offering neonatologists practical tools to assess disease severity.
- By compiling and simplifying complex international recommendations, this article serves as a valuable resource for clinicians managing CDH in the neonatal period.

Introduction

Congenital diaphragmatic hernia (CDH) is a rare but serious developmental anomaly, occurring in approximately one in every 3000 live births.[1-4] Characterized by a defect in the diaphragm that allows abdominal organs to herniate into the thoracic cavity, CDH is associated with significant pulmonary hypoplasia, CDH-associated pulmonary hypertension (CDH-PH), and cardiac dysfunction, which are the main determinants of neonatal morbidity and mortality.[5,6]

Over the past two decades, advances in neonatal intensive care, prenatal diagnosis, and respiratory support strategies have contributed to a gradual improvement in survival rates.[7] Once considered uniformly fatal, the survival of infants with CDH now exceeds 70% in specialized centers.[4,7] However, this progress has not been consistent across all healthcare settings.[4]

Despite improved outcomes, the medical management of CDH remains highly variable.[8] There is no universally accepted protocol, and significant discrepancies persist among international guidelines regarding the timing of interventions, use of pulmonary vasodilators, ventilation strategies, and criteria for extracorporeal life support (ECLS).[9] This lack of standardization poses challenges not only for clinical decision-making but also for comparing outcomes across centers and conducting robust research.[10]

This article aims to review the prognostic factors and the current medical management of CDH from a neonatologist's perspective, highlighting key areas of consensus, ongoing controversies, and opportunities for the standardization of care.

Methods

To prepare this article, the most relevant publications on the medical management of CDH from the last ten years, up to July 1, 2025, were reviewed using the PubMed database. Some older articles referenced in the analyzed papers were also reviewed and are cited in this review. The search terms used were: congenital diaphragmatic hernia, treatment, prenatal diagnosis, prognostic, fetal endoscopic tracheal occlusion, cardiac, delivery, resuscitation, treatment, management, ventilation, sedation, analgesia, pulmonary hypertension (PH), hemodynamic support, vasoactive, vasodilator, surgical repair, extracorporeal membrane oxygenation (ECMO), outcomes, malnutrition, feeding difficulties, gastroesophageal reflux, chronic lung disease, and mortality.

Development

Prognostic implications of the diaphragmatic defect type

The majority of CDH are Bochdalek hernias, which occur posterolaterally and account for approximately 85-90% of cases.[11] These defects arise due to the incomplete closure of the pleuroperitoneal canals during fetal development, predominantly (80-85% of cases) affecting the left hemidiaphragm.[11] The anatomical severity of the diaphragmatic defect has been standardized using the CDH Study Group classification, which categorizes defects as follows: Type A: small, isolated defect with intact diaphragmatic musculature

surrounding the hernia; suitable for primary repair without tension; Type B: moderate-sized defect with partial posterolateral muscular discontinuity; less than 50% of the chest wall is devoid of diaphragm; generally amenable to primary repair but may require reinforcement; Type C: large defect with minimal residual diaphragmatic tissue; more than 50% of the chest wall lacks a diaphragm; primary repair is typically not feasible and requires prosthetic patch reconstruction; Type D: near-total or complete agenesis of the hemidiaphragm; requires extensive patch repair and is often associated with severe PH and malrotation.[12]

There is a well-established correlation between the defect type and postnatal outcomes. Types A and B are associated with favorable prognoses, lower surgical complexity, and a reduced incidence of postnatal complications. These patients typically exhibit better pulmonary function, a shorter duration of mechanical ventilation, and a decreased need for ECLS.[13] Conversely, Types C and D represent severe phenotypes, frequently requiring prosthetic repair, and are associated with significant morbidity and mortality. These neonates exhibit increased rates of CDH-PH, prolonged respiratory support, feeding difficulties, and higher rates of recurrence. Important long-term sequelae, including chronic lung disease (CLD), may occur in patients with CDH.[14,15]

Herniation of the abdominal contents leads to persistent hypoplasia of the ipsilateral lung, while the resulting secondary mass effect contributes to hypoplasia of the contralateral lung.[5] These anatomical changes impact lung mechanics by reducing lung volumes and causing smooth muscle dysregulation, which increases airway resistance. Additionally, the pulmonary vasculature is affected, resulting in a decreased cross-sectional area of the pulmonary vascular bed and thickening of the adventitia and media, leading to elevated pulmonary vascular resistance (PVR). Due to the chronic nature of these changes, the elevated PVR becomes fixed and less responsive to vasodilators such as inhaled nitric oxide (iNO). Over time, this sustained increase in PVR may result in right heart strain and right ventricular (RV) hypertrophy, particularly after the patent foramen ovale (FO) and ductus arteriosus (DA) have closed.[5]

Accurate intraoperative classification of the diaphragmatic defect provides essential prognostic information and should be systematically documented.[16] Additionally, advances in prenatal imaging, particularly fetal magnetic resonance imaging (MRI), allow for a more precise antenatal estimation of the defect size and associated lung volumes, improving risk stratification and perinatal management planning.[16]

Beyond the size of the diaphragmatic defect, estimated indirectly through ultrasound (US) and MRI-based assessments of fetal lung volume, and the extent of visceral herniation, several other factors can impact both the immediate and long-term prognosis of CDH. These include the timing of prenatal diagnosis, gestational age at detection, the side of the defect (laterality), the presence of additional structural or genetic anomalies, gestational age at delivery, and the experience of the delivery center in managing neonates with CDH.[16]

Prenatal issues

The prenatal diagnosis of CDH plays a crucial role in planning perinatal care and assessing prognosis[16]. In high-income countries, the integration of US into routine prenatal care has markedly improved the detection rates of CDH, rising from approximately 15% to over 60%, which has likely contributed to improved postnatal survival outcomes.[7,17,18]

CDH is typically diagnosed during the second-trimester routine obstetric anatomy scan (18-24 weeks of gestation). Sonographic signs include the presence of abdominal organs (e.g., stomach, intestines or liver) within the thoracic cavity, mediastinal shift, and an absent or small stomach bubble in the abdomen[16]. Left-sided hernias, the most common form, are usually easier to detect due to the displacement of the heart and visualization of the stomach in the thorax.[16,19] Fetal MRI may be used to complement US findings and provide a detailed assessment of lung volumes, liver herniation, and the presence of other congenital anomalies, all important prognostic factors.[20] Additionally, MRI images are independent of maternal body habitus, fetal position, or abnormalities in the amniotic fluid.[20]

Approximately 30-50% of CDH are “non-isolated” or “syndromic”.[21] A comprehensive morphological evaluation, including an assessment of the cardiac structure and function, as well as genetic testing, should be conducted in all pregnancies with fetuses diagnosed with CDH.[22] There is no genetic panel for CDH.[23] Invasive genetic testing with chromosomal microarray analysis should be offered in cases of isolated CDH, whereas more targeted mutation identification or expanded genomic analyses (e.g., exome sequencing) are likely to further improve the diagnostic yield in “syndromic” or “non-isolated” cases.[23]

Prognostic indicators

Several prenatal indices have been developed to estimate the severity of CDH and guide clinical decision-making (Table 1). The lung-to-head ratio (LHR) is measured via US and represents the area of the contralateral lung divided by the head circumference. An observed-to-expected (o/e) LHR is often used to standardize measurements across gestational ages. The o/e LHR should be measured with the trace method between 22 and 32 weeks of gestational age in experienced centers. Severe pulmonary hypoplasia is predicted by an o/e LHR of ≤ 25% in left-sided CDH and ≤ 50% for right-sided CDH, with an estimated survival rate of ≤ 30%.[24-28] In cases of left-sided CDH, moderate pulmonary hypoplasia is defined by an o/e LHR ranging from 26 to 34%.[28]

The presence of the liver in the thoracic cavity ("liver up") is considered a negative prognostic factor, as it reflects a larger diaphragmatic defect and more severe lung compression. Intrathoracic liver herniation can be challenging to detect on US. Consequently, stomach position classification has been proposed as a surrogate marker and has been shown to correlate with neonatal mortality and morbidity.[29-33] The position of the stomach is graded I – IV (I: intra-abdominal, II: anterior left chest, III: mid-to-posterior left chest, and IV: retrocardiac) based on the degree of thoracic herniation; a higher grade indicates more severe herniation and a worse prognosis.[31] The o/e total fetal lung volume (o/e TFLV) measured by fetal MRI is another reliable marker.[28] An o/e TFLV < 35% with liver herniation is linked to a higher mortality rate.[28] The optimal timing for MRI appears to be around 26 weeks, as performing it earlier may result in inaccurate measurements. When combined, the o/e TFLV and liver herniation indicators provide improved predictive value for mortality and the need for ECLS.[34]

While MRI offers advantages for prenatal prognostication, US is likely to remain the primary tool due to its broad accessibility. Ideally, both imaging modalities should be used complementarily, especially in high-risk fetuses.[28] MRI for the assessment of o/e TFLV and liver herniation should be considered in all fetuses with CDH, and it is strongly recommended in fetuses with severe or moderate CDH by o/e LHR.[28]

During pregnancy, multidisciplinary counselling is provided, and various management options are discussed, including expectant management, fetoscopic endoluminal tracheal occlusion (FETO), pregnancy termination, and palliative care (in cases that are syndromic, severe, or bilateral).[35]

Table 1. Prenatal imaging parameters and their thresholds for predicting mortality in cases of congenital diaphragmatic hernia that are managed expectantly[16]

Prenatal parameter	Cut-off	Mortality (%)
o/e LHR (on US) Left CDH Right CDH	 < 25% < 50%	 50-70 80
Liver herniation (on MRI)	> 21%	20-52.4
Stomach herniation (on US)	Grade IV/ Retrocardiac	61
o/e TFLV (on MRI)	< 25% < 35%	75-100 30-75
o/e TFLV with liver herniation (on MRI)	< 35% with liver "up"	75

CDH: congenital diaphragmatic hernia; o/e LHR: observed-to-expected lung/head ratio; MRI: magnetic resonance image; o/e TFLV: observed-to-expected total fetal lung volume; US: ultrasound.

Fetal endoscopic tracheal occlusion eligibility

For severe and moderately severe cases of CDH, the use of FETO should be considered a treatment option.[28] Eligibility often depends on prognostic indicators like o/e TFLV and the liver herniation status. A systematic review and meta-analysis including a total of 1187 CDH fetuses from 20 studies demonstrated that FETO is associated with a reduction in mortality, the rate of CDH-PH, and ECMO usage in severe CDH, while it reduces only the risk of mortality in moderate CDH.[36] Although FETO increases the risk of late prematurity, it does not result in extreme prematurity.[36]

The decision to proceed with FETO should be individualized, based on detailed imaging, multidisciplinary evaluation, and careful counselling of the parents regarding the risks and benefits.[28]

Cardiac parameters

Fetuses with CDH are at risk of cardiac chamber abnormalities, particularly left ventricular (LV) hypoplasia, leading to biventricular dysfunction after birth.[37,38] Emerging evidence suggests that cardiac dysfunction plays a key role in CDH pathophysiology. It remains uncertain whether these morphological changes stem from a primary embryological defect or are secondary to altered fetal hemodynamics and cardiac compression due to visceral herniation.[16] Postnatal ventricular imbalance and dysfunction are linked to higher mortality and an increased need for ECLS, although fetal cardiac size does not consistently predict outcomes.

