Congenital Diaphragmatic Hernia

East Bay Newborn Specialists Guideline
Priscilla Joe MD and Stacie Bennett MD
Updated February 2017

Background:
The incidence of congenital diaphragmatic hernia (CDH) is 1/2200 births. It represents 8% of all major congenital anomalies. 85-90% of the defects occur on the left side of the diaphragm through the Foramen of Bochdalek, 11% presenting on the right side, and 2% are bilateral. The abnormality allows herniation of gut, spleen, and/or liver into the chest resulting in pulmonary hypoplasia, which is most severe on the ipsilateral side, but may also occur on the contralateral side due to mediastinal shift. Overall survival has improved to 70-80%.

Ultrasound findings:
Fetal ultrasound shows a heterogeneous chest mass with a right mediastinal shift. Other thoracic lesions, which may be in the differential of a fetal lung mass, include diaphragmatic eventration, congenital pulmonary airway malformation (CPAM), bronchopulmonary sequestration, bronchogenic cysts, bronchial atresia, enteric cysts, and teratomas. Fluid in the bowel or peristalsis distinguishes bowel from other intrathoracic masses or neoplasms. A liver herniation appears as a right sided homogeneous chest mass at the level of the heart with or without a left mediastinal shift. Mechanical consequences of mediastinal shift and compression of the IVC and left heart may cause hydrops fetalis. Polyhydramnios may also be present due to compression or dysmotility of the esophagus. Other common associations are intestinal malrotation and cardiac dextroposition.

Fetal MRI findings:
Fetal MRI is the most accurate way to calculate total lung volume. MRI should be performed between 24-30 weeks gestation and may more reliably determine liver herniation, diagnose associated anomalies, and allow visualization of the lungs.

Genetic disorders:
50-60% of cases are isolated anomalies. The other 40-50% of cases are associated with additional major organ systems abnormalities. More than 10% of infants with congenital diaphragmatic hernia have an underlying syndromic diagnosis, although few gene mutations are currently recognized. Congenital diaphragmatic hernia is a recognized finding in Cornelia de Lange syndrome and also occurs as a prominent feature of Fryns syndrome, an autosomal recessive disorder with variable features, including diaphragmatic hernia, cleft lip or palate, and distal digital hypoplasia. Chromosomal anomalies are found in 10-30%; the most common diagnoses include Trisomy 18, 13, and 21.

Prognosis:
The major determinants of survival are gestational age, the severity of pulmonary hypoplasia and pulmonary hypertension, and associated anomalies. Although various indices have been used to determine the presence of fatal pulmonary hypoplasia (e.g., best post-ductal $_{PaO2}$ < 100 mmHg, PaCO2 > 60 despite a ventilation index [VI = Paw x Rate] > 1000, modified McGoon ratio [RPA + LPA /Ao ratio] and LV mass), none of these have proved to be predictive of survival. Survival is highest in late term infants (≥ 39 weeks gestation) compared to preterm or early term infants. Prenatal prognostic indicators include the presence of hydrops, an abnormal karyotype, severe associated anomalies, liver herniation and fetal lung volume measurements. Liver herniation and lung volumes may predict size of the defect. A large defect is more likely to result in pulmonary hypoplasia and death than a small defect. Right sided lesions, when large, are as or more severe than left side lesions. Bilateral lesions are the most severe. The lung area to head circumference ratio (LHR) is more predictive of morbidity than mortality. Observed/Expected LHR less than 25% is associated with less than 30% survival and an O/E LHR greater than 46% is associated with greater than 85% survival. The predictive value of LHR however is operator dependent.

Pulmonary hypertension is present in ~ 50% of these patients. Morbidity and mortality is rare in infants with CDH, who either do not require respiratory assistance immediately after birth or for those who require respiratory assistance, but do not have echocardiographic evidence of pulmonary hypertension.

Management:

Prenatal:

- Fetal imaging to evaluate for associated anomalies, liver herniation, and to estimate lung volumes
- Fetal echocardiography
- Fetal genetic testing
- Betamethasone prior to delivery for all mothers $\leq$ 34 weeks gestation
- Serial fetal ultrasounds and antepartum fetal testing
- Fetal MRI
- Delivery after a gestational age of 39 weeks gestation in a tertiary center

Delivery room:

- Avoid bag and mask ventilation or blow-by oxygen to avoid gastric distension and lung compression
- Intubate immediately and use a low peak pressure < 25cm H_2O with Neopuff device PEEP 3-5 cmH_2O, rate of 40-60 bpm
- Place a nasogastric tube and decompress stomach
- Infants with CDH have a delayed transition. Target a preductal SpO_2 of 85-95%. Preductal SpO2 as low as 70% is acceptable if it is improving without ventilator changes and perfusion is satisfactory
- Begin with FiO_2 of 21% and increase to maintain desired SpO_2 as necessary
- Delayed cord clamping cannot be recommended because it will interfere with immediate intubation

Stabilization:

- Restrict fluid administration to 50-60ml/kg/day and fluid boluses to 5-10 ml/kg/day for the first 24 hours to minimize edema. Increase intake thereafter
- Vascular access with UAC line. A right radial PIA line is preferable if a UAC cannot be inserted. A UVC may be difficult to position, and a PICC line should be inserted when able
- NGT to low intermittent suction
- Target a **pre-ductal SpO_2 of 85-95%. Post-ductal SpO_2 >70%.** Hyperoxia should be avoided, as it increases PVR by increasing oxidative stress and pulmonary vascular reactivity, and blunting the response to iNO
- In the first 2 hours of life, pre-ductal SpO_2 of 75-80% is acceptable if improving gradually and organ perfusion is adequate
- Avoid barotrauma. Begin with conventional ventilation using PIP < 25, PEEP 3-5, rates 30-70. If using volume guarantee use Vt 4-5 mL/kg. If unable to ventilate on conventional ventilation with a PIP $\leq$ 28, change to HFOV.
- Avoid hyperventilation: keep pCO_2 50-70mmHg and pH > 7.20
- ECHO to rule out congenital heart disease and to evaluate degree of pulmonary hypertension, shunting, and right heart function
- Consider iNO if preductal SpO_2 is < 85%, pre/postductal differential is > 10% despite maximal respiratory support and/or if oxygen index $\geq$ 25. iNO should be discontinued if there is no improvement. IV sildenafil should be considered.
- Keep MAP > 40mm Hg. Begin with normal saline boluses (10mL/kg, no more than two times) and add pressors, hydrocortisone if necessary. In infants with pulmonary hypertension whose oxygenation is BP dependent, higher MAPs may be needed.

- Consider PGE1 to improve ductal shunting and reduce RV afterload in infants with severe pulmonary hypertension.
- In the face of refractory PPHN with failure of iNO, IV sildenafil, milrinone, and hydrocortisone may have possible therapeutic effects
- Minimize handling. Consider sedation when necessary to decrease air swallowing, while maintaining some spontaneous breathing and movement (decrease VAP and edema). Avoid paralysis if possible
- Routine use of surfactant is not recommended regardless of gestational age

Indications for ECMO if any one of the following criteria is met:
- Failure to maintain pre-ductal SpO_2 > 85% or post-ductal SpO_2 > 70%
- Severe hypotension refractory to pressors or fluid support
- Oxygen index > 40 for at least 3 hours, pH < 7.2 with $PaCO_2$ > 70 despite maximal medical therapy
- Poor organ perfusion with worsening lactic acidosis (lactate >5) and urine output < 1ml/kg/hr
- Other standard ECMO inclusion criteria:
    - Birth weight $\geq$ 2.0 kg
    - Gestational age $\geq$ 34 weeks
- Absence of:
    - Lethal congenital anomalies
    - Lethal chromosomal disorder or syndrome
    - Severe intracranial hemorrhage, greater than grade II IVH, or coagulopathy

Timing of surgery:
There is no evidence for the ideal timing of surgical repair. In patients who are either asymptomatic or have mild symptoms without evidence of pulmonary hypertension, repair can be performed electively after the first 48-72 hours of life.

In patients with moderate symptoms and/or pulmonary hypertension, the time course for repair is variable and delayed until the pulmonary hypertension has resolved. Repair can generally be performed in 7-10 days.

In patients with severe disease who require ECMO, timing of repair is controversial. Evidence (level 3-4) exists for and against operating during ECMO versus after decannulation. Success has been reported with all of the following strategies:
- Reported survival rates with repair on ECMO was 68%, as compared to increased survival before or after ECMO which was 90%and 88, respectively. Try to repair after the patient is off of ECMO or can be decannulated soon after repair:
- Repair after a successful trial off ECMO. Decannulate within 24 hr after repair if possible. This approach provides a safety net for those patients who develop recurrent pulmonary hypertension postoperatively.
- Repair after the patient is successfully decannulated and has been observed for a period of time on conventional or high frequency ventilation for recurrent pulmonary hypertension. The duration of ECMO averages more than 10 