Further studies are needed to identify fetal cardiac parameters that may improve the prediction of neonatal outcomes in prenatally diagnosed CDH.[16]

Delivery

The delivery of a fetus with CDH should occur in a high-volume tertiary center equipped with a multidisciplinary team experienced in neonatal intensive care, pediatric surgery, and ECLS, if needed.[39] The mode of delivery should be determined on usual obstetric grounds and should be considered between 38 and 39 weeks of gestation, as earlier delivery has not been shown to improve outcomes and may be associated with an increased risk of prematurity.[40] In the case of an early birth prior to 34 weeks of gestation, antenatal steroids should be given.[41] Planned delivery at term allows for stabilization of the newborn prior to surgical repair, which is associated with improved survival and reduced morbidity.[9,41] Whenever possible, delivery should be scheduled for an early weekday during daytime hours, ensuring the optimal availability of experienced personnel and allowing for timely planning of CDH repair within the first week of life.[9] Obstetric management should prioritize achieving a normal umbilical cord arterial pH at birth in order to minimize the degree of respiratory acidosis during the neonatal transition.[9]

Management of a neonate with congenital diaphragmatic hernia

Neonates with CDH often present with respiratory distress immediately after birth.[42] The severity can vary depending on the degree of pulmonary hypoplasia and CDH-PH. Common clinical signs include tachypnea, nasal flaring, grunting, and cyanosis. On physical examination, breath sounds may be decreased or absent on the affected side, and heart sounds may be displaced due to mediastinal shift. The abdomen may appear scaphoid due to the herniation of abdominal contents into the thoracic cavity. In severe cases, the newborn may present with signs of cardiovascular instability, such as hypotension and poor perfusion. A prenatal diagnosis is common, but undiagnosed cases may first be identified based on postnatal clinical findings and confirmed by chest radiography.[42] About 5% of CDH cases will present after 24 hours of age with mild tachypnoea, or even later with failure to thrive, recurrent chest infections, pleural effusions, or as an incidental finding on a chest X-ray.[42]

The management of neonates affected of CDH requires a multidisciplinary approach and highly specialized neonatal intensive care from birth.[41] Neonatal CDH care focuses on three overlapping domains: pulmonary hypoplasia, CDH-PH, and biventricular cardiac dysfunction.[9] Preoperative medical management involves stabilizing the infant's oxygenation, hemodynamics, and acid-base balance, and providing nutritional support, beginning immediately in the delivery room.[41] The severity of pulmonary and cardiac impairment determines the timing of surgery, which should be deferred until cardiac function and CDH-PH have improved.[43-46]

Delivery room stabilization and resuscitation

The initial management of CDH patients in the delivery room is a critical medical intervention that significantly impacts patient prognosis.[47] The initial approach is based on the 2025 updated newborn life support guidelines from the European Resuscitation Council.[48]

Immediate postnatal care focuses on gentle stabilization rather than aggressive resuscitation. Bag-mask ventilation is contraindicated due to the risk of gastric insufflation and further compromise of lung function. Endotracheal intubation should be performed promptly after birth. A nasogastric or orogastric tube should be inserted to decompress the stomach and reduce thoracic compression. Chest compressions are rarely needed; instead, the focus is on achieving adequate oxygenation and ventilation while avoiding barotrauma. The delivery room management of a newborn with CDH is summarized in table 2.[28,35,41,47,49-52]

Ventilation strategies

Permissive hypercapnia and "gentle ventilation" have been associated with improved survival rates in neonates with CDH.[35,41,52-54] Lung-protective ventilation is the cornerstone of respiratory management. Caring for asymmetric lungs requires clinicians to find a delicate balance between atelectasis of the larger lung and hyperinflation of the smaller lung.[9] The optimal initial ventilation strategy was explored in the VICI trial (NTR1310).[55] Although the primary outcome (death/CLD at day 28) did not differ significantly between the two groups, it was found that infants initially ventilated with conventional mechanical ventilation required a significantly shorter duration of ventilation, had a lower need for iNO or sildenafil, needed less vasoactive medication, and were less likely to require ECMO than the group initially ventilated with high-frequency oscillatory ventilation (HFOV). The CDH EURO Consortium recommends conventional mechanical ventilation as the initial ventilation strategy.[41]

Table 2. Delivery room management of a newborn with congenital diaphragmatic hernia[28,35,41,47,49-52]

Cord clamping	DCC is generally advocated in neonates, including those with CDH. In the case of critical CDH, where immediate resuscitation is required, healthcare providers may opt for a faster intervention over DCC. There is an ongoing trial (*NCT04373902*) aimed at investigating whether cord clamping after lung aeration in CDH, referred to as physiological-based cord clamping, could reduce the incidence of PH in the first 24 hours after birth. Additionally, the Congenital Hernia Intact Cord (CHIC) trial is a prospective, multicenter, open-label, randomized controlled trial designed to assess its primary endpoint in two groups (early and delayed cord clamping): the number of infants with an APGAR score < 4 at one minute or < 7 at five minutes.
Intubation	Avoid using positive-pressure mask ventilation as it may cause gastric distension and lung compression. After delivery, the infant should be intubated. In infants with a prenatal diagnosis and favorable prognostic indicators (e.g., left-sided defect, o/e LHR > 50%, and liver down), intubation may be avoided; however, even vigorous neonates with favorable prenatal predictors often require intubation for surgery and to avoid developing PH. Premedication should be given before intubation, if possible. Neuromuscular blocking agents should be avoided. The position of the ETT should be confirmed by end-tidal CO_2 monitoring if there is no thorax expansion or improvement in SpO_2.
Oxygen	Initiate resuscitation with an FiO_2 below 1.0 (e.g., 0.30 if the liver is abdominal; 0.50 if the liver is intra-thoracic and in right-sided CDH), titrating up to 1.0, if adequate oxygenation is not achieved. FiO_2 is titrated to achieve a pre-ductal oxygen saturation minimum goal of ≥ 85% by 10 min after birth. Saturation (SpO_2) targets: pre-ductal between 85 and 95%; post-ductal saturation above 70%. To avoid hyperoxia, supplemental oxygen should be diminished when pre-ductal saturation exceeds 95%. NIRS cerebral oxygenation may supplement pulse oximetry and heart rate monitoring.
Gastric tube	Insert an orogastric or nasogastric tube (8F for < 34 weeks GA and 10F for > 34 weeks), with continuous or intermittent suction, for abdominal decompression.
Sedation	If the infant is agitated and/or fighting the ventilator, intranasal midazolam may be administered to achieve sedation prior to initiating an intravenous infusion.
Mechanical ventilation	Conventional ventilation (e.g.,: SIPPV) PIP: start with 20 cmH_2O and increase up to 25 cmH_2O (avoiding pressure > 25). PEEP: 3-5 cmH_2O. Frequency: 40-60/min. Inspiratory time: 0.3 seconds. Use volume targeted ventilation (tidal volume 4-6 mL/kg). Permissive hypercapnia: $PaCO_2$ 50-70 mmHg. Arterial pH: 7.25-7.35.
Vascular access	Umbilical venous catheter: may be needed in the event of advanced resuscitation. Consider obtaining a microarray from cord blood or from umbilical catheter, in isolated and non-syndromic cases.
Hemodynamic	Maintain mean arterial blood pressure above the lower limit of normal levels for the gestational age (maintaining 45 to 55 mmHg for term neonates). In the case of hypotension and/or poor tissue perfusion, one fluid bolus of 10-20 ml/kg NaCl 0.9% may be administered.

CDH: congenital diaphragmatic hernia; CO_2: carbon dioxide; DCC: delayed cord clamping; ETT: endotracheal tube; F: French; FiO_2: fraction of inspired oxygen; GA: gestational age; NaCl: sodium chloride; NIRS: near-infrared spectroscopy; o/e LHR: observed-to-expected lung-to-head ratio; $PaCO_2$: arterial partial pressure of carbon dioxide; PEEP: positive end expiratory pressure; PH: pulmonary hypertension; PIP: peak inspiratory pressure; SIPPV: synchronized positive pressure ventilation; SpO_2: peripheral oxygen saturation.

Conventional mechanical ventilation with low peak inspiratory pressures and permissive hypercapnia is preferred to minimize ventilator-induced lung injury. In cases where conventional ventilation is inadequate, rescue HFOV may be used. Oxygenation targets should be tailored to maintain pre-ductal SpO_2 between 85-95%, avoiding both hypoxemia and hyperoxia. Table 3 provides a summary of the medical management for newborns with CDH from delivery room care, including ventilation strategies.[8,9,28,35,41,47,49,56]

The pathophysiology of pulmonary hypoplasia and CDH-PH often results in respiratory failure and hemodynamic instability beginning at birth. Therefore, cerebral oxygenation monitoring using near-infrared spectroscopy (NIRS) may serve as a valuable adjunct to pulse oximetry and heart rate monitoring, which currently guide resuscitation efforts per Neonatal Resuscitation Program guidelines. The use of NIRS from the delivery room is now implemented in some centers.[35]

Sedation and analgesia

Adequate sedation plays a critical role in reducing stress, decreasing oxygen consumption, and preventing patient-ventilator dyssynchrony.[35,56,57] Additionally, patients with CDH-PH should be managed in a calm,

Table 3. Management of a newborn with congenital diaphragmatic hernia in the Neonatal Intensive Care Unit[8,9,28,35,41,47,49,52-56]

Ventilation strategies	Lung-protective ventilation is the cornerstone. Synchronized conventional mechanical ventilation is recommended as the initial strategy: SIPPV or SIMV. Use volume targeted ventilation (4-6 mL/kg). Try to maintain spontaneous respiration, avoiding over-sedation. Start with a ventilator rate of 40-60/min and an inspiratory time (iT) of 0.3 sec.; adjust the rate to maintain a $PaCO_2$ of 40-65 mmHg and arterial pH of 7.25-7.40. PIP should not be higher than 25 cmH_2O. If a PIP greater than 25 cmH_2O is required to achieve the target $PaCO_2$ and saturation levels, alternative treatment modalities, such as HFOV or ECMO, should be considered. If a persistent leak > 25% is present, consider upsizing the ETT. Use a PEEP of 3-5 cmH_2O. If there are oxygenation issues and a chest X-ray shows collapse or underinflated lungs, consider a trial of higher PEEP. Chest X-ray: larger lung to an expansion of 8-9 ribs; the smaller lung ipsilateral to the hernia should not be visible on the pre-operative radiograph. HFOV can be used as rescue ventilation. When transitioning infants to HFOV, particularly term infants, have them well sedated and consider muscle relaxation. Commence at a MAP equal to that on conventional ventilation (11-17cmH_2O). MAP should not exceed 17 cmH_2O; Frequency of 6-8Hz with adjustments made based on gestational age. Use highest frequency that will allow for adequate gas exchange. Delta P of amplitude adjusted until chest oscillation is seen (usually 30-45 cmH_2O). Obtain chest X-ray within one hour to watch for adequate lung inflation. Look at contralateral lung; 7-8 posterior ribs with a curved diaphragm. If chest X-ray shows > 9 posterior ribs and flattened diaphragm, reduce the MAP.
Surfactant	Usually not necessary nor indicated. In preterm infants ≤ 34 weeks GA, if the chest X-ray or lung ultrasound is suggestive of RDS, surfactant is indicated.
Oxygen	Pre-ductal saturation levels: between 85 and 95%. In individual cases, levels as low as 80% may be acceptable, provided that organ perfusion is adequate, as indicated by a pH > 7.2, lactate levels < 5 mmol/L, and urinary output > 1 mL/kg/h. Post-ductal saturations should remain above 70%. Persistent post-ductal saturations < 70% are indicative of PH and require intervention. Oxygen toxicity needs to be prevented; reduce FiO_2 if the pre-ductal saturation is above 95%. FiO_2 should be weaned or increased gradually, typically in 3% increments. Metabolic acidosis should be promptly corrected with sodium bicarbonate. Pre-ductal PaO_2 should be kept > 30 mmHg, although PaO_2 is not recommended to guide ventilator management; if the post-ductal PaO_2 is < 40 mmHg, FiO_2 should not be weaned. NIRS cerebral oxygenation may supplement pulse oximetry and heart rate monitoring; use normal reference ranges for NIRS values (55 to 85%).
Sedation	Judicious sedation is recommended. Deep sedation is contraindicated. Neuromuscular blockade can impair respiratory function, decrease lung compliance, and increase oxygenation indices and mortality. The main goals are to minimize stress and oxygen consumption, prevent patient-ventilator dyssynchrony, prevent abrupt movements that increase intrathoracic pressure, and maintain hemodynamic stability. Opioids such as morphine sulfate or fentanyl may be used. Morphine has a higher risk of hypotension and histamine release than fentanyl. Commence either morphine (5-10 mcg/kg/h) or fentanyl (0.5 at 3 mcg/kg/hour). Neonatal sedation scales (e.g., N-PASS or COMFORT) can guide sedation titration. If fentanyl perfusion is started, after the first 24-48 hours of life infants should be transitioned from fentanyl to morphine infusions to avoid the development of tachyphylaxis. A bolus of opioid may be required for interventions. A midazolam (20-60 mcg/kg/h) or dexmedetomidine (0.2-0.5 mcg/kg/h) infusion may be required for muscle relaxation. Midazolam may cause hypotension, especially when combined with opioids. Consider muscle relaxation (vecuronium 0.1-0.2 mg/kg IV bolus or rocuronium 0.15 mg/kg IV bolus) in severe cases of ventilator dyssynchrony despite optimization of ventilator settings and sedation. Infants should remain sedated until weaning from mechanical ventilation. Sedation plans should be regularly reassessed.
Bladder catheter	To monitor renal function and fluid balance; prevent urinary retention and associated discomfort; help manage abdominal pressure and ventilation complications; and facilitate nursing care by reducing the need for frequent handling.
Vascular access	Umbilical venous catheter (double-lumen) for fluids and medications for up to five days. An umbilical venous line may not be able to be placed, most likely secondary to an intra-thoracic liver. Peripherally inserted central catheter: should be placed to replace UVC. Right radial artery: allows PaO_2 measurement and reflects the level of oxygen delivered to the brain. Umbilical arterial catheter: reflects the post-ductal saturation, but it may give a more secure longer-term arterial access.

(Continues)

Table 3. Management of a newborn with congenital diaphragmatic hernia in the Neonatal Intensive Care Unit[8,9,28,35,41,47,49,52-56] *(continued)*

Fluid management	Fluid intake restriction is recommended (60-80 mL/kg/day) to prevent pulmonary edema. Pre-operative and post-operative fluid status is crucial. It is important to monitor for signs of fluid overload (CVP persistently > 5 cmH_2O; CVP trending up after fluid bolus; peripheral edema; and worsening respiratory function). If there are signs of fluid overload or pulmonary congestion, then: reduce sedation and muscle relaxation to allow some spontaneous movement; judicious use of diuretics; and consider fluid restriction. Diuretics may be used in selected cases. Diuretics should be considered in the case of persisting positive fluid balance: aim for a diuresis > 1 ml/kg/h. Parenteral nutrition should be initiated early (see Table 6).
Antibiotics	Use antibiotics based on risk factors for perinatal infection (e.g., ampicillin and gentamycin). Does not require empiric prophylactic antibiotic coverage. Cefazolin may be used for perioperative antibiotic prophylaxis.
Hemodynamic	Sedation, acid-base status, and lung recruitment should always be optimized. Early and regular echocardiographic assessment of cardiac function and pulmonary artery pressure can guide therapeutic decision-making. When the heart rate is within the normal range, urine output exceeds 1.0 ml/kg/h, lactate levels are below 3 mmol/L, and there are no other signs of inadequate tissue perfusion, the use of inotropic or vasopressor support is unnecessary. If symptoms of poor perfusion and/or BP below the normal level for GA occur and are associated with pre-ductal saturation below 80%, echocardiographic assessment should be performed. Mean BP maintained within normal limits. Historically, PH treatment involved aggressive vasoconstriction to raise systemic BP and promote left-to-right ductal shunting. However, this approach can be detrimental. Additionally, in patients with severe LV dysfunction (phenotype 3), excessive afterload can worsen LV function. Careful, targeted use of lower-dose systemic vasoconstrictors is now preferred to optimize blood pressure without causing harm. In the case of hypovolemia, fluid therapy (10-20 ml/kg NaCl 0.9%) may be given up to two times. Consider initiating inotropes if there is a minimal response to the fluid bolus and no signs of excessive fluid loss. If the echocardiogram reveals predominant RV dysfunction (usually associated with PH), agents to reduce PVR and enhance RV function such as iNO, milrinone, dobutamine, low-dose epinephrine, and PGE1, may need to be used. The use of prostaglandin E1 (PGE1) is recommended when a dilated and dysfunctional RV is present, accompanied by systemic or supra-systemic pulmonary arterial pressures and a restrictive PDA. If the echocardiogram reveals predominant LV dysfunction (usually with reduced cardiac output and systemic hypotension), myocardial function should be supported with low-dose epinephrine and/or dobutamine. Milrinone can also be used if needed, and it can be combined with epinephrine. PGE1 may be indicated in newborns whose circulation depends on a PDA, providing temporary support until inotropic support is effective. In the presence of systemic hypotension with preserved cardiac function, norepinephrine or vasopressin may be used. Frequent review of the volume status is required prior to and after commencing inotropes. An echocardiogram should be considered to evaluate cardiac function and filling before and after inotropes whenever possible. Hydrocortisone may be used to treat hypotension after other treatment has failed.

BP: blood pressure; CV: conventional ventilation; CVP: central venous pressure; ECMO: extracorporeal membrane oxygenation; ETT: endotracheal tube; FiO_2: fraction of inspired oxygen; GA: gestational age; IV: intra-venous; iNO: inhaled nitric oxide; HFOV: high-frequency oscillatory ventilation; LV: left ventricle; MAP: mean airway pressure; NaCl: sodium chloride; NIRS: near-infrared spectroscopy; SIMV: synchronized intermittent mandatory ventilation; SIPPV: synchronized intermittent positive pressure ventilation; PaO_2: arterial partial pressure of oxygen; $PaCO_2$: arterial partial pressure of carbon dioxide; PEEP: positive end expiratory pressure; PDA: patent ductus arteriosus; PH: pulmonary hypertension; PIP: peak inspiratory pressure; PVR: pulmonary vascular resistance; RDS: respiratory distress syndrome; RV: right ventricle.

noise-free environment, with minimal and gentle handling to reduce the risk of hypoxic episodes. Continuous opioid infusions are commonly employed, with benzodiazepines or dexmedetomidine added in certain cases to enhance sedation.[35,41] While neuromuscular blocking agents may be considered in specific situations, such as severe CDH-PH or refractory hypoxemia, their use is generally reserved for critical scenarios, particularly during HFOV, as its use has been associated with increased mortality.[35,58] Effective analgesia is required after surgical repair.[59]

Fluid management and nutrition

Careful fluid management is critical. Initial fluid intake needs to be restricted to prevent pulmonary edema.[35,41,56,60] Diuretics may be used in selected cases.[40] Parenteral nutrition should be initiated early, as enteral feeds are often delayed until after surgical repair and hemodynamic and respiratory stabilization.[35,56,60] Once stable, minimal enteral feeding may be cautiously introduced to promote gut integrity.[56,60]

Antibiotics

Empirical broad-spectrum antibiotics (e.g., ampicillin and gentamicin) are started upon admission if there is any risk of bacterial perinatal infection, possible bowel ischemia, or risk deriving from the invasive procedures. Therapy is adjusted in accordance with the clinical course and culture results. Cefazolin may be used for perioperative antibiotic prophylaxis.[61]

Hemodynamic support

Newborns with CDH often present with compromised cardiac function.[62] Ventricular dysfunction plays a key role in determining disease severity and mortality.[63,64]

The goal of hemodynamic management should be to ensure adequate end-organ perfusion, as assessed by heart rate, urine output, and lactate levels.[41,65] Echocardiography is recommended whenever there are signs of poor perfusion or if blood pressure falls below the normal range for the gestational age, combined with a pre-ductal oxygen saturation under 80%. It can help to determine whether the poor perfusion is caused by hypovolemia or myocardial dysfunction.[41]

Currently, echocardiography plays a central role in the evaluation of infants with CDH, not only in the assessment of hypoxemic respiratory failure, but also as a key tool for early screening, phenotypic classification, and longitudinal monitoring of PH and cardiovascular dysfunction.[5,66,67]

Whenever feasible, a comprehensive baseline echocardiographic assessment should be performed prior to the initiation of cardiovascular therapies, allowing for accurate characterization of the predominant hemodynamic phenotype. This initial evaluation should include an assessment of PH severity, RV and LV systolic and diastolic function, ventricular interdependence, atrial and ductal shunting patterns, and the exclusion of associated congenital heart disease.[5,66,67]

Given the dynamic and frequently mixed nature of CDH-PH phenotypes, serial echocardiographic evaluations are essential to guide phenotype-directed therapy, monitor response to interventions, and detect evolving changes in cardiac function and pulmonary or systemic hemodynamics at the bedside.[5,66-70]

Echocardiographic assessment should be performed and interpreted by experienced pediatric cardiologists and/or neonatologists with expertise in functional echocardiography, ensuring an accurate incorporation of imaging findings into individualized clinical decision-making.[69]

Additionally, echocardiography helps to determine the appropriate timing of surgical repair. It is also essential for identifying candidates for ECMO and for monitoring postoperative cardiac function and pulmonary hemodynamics. Postoperatively, echocardiography is used to assess residual PH and ventricular performance. In severe cases, it also supports decisions regarding ECMO initiation, management, and weaning. Thus, echocardiography is an indispensable, non-invasive tool for the diagnosis, management, and longitudinal monitoring of the hemodynamic status in CDH patients.[5,41,57,58,71-75]

Hypovolemia requires correction through appropriate fluid administration.[41] However, hypovolemia generally does not represent the primary cause of hemodynamic instability in CDH. Given the risk of both left and right ventricular dysfunction, fluid administration should be undertaken cautiously and guided by echocardiographic assessment.[41]

Due to the pathophysiology of CDH, structural pulmonary hypoplasia with a reduced pulmonary vascular bed, increased vascular muscularization, and heightened vasoreactivity, CDH-PH usually comprises varying degrees of both pre-capillary and post-capillary components. Accordingly, CDH-PH can be broadly categorized into three phenotypes.[5,67,76] Phenotype 1 is characterized by mild or absent PH with a compliant RV, preserved biventricular function, and predominantly left-to-right shunting at both the ductal and atrial levels. Phenotype 2 represents mainly pre-capillary PH, with increased PVR and either preserved cardiac function, primary RV dysfunction, or secondary LV impairment due to ventricular interdependence, typically associated with predominant right-to-left shunting. Phenotype 3 corresponds to mainly post-capillary PH, driven by primary LV dysfunction with elevated left-sided filling pressures, and characterized by right-to-left ductal shunting with left-to-right atrial shunting. Importantly, these phenotypes should not be regarded as fixed entities; rather, they exist along a dynamic spectrum and may evolve over time, being significantly influenced by disease progression, cardiopulmonary interactions, and the initiation of vasoactive and pulmonary vasodilator therapies, which can modify both echocardiographic findings and shunt patterns.[5,67,76]

Some authors prefer to describe CDH-PH as associated with predominantly RV dysfunction (mainly pre-capillary), predominantly LV dysfunction (mainly post-capillary), or mild PH with no significant ventricular dysfunction, since these phenotypes are dynamic and may coexist, with one component being predominant.[35]

Accurate characterization of the underlying hemodynamic phenotype can be challenging, as pulmonary vasodilators (such as oxygen or iNO), positive inotropes, and non-specific vasopressors are often initiated before the first echocardiographic assessment, potentially modifying the baseline physiology. In addition, the spontaneous or therapeutic closure of the PDA, although uncommon, or the absence of an atrial-level communication may further complicate phenotypic classification.

Heart–lung interactions are also an important consideration, as lung derecruitment or hyperinflation can significantly impact PVR and cardiac performance. Since these phenotypes are dynamic rather than static, the serial clinical and echocardiographic assessment of the hemodynamic effects of treatment may therefore provide valuable additional insights.[5]

When RV dysfunction associated with significant CDH-PH is the predominant presentation (phenotype 2; predominantly pre-capillary PH), management should primarily focus on reducing PVR, optimizing RV-pulmonary arterial coupling, and supporting RV function.[35,67] Targeted pulmonary vasodilators such as iNO and milrinone are commonly used in this setting, alongside inotropic support when indicated. Milrinone, dobutamine, and low-dose epinephrine are generally the preferred agents for improving myocardial performance due to their more favorable pulmonary vascular profile.[35,38,67] Systemic hypotension in this phenotype can also contribute to clinical deterioration, often reflecting RV dysfunction and impaired diastolic filling, with reduced coronary perfusion.[67] Vasopressors may restore systemic pressure and coronary blood flow. Epinephrine, norepinephrine, or vasopressin are the preferred agents.[67] Norepinephrine enhances diastolic pressure and coronary blood flow when LV function is preserved.[67]

Dopamine, a non-specific vasopressor with dose-dependent adrenergic effects, has historically been used in some centers to support systemic blood pressure. However, experimental and clinical data suggest that dopamine may increase PVR and worsen RV afterload, particularly in neonates with reactive pulmonary vasculature such as those with CDH. Therefore, dopamine is not recommended as first-line therapy in CDH patients with RV dysfunction and PH, and its use is increasingly discouraged.[5,67,76-78] If considered, dopamine should be reserved for exceptional circumstances, administered at the lowest effective dose, and guided by close clinical and echocardiographic monitoring, while carefully weighing alternative agents with a more favorable hemodynamic profile.[35,38]

High doses of dopamine (> 15 mcg/kg/min) should be avoided, as they are associated with excessive systemic and pulmonary vasoconstriction, increased myocardial oxygen demand, and the potential worsening of global hemodynamics.[35] The combination of dopamine with pulmonary vasodilators such as milrinone should be approached with caution, as dopamine-induced vasoconstriction may offset the beneficial pulmonary and lusitropic effects of milrinone.

Prostaglandin E1 (PGE1) is indicated when a dilated and dysfunctional RV is present in the setting of systemic or supra-systemic pulmonary arterial pressures and a restrictive or closing ductus arteriosus, as maintaining ductal patency may help unload the RV and support systemic perfusion.[67,69]

When LV dysfunction predominates (phenotype 3; predominantly post-capillary PH), management should aim to improve myocardial contractility, optimize preload, and reduce LV afterload. Low-dose epinephrine and dobutamine are commonly used in this setting.[35,38,67] Low-dose epinephrine improves myocardial contractility and cardiac output, making it suitable for treating LV dysfunction and RV dysfunction in CDH. However, higher doses may lead to vasoconstriction, potentially increasing PVR and worsening PH.[67] Milrinone may be beneficial due to its inotropic, lusitropic, and afterload-reducing effects; however, careful monitoring is required because of its potential to cause systemic hypotension.[35,38] Low-dose dopamine may be used, although it is not the first choice and the potential to worsen pulmonary pressure should always be considered.[35] In cases of systemic hypotension with preserved cardiac function, vasopressors with a more favorable pulmonary vascular profile are preferred, such as norepinephrine and epinephrine. Norepinephrine increases SVR and diastolic blood pressure and coronary perfusion while modestly improving pulmonary hemodynamics via α-2-mediated vasodilation.[67] Nonetheless, norepinephrine may be used cautiously when cardiac function is adequate, acknowledging its potential to increase pulmonary arterial pressure.[28] Vasopressin may be considered at low doses, as it predominantly increases SVR while relatively sparing the pulmonary circulation, although excessive afterload may further impair LV function.[35,76,77] Vasopressin is generally reserved as rescue therapy for refractory hypotension; however, some centers have adopted it as a first-line vasopressor in selected cases. Also, vasopressin has minimal beneficial effects on PH.[35,76,77] It should be administered cautiously and at low doses, as it may increase cardiac afterload and further impair LV function.[76,77] Hydrocortisone should be considered in cases of vasopressor-refractory hypotension, particularly when relative adrenal insufficiency is suspected. Its use should be limited to short-term rescue therapy and guided by clinical response.[79–89]

Table 4 provides a summary of the effects of the vasoactive drugs used in treating CDH.[5,28,35,38,41,62-65,67,69,72,73,75-95]

Table 4. Summary of the effects and doses of vasoactive agents[5,28,35,38,41,62-65,67,69, 72,73,75-95]

Vasoactive agent	Effects and doses
Milrinone	Consider in cases with predominant RV dysfunction and severe PH (phenotype 2). Inotropic effects → improves RV contractility. Pulmonary vasodilator effects → reduces PVR, lowering RV afterload. Caution: may precipitate systemic hypotension. Consider also in cases with LV dysfunction/biventricular failure (phenotype 3). Loading dose: this is usually not used, as in neonates with CDH and hemodynamic instability it may worsen or cause hypotension, with the harmful effects outweighing the benefits. It can be used when systemic blood pressure is at the upper limit of normal. A loading dose achieves therapeutic levels faster: 50 mcg/kg over 15 minutes (in pre-term neonates < 30 weeks, with infusion over three hours). Maintenance infusion: initial dose: 0.2-0.33 µg/kg/min (minimizes risk of hypotension). Titration: can be gradually increased up to 0.66 µg/kg/min, and in some cases, up to 1.0 µg/kg/min if tolerated (monitor for BP and perfusion). In the case of milrinone-associated systemic hypotension, the combination with norepinephrine or epinephrine may be a good option, as it allows for an inotropic effect, pulmonary vasodilation, and BP to be maintained. The use of milrinone in patients with renal failure and oliguria demands caution due to the drug's predominantly renal clearance and the increased risk of accumulation and toxicity, including hypotension, arrhythmias, and thrombocytopenia.
Dopamine	Non-selective vasoactive agent with dose-dependent adrenergic effects; historically used for systemic blood pressure support in neonates with CDH. Not recommended as first-line therapy in CDH associated with PH due to its potential to increase PVR and RV afterload. May be considered only in selected cases of systemic hypotension with impaired cardiac output, when alternative agents with a more favorable pulmonary vascular profile are unavailable or contraindicated. Effects on myocardial contractility and systemic vascular resistance are highly variable and unpredictable in critically ill neonates and should be guided by close clinical and echocardiographic monitoring. Dose-dependent effects (variable and overlapping): – 2-5 mcg/kg/min: dopaminergic effects on splanchnic and renal circulation (limited clinical relevance in CDH). – 5-10 mcg/kg/min: β1-adrenergic effects (variable inotropic response). – > 10 mcg/kg/min: α-adrenergic vasoconstriction with increased SVR and potential increase in PVR. Dosing considerations: suggested starting dose (if used): 3-5 mcg/kg/min; titrate cautiously, usually not exceeding 10-15 mcg/kg/min, based on systemic BP, markers of end-organ perfusion (lactate and urine output), and echocardiographic assessment. Avoid doses > 15mcg/kg/min, as they are associated with excessive systemic and pulmonary vasoconstriction, increased myocardial oxygen demand, and potential worsening of global hemodynamics. Dosage should be titrated according to the hemodynamic effect but not the standardized dosing regimen.
PGE1	Prostaglandin E1 (PGE1) is reserved for specific situations, guided by echocardiographic findings. In CDH with severe PH, the RV may not be able to pump effectively into the high-resistance pulmonary circulation. PGE1 keeps the ductus arteriosus open, allowing right-to-left shunting through the ductus. This offloads the RV and allows systemic perfusion to be maintained via the ductus. This way, PGE1 may optimize shunting patterns temporarily, buying time for pulmonary vasodilators (like iNO) to take effect. Also, the indication for PGE1 in LV dysfunction is to maintain systemic perfusion in newborns whose circulation depends on a patent ductus arteriosus, providing temporary support until inotropic support is effective. It is also favored in infants with evidence of structural heart disease to maintain ductal patency. Side effects: apnea, hypotension, and fever. Initial dose: 0.01 mcg/kg/min. Maintenance range: 0.01-0.05 mcg/kg/min. Maximum dose: 0.1 mcg/kg/min.
Epinephrine	May be used in CDH patients: (1) to support myocardial contractility (inotropy), since both right and left ventricular dysfunction may occur; (2) to increase systemic BP (MAP); (3) in cases of severe cardiogenic shock or refractory hypotension. Starting dose: 0.01 mcg/kg/min; low dose: 0.01-0.05 mcg/kg/min (↑ inotropy and ↑ HR); moderate dose: 0.05-0.1 mcg/kg/min (↑ cardiac output and ↑ SVR); high dose: > 0.1 mcg/kg/min (vasoconstriction, ↑ SVR, and potential ↑ afterload) and should not be used in CDH-PH. Caution in CDH patients: increased afterload from high doses may worsen RV function or increase PH. Tachycardia and increased myocardial oxygen demand can be harmful. Always use echocardiography to guide use in the context of RV/LV performance and shunt direction.
Dobutamine	Increases myocardial contractility (positive inotrope). Improves cardiac output; especially useful in LV dysfunction. Improved LV output helps lower left atrial pressure, which can improve pulmonary venous drainage. Mild vasodilation (from beta-2 activity), which can help reduce afterload without significantly dropping BP. Initial dose: 2 to 5 mcg/kg/min. Titration: dose is usually increased in increments of 1-2 mcg/kg/min if the desired hemodynamic effect is not achieved, aiming for optimal cardiac output and BP. Maximum dose: 10 mcg/kg/min; higher doses may be used in some situations (under close monitoring), but the risk of tachycardia or arrhythmias increases.

(Continues)

Table 4. Summary of the effects and doses of vasoactive agents[5,28,35,38,41,62-65,67,69, 72,73,75-95] *(continued)*

Norepinephrine	This is sometimes used in the management of CDH, particularly in cases of severe hypotension, shock, or poor perfusion. It is a potent vasopressor that works by constricting blood vessels, thereby increasing SVR and MAP. Useful when cardiac output is normal but vasoconstriction is required. Usual dose: 0.05 to 0.1 mcg/kg/min. Titration: the dose can be gradually increased by increments of 0.05 mcg/kg/min depending on the clinical response (blood pressure, urine output, and overall perfusion). Maximum dose: while neonates can tolerate doses up to 1-2 mcg/kg/min, the goal is to use the lowest effective dose to maintain adequate perfusion and avoid excessive vasoconstriction. When norepinephrine doses exceed 0.5 mcg/kg/min in patients with CDH, hemodynamics should be reassessed and alternative vasopressors or inotropes considered (or ECMO), as further dose escalation offers limited benefit and increases the risk of excessive vasoconstriction and impaired microcirculatory perfusion. Can cause excessive peripheral vasoconstriction, renal ischemia, and arrhythmias/tachycardia. Norepinephrine should be used cautiously when FiO_2 > 0.6, as its vasoconstrictive effect may increase PVR and worsen right-to-left shunting. Use should be guided by echocardiographic and perfusion parameters.
Hydrocortisone	Consider hydrocortisone if inadequate response from fluid resuscitation and inotropic support. Hydrocortisone can help improve vascular responsiveness to fluid management, thereby supporting BP and preventing hypertension from fluid overload. Its use in pre-term or critically ill neonates has been shown to improve cardiovascular stability, particularly in those with shock or hypotension. Loading dose: 1-2 mg/kg IV. Maintenance dose: 1 to 2 mg/kg/day in divided doses, every eight to 12 hours. Maximum dose: up to 3 mg/kg/day (in severe cases). High doses can lead to immunosuppression and hyperglycemia. Tapering: reduction of 25-50% every 24-48 hours, as the neonate stabilizes.
Vasopressin	Vasopressin is generally reserved as rescue therapy for refractory hypotension and PH unresponsive to catecholamines and iNO; however, some centers have adopted it as a first-line vasopressor in selected cases. Vasopressin has minimal beneficial effects on PH. Starting dose: 0.01-0.1 units/kg/h, started at the lowest dose and titrated based on BP response. Titration: dose may be increased gradually in increments of 0.01-0.05 units/kg/h if there is an insufficient response in MAP or perfusion. Maximum dose used in neonates is typically around 0.3 units/kg/h.

BP: blood pressure; CDH: congenital diaphragmatic hernia; ECMO: extracorporeal membrane oxygenation; HR: heart rate; iNO: inhaled nitric oxide; LV: left ventricle; MAP: mean arterial pressure; PH: pulmonary hypertension; PVR: pulmonary vascular resistance; RV: right ventricle; SVR: systemic vascular resistance.

Management of pulmonary hypertension

CDH-PH is a major cause of morbidity and mortality in CDH.[5,7] Echocardiographic evaluation is essential for diagnosis and monitoring.[41,47] Although oxygen is a powerful pulmonary vasodilator, using concentrations greater than 50% has not demonstrated additional benefits for pulmonary vasodilation.[93] In fact, studies have shown that hyperoxic ventilation can increase oxidative stress and lung injury, and may paradoxically reduce the vasodilatory response to iNO.[93] iNO is the first-line therapy for PH, particularly in the presence of pre-capillary hypertension and right-to-left shunting across an atrial shunt and PDA, because it selectively dilates the pulmonary arterial vasculature, reducing PVR, improving blood flow through the lungs, enhancing oxygenation, and decreasing the magnitude of the shunt, all without causing systemic hypotension.[41,94,95] iNO should be started when the oxygenation index (OI: mean airway pressure × FiO_2/PaO_2) is over 20 and/or the pre- and post-ductal saturation difference is greater than 10%.[41] iNO should be postponed until LV function improves, because its pulmonary vasodilatory effect can increase pulmonary venous return to a compromised LV, potentially worsening existing LV dysfunction and causing systemic hypotension or pulmonary edema.[96] iNO responders are defined by any of the following criteria: a 10-20% reduction in the pre- and post-ductal saturation difference, a 10-20% increase in PaO_2, an improvement in hemodynamic parameters (e.g., a 10% rise in mean blood pressure), or a decrease in lactate levels.[41] In non-responders, iNO should be discontinued.[41] Sildenafil and/or prostacyclin analogs, as well as bosentan, may be used as adjuncts to vasoactive agents, particularly after milrinone.[35] Intravenous sildenafil should be considered in severe CDH-PH.[41] Sildenafil can be used both in acute situations, as an adjunct therapy when iNO and/or milrinone are insufficient, and in chronic use to maintain the pulmonary pressure reduction after stabilization.[97-102] Bosentan, on the other hand, is generally reserved for chronic use in the postoperative period.[101,102]

Optimization of oxygenation, ventilation, and acid-base balance are also key components of management.[80] Table 5 summarizes the mechanism of action and dosage of pulmonary vasodilator agents used in CDH-PH.[35,41,67,80,93-102]

Table 5. Mechanism of action and dosage of pulmonary vasodilator agents used in pulmonary hypertension associated with congenital diaphragmatic hernia[35,41,67,80,93-102]

Agent	Effects and doses
Nitric oxide	Selective pulmonary vasodilator without causing systemic hypotension; helps to improve ventilation-perfusion matching and oxygenation. It is delivered via ventilator circuit as a continuous inhaled gas. Typical initial dose: 20 ppm; dose may be adjusted based on response and oxygenation. The focus is on titrating down once improvement occurs to minimize side effects. Doses above 20 ppm (up to 40 ppm) have not shown additional benefit and may increase the risk of side effects such as methemoglobinemia and NO_2 toxicity. iNO should be part of a multimodal approach including optimal ventilation strategies. Needs careful monitoring of oxygenation (e.g., oxygenation index and arterial blood gases) and hemodynamics. Response may be variable in CDH patients because pulmonary hypoplasia limits the number of vessels available to vasodilate, and also due to the possibility of primary LV dysfunction in mixed phenotypes or those predominantly with post-capillary PH. Lack of response or rebound PH may occur; iNO is not universally effective in CDH. A negative response to iNO should prompt early echocardiography to rule out a primary left heart phenotype and weaning of treatment. Once oxygenation improves, gradual weaning of iNO is recommended to avoid rebound PH.
Sildenafil	Sildenafil is a phosphodiesterase type 5 (PDE5) inhibitor, which works by increasing the levels of cyclic-GMP within smooth muscle cells in the pulmonary vasculature. This leads to vasodilation and a reduction in PVR. It reduces right ventricular afterload, improving right ventricular function and cardiac output. It improves pulmonary blood flow, which leads to better ventilation–perfusion matching in the lungs. Sildenafil is often used in combination with other therapies, such as iNO or inotropes. It can also be used alongside mechanical ventilation or ECMO (if needed). It is indicated when other treatments like iNO or HFOV are either insufficient or require additional support. Starting oral dose: 0.25-0.5 mg/kg administered every six to eight hours. Maximum oral dose: 2 mg/kg every six hours. IV: 0.4 mg/kg loading dose over 3 h → infusion 1.6-2 mg/kg/ day; omit loading if hypotensive. Careful monitoring of BP, heart rate, and oxygenation is essential during sildenafil therapy to avoid potential side effects, such as hypotension or bradycardia. Special considerations: pulmonary vasodilatory effects are not confined to well-ventilated portions of the lung, as in the case with iNO, which could contribute to a worsened V:Q mismatch. The duration of IV sildenafil therapy varies but is typically used for a short period while transitioning to oral sildenafil if ongoing treatment is required. Once the neonate stabilizes and the risk of PH decreases, the IV formulation can be transitioned to oral sildenafil at similar doses (around 0.25-1 mg/kg every six to eight hours).
Prostacyclin analogs	Prostacyclin analogs are used as part of advanced pulmonary vasodilator therapy, especially when iNO is insufficient or not effective. They act by vasodilation of pulmonary arteries and inhibiting smooth muscle proliferation. Reserved for severe or refractory PH. Often used in combination with other therapies like iNO, phosphodiesterase inhibitors (e.g., sildenafil), and ECMO. Iloprost (inhaled): can be used as an adjunct to iNO or when iNO response is limited; short half-life; multiple daily doses or continuous nebulization needed. Limited data in neonates but used off-label. Dose: 0.5-2 mcg/kg per inhalation, nebulized every two to three hours, six to nine times per day (due to short half-life ~30 minutes); some centers use continuous nebulization via ventilator circuit. Epoprostenol (IV): continuous IV infusion; potent vasodilator and inhibitor of platelet aggregation. Starting dose: 1-2 nanograms/kg/min; titration: increase by 1-2 ng/kg/min every 30-60 minutes based on response and tolerance; typical range: 7-10 ng/kg/min. Inhalation dose: 20-50 ng/kg/min. Treprostinil: available in IV, subcutaneous, and inhaled forms; less commonly used in neonates; more data in older children and adults; longer half-life than epoprostenol. IV starting dose: 1-2 ng/kg/min; titration: increase by 1-2 ng/kg/min every 12-24 hours; typical dose range: 5-20 ng/kg/min.
Bosentan	Bosentan, an oral endothelin receptor antagonist, blocks ET-A and ET-B receptors, reducing vasoconstriction and vascular proliferation. It is used in infants with CDH and PH to help lower PVR and improve long-term outcomes. It is typically part of a chronic management strategy, not for acute neonatal stabilization. Even after initial stabilization, some CDH survivors develop persistent or progressive PH that worsens over weeks to months. Sometimes used before discharge to support pulmonary transition. Oral: 0.5-2 mg/kg/dose, twice daily. Commence at 0.5 mg/kg/dose 12 hourly. Increase incrementally in consultation with cardiologist to a maximum of 2 mg/kg/dose 12 hourly.

CDH: congenital diaphragmatic hernia; cGMP: cyclic guanosine monophosphate; iNO: inhaled nitric oxide; IV: intravenous; HFOV: high-frequency oscillatory ventilation; NO_2: nitrogen dioxide; PH: pulmonary hypertension; ppm: parts per million; PVR: pulmonary vascular resistance.

Extracorporeal membrane oxygenation

If maximal medical management fails to stabilize oxygenation and/or hemodynamics, ECMO should be considered.[41,103] The benefit of ECMO in the treatment of infants with CDH remains unclear.[41] The ELSO Registry showed a survival rate of 51% of patients with CDH who required ECMO. ECMO seems to improve survival rates in CDH patients who are most severely affected, but the potential complications of ECMO delivery

outweigh the benefit in patients who are less severely affected.[102] Criteria typically include an OI > 40 for at least three hours despite maximal support, inability to maintain pre-ductal saturations > 85% or post-ductal saturations > 70%, increased $PaCO_2$ and respiratory acidosis, peak inspiratory pressure ≥ 28 cmH_2O, or mean airway pressure > 17 cmH_2O required to achieve saturation > 85%, inadequate oxygen delivery with metabolic acidosis as measured by elevated lactate ≥ 5 mmol/L and pH, systemic hypotension, resistance to fluid and inotropic therapy, resulting in urine output or severe cardiovascular compromise that is unresponsive to inotropes.[41] Venoarterial (VA) is often preferred over venovenous (VV) ECMO in infants with CDH due to the need for both respiratory and cardiac support. However, several studies comparing VA and VV ECMO in this population have not demonstrated a significant difference in mortality between the two modes. Given that VA and VV ECMO have similar outcomes, the choice should be based on institutional expertise.[35] ECMO provides time for pulmonary vasculature and lung function to improve before surgical repair. Relative contraindications should be evaluated individually in consultation with the surgical, neonatology, and ECMO teams to assess eligibility. These include a birth weight under 1.7-2 kg, gestational age under 32 weeks, significant congenital or chromosomal anomalies, and complex congenital heart disease, especially those involving single-ventricle physiology. Intracranial hemorrhage of grade III or higher is generally considered an absolute contraindication.[35]

Surgical repair

Surgical repair plays a crucial role in the management of CDH, aiming to restore the normal anatomy by repositioning herniated abdominal organs into the abdomen and closing the diaphragmatic defect. Surgery is not an emergency procedure and should be performed only after the infant is stabilized. Cardiac dysfunction is common in CDH and has a significant impact on morbidity and mortality.[70] Stabilization for surgery should be considered in the presence of clinical, blood gas, and echocardiographic criteria: a normal mean arterial pressure for the gestational age (> 3rd centile), pre-ductal oxygen saturation of 85-95% on $FiO_2 \leq 50\%$ (tolerating ≤ 60%) , lactate level < 3 mmol/L, and urine output > 2 mL/kg/h, tolerance of nursing care without instability and with adequate sedation, arterial pH > 7.25, $PaCO_2$ < 60 mmHg (pre-ductal) or < 65 mmHg (post-ductal), stable ventilation settings, normal biventricular function on stable inotropes (if needed), PDA shunt > 50% left-to-right, pulmonary pressures that are stable or not worsening, and stability on serial echocardiograms (≥ 2) at least 24 hours apart.[9,35,41,70] The assessment, including the aforementioned parameters, should be performed daily during the preoperative period, and once this window of clinical stability is achieved, surgery should be carried out within 24 hours.[70] Unlike ventricular function, we should not expect or require the normalization of pulmonary arterial pressure/PH prior to surgical repair.[70] Indeed, the optimal repair window includes some degree of stable PH or PH that is not worsening.[70] Given the close association of heart function and outcomes of CDH, cardiotropic medications, when needed, should not be discontinued prior to operative repair.[70]

In CDH patients on ECLS, normalization of LV function is required as a criterion for surgical repair or decannulation for surgery. Due to RV unloading by the ECMO cannula, mild-to-moderate RV dysfunction may persist and should not delay surgery.[70]

To enhance understanding of echocardiographic assessment in determining the optimal timing for surgery, reading the article by Wren JT et al.[70] is recommended.

In infants with no evidence of liver herniation, requiring minimal ventilatory support, and with no significant evidence of CDH-PH or pulmonary hypoplasia, surgical repair can be performed on the second or third day of life.[35] In infants with moderate-to-severe pulmonary hypoplasia and CDH-PH, surgical repair is often delayed. Although most of these infants initially exhibit clinical instability, they typically demonstrate subsequent improvement and stabilization, allowing surgical repair to be performed around days five to ten of life.[35] The timing and approach of the repair, whether open or minimally invasive, are determined based on the patient's clinical status and institutional protocols. Depending on the infrastructure and clinical protocols of the unit, CDH repair can be performed at the infant's bedside. This approach may reduce the risks associated with transporting a hemodynamically unstable neonate who requires extensive supportive equipment and continuous monitoring.[35] Repair can be performed while the patient is on ECMO.[35,41]

Chronic lung disease

The definition of CLD in infants with CDH has traditionally followed that used for preterm infants with bronchopulmonary dysplasia, based on oxygen dependency at 28-30 days of life. However, due to the different pathophysiology, a more appropriate definition for CLD

in CDH may be oxygen dependency 30 days after surgical repair. Studies show this is linked to important clinical outcomes, such as reduced lung function and increased respiratory and developmental morbidity. Respiratory management should be individualized, considering the heterogeneity of lung involvement and the high prevalence of CDH-PH in these infants. Strategies like careful PEEP use, adjusting respiratory rate and expiratory time, and bronchodilator therapy may be beneficial. Importantly, lung growth continues throughout childhood.[35]

Sildenafil and bosentan can be considered for the treatment of PH in postoperative patients with CLD, although the evidence in the literature remains limited.[98] Their use in CDH patients requires careful monitoring of pulmonary, cardiac, and hepatic function due to potential complications and drug interactions. The choice of treatment should be individualized, considering the severity of PH, comorbidities, and the patient's post-surgical recovery status. Close follow-up, including a pediatric cardiologist and a pulmonologist, is essential to ensure efficacy and to minimize adverse effects.[101,102]

Malnutrition and feeding difficulties

Malnutrition and feeding difficulties are common in infants with CDH and often persist into early childhood. Enteral feeds can be commenced within 24 hours of surgery, after discussion with the surgical team. Intestinal ileus and reflux are common and continuous feeds (gastric or transpyloric) may be required in the first few days (Table 6).[35,103-105]

Implementing strategies such as human milk feeding, early recognition of growth failure, and earlier initiation of higher-calorie feeds is paramount. The transition from parenteral to enteral nutrition is a vulnerable period for calorie deficits and is often prolonged due to feeding intolerance. In some patients, surgical complications such as traumatic chylothorax and diaphragmatic paresis further exacerbate these feeding challenges.[106-108]

In cases of gastroesophageal reflux, non-pharmacological measures such as upright positioning, small frequent feeds, and slow feeding techniques should be prioritized, while pharmacological therapy with proton pump inhibitors or prokinetic agents may be considered when there is documented esophagitis, when symptoms persist, or when complications arise. Gastroesophageal reflux must be adequately managed through medical or surgical interventions.[109]

Feeding guidelines recommend starting with human milk and adjusting feeding progress based on tolerance. A hypercaloric diet may be necessary for selected patients, and a specialized nutritional plan should be individualized. Continuous monitoring by a dietitian is essential to support growth and meet nutritional goals.[35,110,111]

Outcomes in congenital diaphragmatic hernia

The prognosis of infants with CDH has improved over recent decades due to advances in perinatal care, surgical techniques, and neonatal intensive care. However, CDH continues to be associated with significant morbidity and mortality, particularly in cases involving severe pulmonary hypoplasia and CDH-PH.[111]

Infants with CDH are at risk for a wide range of complications that span multiple organ systems.[111,112] Respiratory complications are among the most frequent and severe, including pulmonary hypoplasia, persistent CDH-PH, CLD, recurrent respiratory infections, and prolonged dependence on supplemental oxygen or mechanical ventilation. Nutritional and gastrointestinal problems are also common, with feeding difficulties, gastroesophageal reflux disease, malnutrition, growth failure, and feeding intolerance with frequent vomiting frequently reported. Cardiac complications may occur due to cardiac displacement and the presence of associated congenital heart defects, which are identified in up to 40% of cases. Neurological and developmental outcomes may be affected, as neurodevelopmental delays, neuromuscular hypotonia, and mild-to-moderate cognitive or motor impairments are frequently observed. Sensory impairments, such as hearing and visual deficits, can also occur. Surgical complications include hernia recurrence, surgical wound infections, prosthetic mesh-related problems, diaphragmatic paresis, and chylothorax. In addition, musculoskeletal abnormalities such as scoliosis and pectus excavatum may develop over time, often as a result of thoracic deformities or prolonged respiratory support.[113,114]

Overall, the management of CDH requires a multidisciplinary approach, with long-term follow-up to address the complex interplay between respiratory, nutritional, cardiac, neurological, and musculoskeletal sequelae.[111-113]

Survival rates vary widely and depend on several factors, including the size and side of the hernia, the presence of liver herniation, the degree of lung underdevelopment, and the need for ECMO. Overall survival in high-resource settings ranges from 60 to 80%, but may be lower in severe cases or in the presence of associated anomalies.[114]

Table 6. Nutritional approach to infants with congenital diaphragmatic hernia[35,103-105]

Aspect	Key points/recommendations
Nutritional risk	Malnutrition and feeding difficulties are common in infants with CDH; early recognition of growth failure is essential.
Fluid management	Initial fluids: 60-80 mL/kg/day. Management should be restrictive. Before surgical repair, fluid progression should be cautious and always guided by the infant's hemodynamic and respiratory status, to avoid pulmonary edema and the worsening of PH and cardiac function. Fluids are increased gradually as the infant stabilizes hemodynamically and metabolically. Gradual increase progressed by 10-20 mL/kg/day up to 120-150 mL/kg/day after stabilization. Monitor urine output (1-3 mL/kg/h), weight, electrolytes, and signs of fluid retention or pulmonary congestion.
Caloric requirements	Start at 40-60 kcal/kg/day and increase as possible up to 100-110 kcal/kg/day. To reduce failure to thrive and promote growth, once enteral feedings are tolerated, caloric intake should aim for 120-140 kcal/kg/day; target daily weight gain should be comparable to other term infants.
Protein	Start at 1.5-2 g/kg/day; progress to 3 g/kg/day to prevent catabolism.
Glucose	Start at 4-6 mg/kg/min; may increase to 8-10 mg/kg/min. Maintain blood glucose 70-120 mg/dL.
Lipids	Start at 0.5-1 g/kg/day; increase up to 3 g/kg/day (30-40% of total calories).
Parenteral nutrition (PN)	Initiation in the first 24 hours of life; monitor electrolytes, fluid balance, and metabolic parameters until enteral feeding can be introduced. Infants who require prolonged PN are at high risk of developing PN-associated cholestasis (conjugated bilirubin 1.5-2.0 mg/dL). In cholestasis lipid intake from pure soybean oil emulsions should be reduced to around 1 g/kg/day or replaced with mixed or fish oil-based emulsions (such as SMOFlipid or Omegaven), which can usually be administered at standard doses because they are less likely to induce or worsen cholestasis. In patients on ECMO, augment fluid removal with diuretic or continuous renal replacement therapy to maintain nutritional goals.
Enteral nutrition (EN) initiation	EN should be initiated only after surgical repair, once the infant is hemodynamically and respiratory stable and shows signs of intestinal readiness (bowel sounds, minimal gastric output, and absence of bilious drainage), according to the surgeon's indication. It can also be initiated in infants on ECMO. NOTE: The presence of low-dose, weaning vasoactive support is not an absolute contraindication to initiating EN, provided perfusion is adequate (normal lactate levels and urine output). Small trophic feeds with breast milk can usually be started 48-72 hours postoperatively and progressed gradually as tolerated.
Feeding method	There is no clear evidence to support initiation with bolus *versus* continuous enteral feedings. The method of enteral feeding should be individualized based on hemodynamic stability, risk of aspiration, and intestinal function. Low-risk patients who are hemodynamically stable with adequate gastric motility and low aspiration risk are likely to tolerate bolus feeding: a bolus should be administered slowly (10-15 minutes) at small volumes (10-20 mL/kg per dose) every two to three hours, with gradual progression according to tolerance. Early trophic feeding, even in small amounts, is encouraged to stimulate intestinal maturation and reduce parenteral nutrition-associated cholestasis. High-risk unstable neonates, those on low-dose vasoactive support, or cases of postoperative gastric dysmotility may benefit from continuous feeding. Transpyloric feeding, delivered continuously, is reserved for patients with high aspiration risk or severe gastric intolerance/gastroparesis. Oral feeding by breast or bottle should begin at < 2 liters per minute respiratory support, in the absence of any contraindication to oral feeding. Preventive anti-reflux therapy (e.g., omeprazole) should not be started alongside enteral feeding in all patients, unless esophagitis is documented. The benefits of reducing gastric acid secretion in reflux treatment must be weighed against the associated risks. Also, preventive anti-reflux surgery at the time of CDH repair should not be routinely performed.
Milk choice	Breast milk preferred; if unavailable, term formula. In the case of intolerance: transpyloric feeding or hydrolyzed formulas. May require fortification, modular diets, or high-calorie formulas, as guided by a nutrition specialist.
Transition from PN to EN	Vulnerable period; may result in temporary calorie and protein deficits. Overlaps with weaning from respiratory support and sedation; prolonged in CDH due to feeding intolerance.
Weight gain goals	Gradual and individualized. Target weight gain should be comparable to other term infants (25-35 g/day) after EN initiation. Weight maintenance or 5-10% loss expected during PN. Ensure growth reflects lean body mass; monitor length and head circumference.
Monitoring	Daily weight, growth curve, tolerance, vomiting, abdominal distension, gastric residuals, and signs of malnutrition. In cholestasis, monitor liver enzymes (AST and ALT), GGT, and bilirubin levels. Long-term multidisciplinary nutritional support often required. Feeding support by pediatric occupational and speech therapists is an important component of outpatient management and should be available for infants who are not taking full oral feeds at discharge. The potential risk and benefit of home nasogastric and gastric tube should be carefully weighed for each individual patient.

CDH: congenital diaphragmatic hernia; ECMO: extracorporeal membrane oxygenation; PH: pulmonary hypertension.

In summary, while survival rates for CDH have improved, affected infants remain at high risk for multiple complications. A multidisciplinary approach and long-term follow-up are critical to managing the complex needs of these patients and improving quality of life. Even in cases with favorable short-term outcomes, long-term morbidity is common and may significantly affect quality of life.[112,115]

Conclusion

The treatment of neonates with CDH is complex and requires an individualized, multidisciplinary approach. Advances in perinatal management, gentle ventilation, hemodynamic support, and the selective use of ECMO have contributed to improved outcomes. Continued research and standardized protocols are essential to optimize survival and long-term quality of life in this vulnerable population.

Author contributions

The author was solely responsible for all aspects of the study and manuscript preparation.

Funding

None.

Conflicts of interest

None.

Ethical considerations

Protection of human subjects and animals. The authors declare that no experiments on humans or animals were performed for this research.

Confidentiality, informed consent, and ethical approval. This study does not involve personal patient data, medical records, or biological samples, and does not require ethical approval. SAGER guidelines do not apply.

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

References

1. McGivern MR, Best KE, Rankin J, Wellesley D, Greenlees R, Addor MC, et al. Epidemiology of congenital diaphragmatic hernia in Europe: a register-based study. Arch Dis Child Fetal Neonatal Ed 2015;100(2): F137-44.
2. Peppa M, De Stavola BL, Loukogeorgakis S, Zylbersztejn A, Gilbert R, De Coppi P. Congenital diaphragmatic hernia subtypes: Comparing birth prevalence, occurrence by maternal age, and mortality in a national birth cohort. Paediatr Perinat Epidemiol 2023;37(2):143-153.
3. Paoletti M, Raffler G, Gaffi MS, Antounians L, Lauriti G, Zani A. Prevalence and risk factors for congenital diaphragmatic hernia: A global view. J Pediatr Surg 2020;55(11):2297-2307.
4. Politis MD, Bermejo-Sánchez E, Canfield MA, Contiero P, Cragan JD, Dastgiri S, et al; International Clearinghouse for Birth Defects Surveillance and Research. Prevalence and mortality in children with congenital diaphragmatic hernia: a multicountry study. Ann Epidemiol 2021;56: 61-69.e3.
5. Holden KI, Rintoul NE, McNamara PJ, Harting MT. Congenital diaphragmatic hernia-associated pulmonary hypertension. Semin Pediatr Surg 2024;33(4):151437.
6. Antounians L, Zani A. Beyond the diaphragm and the lung: a multisystem approach to understanding congenital diaphragmatic hernia. Pediatr Surg Int 2023;39(1):194.
7. Gupta VS, Harting MT, Lally PA, Miller CC, Hirschl RB, Davis CF, et al; Congenital Diaphragmatic Hernia Study Group. Mortality in Congenital Diaphragmatic Hernia: A Multicenter Registry Study of Over 5000 Patients Over 25 Years. Ann Surg 2023;277(3):520-527.
8. Jancelewicz T, Brindle ME, Guner YS, Lally PA, Lally KP, Harting MT; Congenital Diaphragmatic Hernia Study Group (CDHSG); Pediatric Surgery Research Collaborative (PedSRC). Toward Standardized Management of Congenital Diaphragmatic Hernia: An Analysis of Practice Guidelines. J Surg Res 2019;243:229-235.
9. Baschat AA, Desiraju S, Bernier ML, Kunisaki SM, Miller JL. Management advances for congenital diaphragmatic hernia: integrating prenatal and postnatal perspectives. Transl Pediatr 2024;13(4):643-662.
10. Dimmer A, Baird R, Puligandla P. Role of practice standardization in outcome optimization for CDH. World J Pediatr Surg 2024;7(2):e000783.
11. Klein J, Sirota M. Congenital Diaphragmatic Hernia. N Engl J Med 2017;377(17):e25.
12. Lally KP, Lasky RE, Lally PA, Bagolan P, Davis CF, Frenckner BP, et al; Congenital Diaphragmatic Hernia Study Group. Standardized reporting for congenital diaphragmatic hernia--an international consensus. J Pediatr Surg 2013;48(12):2408-15.
13. Chandrasekharan PK, Rawat M, Madappa R, Rothstein DH, Lakshminrusimha S. Congenital Diaphragmatic hernia - a review. Matern Health Neonatol Perinatol 2017;3:6.
14. Guglielmetti LC, Estrada AE, Phillips R, Staerkle RF, Gien J, Kinsella JP, et al. Congenital diaphragmatic hernias: Severe defect grade predicts the need for fundoplication. Medicine (Baltimore) 2020 Dec;99(49):e23383.
15. Otaño JC, Murua V, Rugilo J, Reusmann A, Ruhrnschopf CG, Fariña D, et al. Congenital diaphragmatic hernia: relationship between defect size and outcome. Experience in a reference centre. An Pediatr (Engl Ed) 2024;101(1):29-35.
16. Abbasi N, Backley S, Ryan G, Johnson A. Prenatal diagnosis and risk stratification of congenital diaphragmatic hernia. World J Pediatr Surg 2024;7(4):e000892.
17. LaRusso K, Baird R, Keijzer R, Skarsgard E, Puligandla P. Standardizing congenital diaphragmatic hernia care in Canada: Implementing national clinical practice guidelines. J Pediatr Surg 2020;55(5):835-843.
18. Doné E, Gucciardo L, Van Mieghem T, Jani J, Cannie M, Van Schoubroeck D, et al. Prenatal diagnosis, prediction of outcome and in utero therapy of isolated congenital diaphragmatic hernia. Prenat Diagn 2008;28(7):581-91.
19. Jani J, Keller RL, Benachi A, Nicolaides KH, Favre R, Gratacos E, et al; Antenatal-CDH-Registry Group. Prenatal prediction of survival in isolated left-sided diaphragmatic hernia. Ultrasound Obstet Gynecol 2006;27(1):18-22.
20. Cordier AG, Russo FM, Deprest J, Benachi A. Prenatal diagnosis, imaging, and prognosis in Congenital Diaphragmatic Hernia. Semin Perinatol 2020;44(1):51163.
21. Dott MM, Wong LY, Rasmussen SA. Population-based study of congenital diaphragmatic hernia: risk factors and survival in Metropolitan Atlanta, 1968-1999. Birth Defects Res A Clin Mol Teratol 2003;67(4):261-7.
22. Renik-Jankowska W, Buczyńska A, Sidorkiewicz I, Kosiński P, Zbucka-Krętowska M. Exploring new perspectives on congenital diaphragmatic hernia: A comprehensive review. Biochim Biophys Acta Mol Basis Dis 2024;1870(4):167105.
23. Russo FM, Cordier AG, De Catte L, Saada J, Benachi A, Deprest J; Workstream Prenatal Management, ERNICA European reference network. Proposal for standardized prenatal ultrasound assessment of the fetus with congenital diaphragmatic hernia by the European reference network on rare inherited and congenital anomalies (ERNICA). Prenat Diagn 2018;38(9):629-637.
24. Oluyomi-Obi T, Kuret V, Puligandla P, Lodha A, Lee-Robertson H, Lee K, et al. Antenatal predictors of outcome in prenatally diagnosed congenital diaphragmatic hernia (CDH). J Pediatr Surg 2017;52(5):881-888.
25. Masahata K, Yamoto M, Umeda S, Nagata K, Terui K, Fujii M, et al. Prenatal predictors of mortality in fetuses with congenital diaphragmatic hernia: a systematic review and meta-analysis. Pediatr Surg Int 2022;38(12):1745-1757.

26. Basurto D, Russo FM, Van der Veeken L, Van der Merwe J, Hooper S, Benachi A, et al. Prenatal diagnosis and management of congenital diaphragmatic hernia. Best Pract Res Clin Obstet Gynaecol 2019;58: 93-106.
27. Jani J, Nicolaides KH, Keller RL, Benachi A, Peralta CF, Favre R, et al; Antenatal-CDH-Registry Group. Observed to expected lung area to head circumference ratio in the prediction of survival in fetuses with isolated diaphragmatic hernia. Ultrasound Obstet Gynecol 2007;30(1):67-71.
28. Puligandla P, Skarsgard E, Baird R, Guadagno E, Dimmer A, Ganescu O, et al; Canadian Congenital Diaphragmatic Hernia Collaborative. Diagnosis and management of congenital diaphragmatic hernia: a 2023 update from the Canadian Congenital Diaphragmatic Hernia Collaborative. Arch Dis Child Fetal Neonatal Ed 2024;109(3):239-252.
29. Kitano Y, Okuyama H, Saito M, Usui N, Morikawa N, Masumoto K, et al. Re-evaluation of stomach position as a simple prognostic factor in fetal left congenital diaphragmatic hernia: a multicenter survey in Japan. Ultrasound Obstet Gynecol 2011;37(3):277-82.
30. Cordier AG, Cannie MM, Guilbaud L, De Laveaucoupet J, Martinovic J, Nowakowska D, et al. Stomach position versus liver-to-thoracic volume ratio in left-sided congenital diaphragmatic hernia. J Matern Fetal Neonatal Med 2015;28(2):190-5.
31. Basta AM, Lusk LA, Keller RL, Filly RA. Fetal Stomach Position Predicts Neonatal Outcomes in Isolated Left-Sided Congenital Diaphragmatic Hernia. Fetal Diagn Ther 2016;39(4):248-55.
32. Abbasi N, Ryan G, Ruano R, Sanz Cortes M, Ye XY, Shah PS, et al; NAFTNet. Interrater agreement for sonographic stomach position classification in fetal diaphragmatic hernia across the North American Fetal Therapy Network. Prenat Diagn 2022;42(3):348-356.
33. Weller K, Peters NCJ, van Rosmalen J, Cochius-Den Otter SCM, DeKoninck PLJ, Wijnen RMH, et al. Prenatal stomach position and volume in relation to postnatal outcomes in left-sided congenital diaphragmatic hernia. Prenat Diagn 2022;42(3):338-347.
34. Ruano R, Lazar DA, Cass DL, Zamora IJ, Lee TC, Cassady CI, et al. Fetal lung volume and quantification of liver herniation by magnetic resonance imaging in isolated congenital diaphragmatic hernia. Ultrasound Obstet Gynecol 2014;43(6):662-9.
35. Wild KT, Hedrick HL, Ades AM, Fraga MV, Avitabile CM, Gebb JS, et al. Update on Management and Outcomes of Congenital Diaphragmatic Hernia. J Intensive Care Med 2024;39(12):1175-1193.
36. Chen Y, Xu R, Xie X, Wang T, Yang Z, Chen J. Fetal endoscopic tracheal occlusion for congenital diaphragmatic hernia: systematic review and meta-analysis. Ultrasound Obstet Gynecol 2023;61(6):667-681.
37. Pugnaloni F, Bo B, Hale L, Capolupo I, Dotta A, Bagolan P, et al. Early Postnatal Ventricular Disproportion Predicts Outcome in Congenital Diaphragmatic Hernia. Am J Respir Crit Care Med 2023;208(3):325-328.
38. Fraga MV, Hedrick HL, Rintoul NE, Wang Y, Ash D, Flohr SJ, et al. Congenital Diaphragmatic Hernia Patients with Left Heart Hypoplasia and Left Ventricular Dysfunction Have Highest Odds of Mortality. J Pediatr 2024;271:114061.
39. Nasr A, Langer JC; Canadian Pediatric Surgery Network. Influence of location of delivery on outcome in neonates with congenital diaphragmatic hernia. J Pediatr Surg 2011;46(5):814-6.
40. Bouchghoul H, Dumery G, Russo FM, Cordier AG, Le Sache N, Debeer A, et al. Optimal gestational age at delivery in isolated left-sided congenital diaphragmatic hernia. Ultrasound Obstet Gynecol 2021;57(6): 968-973.
41. Snoek KG, Reiss IK, Greenough A, Capolupo I, Urlesberger B, Wessel L, et al; CDH EURO Consortium. Standardized Postnatal Management of Infants with Congenital Diaphragmatic Hernia in Europe: The CDH EURO Consortium Consensus - 2015 Update. Neonatology 2016;110(1):66-74.
42. Dumpa V, Chandrasekharan P. Congenital Diaphragmatic Hernia. 2023 Aug 8. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–.
43. Frenckner B, Ehrén H, Granholm T, Lindén V, Palmér K. Improved results in patients who have congenital diaphragmatic hernia using preoperative stabilization, extracorporeal membrane oxygenation, and delayed surgery. J Pediatr Surg 1997;32(8):1185-9.
44. Reickert CA, Hirschl RB, Schumacher R, Geiger JD, Cox C, Teitelbaum DH, et al. Effect of very delayed repair of congenital diaphragmatic hernia on survival and extracorporeal life support use. Surgery 1996;120(4):766-72; discussion 772-3.
45. Kays DW, Langham MR Jr, Ledbetter DJ, Talbert JL. Detrimental effects of standard medical therapy in congenital diaphragmatic hernia. Ann Surg 1999;230(3):340-8; discussion 348-51.
46. Downard CD, Jaksic T, Garza JJ, Dzakovic A, Nemes L, Jennings RW, et al. Analysis of an improved survival rate for congenital diaphragmatic hernia. J Pediatr Surg 2003;38(5):729-32.
47. Ito M, Terui K, Nagata K, Yamoto M, Shiraishi M, Okuyama H, et al; Japanese Congenital Diaphragmatic Hernia Study Group. Clinical guidelines for the treatment of congenital diaphragmatic hernia. Pediatr Int 2021;63(4):371-390.
48. Hogeveen M, Monnelly V, Binkhorst M, Cusack J, Fawke J, Kardum D, et al. European Resuscitation Council Guidelines 2025 Newborn Resuscitation and Support of Transition of Infants at Birth. Resuscitation. 2025 Oct;215 Suppl 1:110766.
49. Kirby E, Keijzer R. Congenital diaphragmatic hernia: current management strategies from antenatal diagnosis to long-term follow-up. Pediatr Surg Int 2020;36(4):415-429.
50. Foglia EE, Ades A, Hedrick HL, Rintoul N, Munson DA, Moldenhauer J, et al. Initiating resuscitation before umbilical cord clamping in infants with congenital diaphragmatic hernia: a pilot feasibility trial. Arch Dis Child Fetal Neonatal Ed 2020;105(3):322-326.
51. Le Duc K, Mur S, Rakza T, Boukhris MR, Rousset C, Vaast P, et al. Efficacy of Intact Cord Resuscitation Compared to Immediate Cord Clamping on Cardiorespiratory Adaptation at Birth in Infants with Isolated Congenital Diaphragmatic Hernia (CHIC). Children (Basel). 2021;8(5): 339.
52. Horn-Oudshoorn EJJ, Vermeulen MJ, Knol R, Bout-Rebel R, Te Pas AB, Hooper SB, et al. Multicentre, randomised controlled trial of physiological-based cord clamping versus immediate cord clamping in infants with a congenital diaphragmatic hernia (PinC): statistical analysis plan. Trials 2024;25(1):198. doi: 10.1186/s13063-024-08027-7. Erratum in: Trials. 2025 Jul 3;26(1):235. doi: 10.1186/s13063-025-08939-y.
53. Guidry CA, Hranjec T, Rodgers BM, Kane B, McGahren ED. Permissive hypercapnia in the management of congenital diaphragmatic hernia: our institutional experience. J Am Coll Surg 2012;214(4):640-645, 647.e1; discussion 646-7. doi: 10.1016/j.jamcollsurg.2011.12.036. Epub 2012 Feb 28.
54. Lupo E, Castoldi F, Maestri L, Rustico M, Dani C, Lista G. Outcome of congenital diaphragmatic hernia: analysis of implicated factors. Minerva Pediatr 2013;65(3):279-85.
55. van den Hout L, Tibboel D, Vijfhuize S, te Beest H, Hop W, Reiss I; CDH-EURO Consortium. The VICI-trial: high frequency oscillation versus conventional mechanical ventilation in newborns with congenital diaphragmatic hernia: an international multicentre randomized controlled trial. BMC Pediatr 2011;11:98.
56. Pitetti RD, Singh S, Pierce MC. Safe and efficacious use of procedural sedation and analgesia by nonanesthesiologists in a pediatric emergency department. Arch Pediatr Adolesc Med 2003;157(11):1090-6.
57. Weems MF, Grover TR, Seabrook R, DiGeronimo R, Gien J, Keene S, et al; Children's Hospitals Neonatal Consortium Congenital Diaphragmatic Hernia Focus Group. Analgesia, Sedation, and Neuromuscular Blockade in Infants with Congenital Diaphragmatic Hernia. Am J Perinatol 2023;40(4):415-423.
58. Lakshminrusimha S, Keszler M. Persistent Pulmonary Hypertension of the Newborn. Neoreviews 2015;16(12):e680-e692.
59. Pilkington M, Pentz B, Short K, Marchand T, Aziz S, Lam JY, et al. Enhanced Recovery After Surgery (ERAS) consensus recommendations for opioid-minimising pharmacological neonatal pain management. BMJ Paediatr Open 2024;8(1):e002824.
60. Yoshida T, Goya H, Iida N, Arakaki M, Sanabe N, Nakanishi K. Early parenteral nutrition in neonates with congenital diaphragmatic hernia. Pediatr Int 2020;62(2):200-205.
61. Bianchini S, Nicoletti L, Monaco S, Rigotti E, Corbelli A, Colombari A, et al, On Behalf Of The Peri-Operative Prophylaxis In Neonatal And Paediatric Age Pop-NeoPed Study Group. Peri-Operative Prophylaxis in Patients of Neonatal and Pediatric Age Subjected to Cardiac and Thoracic Surgery: A RAND/UCLA Appropriateness Method Consensus Study. Antibiotics (Basel) 2022;11(5):554.
62. Aggarwal S, Stockmann P, Klein MD, Natarajan G. Echocardiographic measures of ventricular function and pulmonary artery size: prognostic markers of congenital diaphragmatic hernia? J Perinatol 2011;31(8):561-6.
63. Patel N, Lally PA, Kipfmueller F, Massolo AC, Luco M, Van Meurs KP, et al. Ventricular Dysfunction Is a Critical Determinant of Mortality in Congenital Diaphragmatic Hernia. Am J Respir Crit Care Med 2019;200(12):1522-1530.
64. Patel N, Massolo AC, Kraemer US, Kipfmueller F. The heart in congenital diaphragmatic hernia: Knowns, unknowns, and future priorities. Front Pediatr 2022;10:890422.
65. Bonafide CP, Brady PW, Keren R, Conway PH, Marsolo K, Daymont C. Development of heart and respiratory rate percentile curves for hospitalized children. Pediatrics 2013;131(4):e1150-7.
66. Altit G, Lapointe A, Kipfmueller F, Patel N. Cardiac function in congenital diaphragmatic hernia. Semin Pediatr Surg 2024;33(4):151438.
67. Foth A, Tingay D, Kipfmueller F. "Gentle" cardio-respiratory management in congenital diaphragmatic hernia: Time for a precision-medicine approach? Semin Fetal Neonatal Med 2025;30(3):101660.
68. Abman SH, Hansmann G, Archer SL, Ivy DD, Adatia I, Chung WK, et al; American Heart Association Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation; Council on Clinical Cardiology; Council on Cardiovascular Disease in the Young; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular Surgery and Anesthesia; and the American Thoracic Society. Pediatric Pulmonary Hypertension: Guidelines From the American Heart Association and American Thoracic Society. Circulation 2015 Nov;132(21):2037-99. doi: 10.1161/CIR.0000000000000329. Erratum in: Circulation 2016;133(4):e368. doi: 10.1161/CIR.0000000000000363.

69. Surak A, Mahgoub L, Ting JY. Hemodynamic management of congenital diaphragmatic hernia: the role of targeted neonatal echocardiography. World J Pediatr Surg 2024;7(2):e000790.
70. Wren JT Jr, Patel N, Harting MT, McNamara PJ. Hemodynamic precision to guide surgical timing for neonates with congenital diaphragmatic hernia: a narrative review. J Perinatol 2025;45(4):552-561.
71. Gowda SH, Patel N. "Heart of the Matter": Cardiac Dysfunction in Congenital Diaphragmatic Hernia. Am J Perinatol 2024;41(S 01):e1709-e1716.
72. Moore SS, Keller RL, Altit G. Congenital Diaphragmatic Hernia: Pulmonary Hypertension and Pulmonary Vascular Disease. Clin Perinatol 2024;51(1):151-170.
73. Agakidou E, Chatziioannidis I, Kontou A, Stathopoulou T, Chotas W, Sarafidis K. An Update on Pharmacologic Management of Neonatal Hypotension: When, Why, and Which Medication. Children (Basel) 2024;11(4):490.
74. Lawrence KM, Berger K, Herkert L, Franciscovich C, O'Dea CLH, Waqar LN, et al. Use of prostaglandin E1 to treat pulmonary hypertension in congenital diaphragmatic hernia. J Pediatr Surg 2019;54(1):55-59.
75. Wehrmann M, Patel SS, Haxel C, Cassidy C, Howley L, Cuneo B, et al. Implications of Atrial-Level Shunting by Echocardiography in Newborns with Congenital Diaphragmatic Hernia. J Pediatr 2020;219:43-47.
76. Patel N, Massolo AC, Kipfmueller F. Congenital diaphragmatic hernia-associated cardiac dysfunction. Semin Perinatol 2020;44(1):151168.
77. Capolupo I, De Rose DU, Mazzeo F, Monaco F, Giliberti P, Landolfo F, et al. Early vasopressin infusion improves oxygenation in infants with congenital diaphragmatic hernia. Front Pediatr 2023;11:1104728.
78. Noori S, Friedlich P, Wong P, Ebrahimi M, Siassi B, Seri I. Hemodynamic changes after low-dosage hydrocortisone administration in vasopressor-treated preterm and term neonates. Pediatrics 2006;118(4):1456-66.
79. Robertson JO, Criss CN, Hsieh LB, Matsuko N, Gish JS, Mon RA, et al. Steroid use for refractory hypotension in congenital diaphragmatic hernia. Pediatr Surg Int 2017;33(9):981-987.
80. Pittinger TP, Sawin RS. Adrenocortical insufficiency in infants with congenital diaphragmatic hernia: a pilot study. J Pediatr Surg 2000;35(2):223-5; discussion 225-6.
81. Kumbhat N, Noori S. Corticosteroids for Neonatal Hypotension. Clin Perinatol 2020;47(3):549-562.
82. Baker CF, Barks JD, Engmann C, Vazquez DM, Neal CR Jr, Schumacher RE, et al. Hydrocortisone administration for the treatment of refractory hypotension in critically ill newborns. J Perinatol 2008;28(6):412-9.
83. Ng PC, Lee CH, Bnur FL, Chan IH, Lee AW, Wong E, et al. A double-blind, randomized, controlled study of a "stress dose" of hydrocortisone for rescue treatment of refractory hypotension in preterm infants. Pediatrics 2006;117(2):367-75.
84. Seri I, Tan R, Evans J. Cardiovascular effects of hydrocortisone in preterm infants with pressor-resistant hypotension. Pediatrics 2001; 107(5):1070-4.
85. Subhedar NV, Duffy K, Ibrahim H. Corticosteroids for treating hypotension in preterm infants. Cochrane Database Syst Rev 2007;(1):CD003662. doi: 10.1002/14651858.CD003662.pub3. Update in: Cochrane Database Syst Rev 2011;(12):CD003662. doi: 10.1002/14651858.CD003662.pub4.
86. Peeples ES. An evaluation of hydrocortisone dosing for neonatal refractory hypotension. J Perinatol 2017;37(8):943-946.
87. Marino BS, Tabbutt S, MacLaren G, Hazinski MF, Adatia I, Atkins DL, et al; American Heart Association Congenital Cardiac Defects Committee of the Council on Cardiovascular Disease in the Young; Council on Clinical Cardiology; Council on Cardiovascular and Stroke Nursing; Council on Cardiovascular Surgery and Anesthesia; and Emergency Cardiovascular Care Committee. Cardiopulmonary Resuscitation in Infants and Children With Cardiac Disease: A Scientific Statement From the American Heart Association. Circulation 2018;137(22):e691-e782.
88. Kovacs K, Szakmar E, Meder U, Szakacs L, Cseko A, Vatai B, et al. A Randomized Controlled Study of Low-Dose Hydrocortisone Versus Placebo in Dopamine-Treated Hypotensive Neonates Undergoing Hypothermia Treatment for Hypoxic-Ischemic Encephalopathy. J Pediatr 2019;211:13-19.e3. doi: 10.1016/j.jpeds.2019.04.008.Kovacs K, Szakmar E, Meder U, et al.
89. Kamath BD, Fashaw L, Kinsella JP. Adrenal insufficiency in newborns with congenital diaphragmatic hernia. J Pediatr 2010;156(3):495-497.e1.
90. Giesinger RE, McNamara PJ. Hemodynamic instability in the critically ill neonate: An approach to cardiovascular support based on disease pathophysiology. Semin Perinatol 2016;40(3):174-88.
91. Joynt C, Cheung PY. Cardiovascular Supportive Therapies for Neonates With Asphyxia - A Literature Review of Pre-clinical and Clinical Studies. Front Pediatr 2018;6:363.
92. Ruoss JL, Moronta SC, Bazacliu C, Giesinger RE, McNamara PJ. Management of cardiac dysfunction in neonates with pulmonary hypertension and the role of the ductus arteriosus. Semin Fetal Neonatal Med 2022;27(4):101368.
93. Steinhorn RH. Advances in Neonatal Pulmonary Hypertension. Neonatology 2016;109(4):334-44.
94. Chaudhari T, Schmidt Sotomayor N, Maheshwari R. Diagnosis, management and long term cardiovascular outcomes of phenotypic profiles in pulmonary hypertension associated with congenital diaphragmatic hernia. Front Pediatr 2024;12:1356157.
95. Bhombal S, Patel N. Diagnosis & management of pulmonary hypertension in congenital diaphragmatic hernia. Semin Fetal Neonatal Med 2022;27(4):101383.
96. Kinsella JP, Steinhorn RH, Mullen MP, Hopper RK, Keller RL, Ivy DD, et al; Pediatric Pulmonary Hypertension Network (PPHNet). The Left Ventricle in Congenital Diaphragmatic Hernia: Implications for the Management of Pulmonary Hypertension. J Pediatr 2018;197:17-22.
97. Lakshminrusimha S, Mathew B, Leach CL. Pharmacologic strategies in neonatal pulmonary hypertension other than nitric oxide. Semin Perinatol. 2016 Apr;40(3):160-73.
98. Falcão MC, Telles APA, Aguiar MLMD, Bigio JZD. Use of sildenafil in late postoperative period of congenital diaphragmatic hernia. J Bras Pneumol 2021;47(4):e20210143.
99. Li Z, Lv X, Liu Q, Dang D, Wu H. Update on the use of sildenafil in neonatal pulmonary hypertension: a narrative review of the history, current administration, and future directions. Transl Pediatr 2021;10(4):998-1007.
100. Kipfmueller F, Schroeder L, Berg C, Heindel K, Bartmann P, Mueller A. Continuous intravenous sildenafil as an early treatment in neonates with congenital diaphragmatic hernia. Pediatr Pulmonol 2018;53(4):452-460.
101. De Vadder A, Lemloh L, Bo B, Hale L, Patel N, Mueller A, et al. Bosentan as adjunctive therapy in neonates with congenital diaphragmatic hernia-associated pulmonary hypertension: a case series. Eur J Pediatr 2025;184(3):198.
102. Yang MJ, Russell KW, Yoder BA, Fenton SJ. Congenital diaphragmatic hernia: a narrative review of controversies in neonatal management. Transl Pediatr 2021;10(5):1432-1447.
103. Kays DW. ECMO in CDH: Is there a role? Semin Pediatr Surg 2017;26(3):166-170.
104. Sloan P, Johng S, Daniel JM, Rhee CJ, Mahmood B, Gravari E, et al. A clinical consensus guideline for nutrition in infants with congenital diaphragmatic hernia from birth through discharge. J Perinatol 2024;44(5):694-701.
105. Marseglia L, Manti S, D'Angelo G, Gitto E, Salpietro C, Centorrino A, et al. Gastroesophageal reflux and congenital gastrointestinal malformations. World J Gastroenterol 2015;21(28):8508-15.
106. Schreiner Y, Sahin S, Otto C, Weis M, Hetjens S, Zahn K, et al. Pleural Effusion and Chylothorax in Congenital Diaphragmatic Hernia-Risk Factors, Management and Outcome. J Clin Med 2024;13(6):1764.
107. Rocha G, Arnet V, Soares P, Gomes AC, Costa S, Guerra P. Chylothorax in the neonate-A stepwise approach algorithm. Pediatr Pulmonol. 2021 Oct;56(10):3093-3105.
108. O'Toole SM, Kramer J. Unilateral Diaphragmatic Paralysis. [Updated 2023 Jan 26]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557388/
109. Rosen R, Vandenplas Y, Singendonk M, Cabana M, DiLorenzo C, Gottrand F, et al. Pediatric Gastroesophageal Reflux Clinical Practice Guidelines: Joint Recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition. J Pediatr Gastroenterol Nutr. 2018 Mar;66(3):516-554.
110. Pulvirenti R, IJsselstijn H, Mur S, Morini F. Approaches to nutrition and feeding in congenital diaphragmatic hernia. Semin Pediatr Surg 2024;33(4):151442.
111. Wynn J, Krishnan U, Aspelund G, Zhang Y, Duong J, Stolar CJ, et al. Outcomes of congenital diaphragmatic hernia in the modern era of management. J Pediatr 2013;163(1):114-9.e1.
112. Obed M, Doktor F, Bercovitch R, Zani A, Pederiva F. Long-term outcomes beyond childhood in patients treated for congenital diaphragmatic hernia- a systematic review. Pediatr Surg Int 2025;41(1):96.
113. Pollack JC, Hollinger LE, Buchmiller TL, Jancelewicz T. Long-term follow-up in congenital diaphragmatic hernia. Semin Pediatr Surg 2024;33(4):151443.
114. Hagadorn JI, Brownell EA, Herbst KW, Trzaski JM, Neff S, Campbell BT. Trends in treatment and in-hospital mortality for neonates with congenital diaphragmatic hernia. J Perinatol 2015;35(9):748-54.
115. Rocha G, Azevedo I, Pinto JC, Guimarães H. Follow-up of the survivors of congenital diaphragmatic hernia. Early Hum Dev 2012;88(4):255-8.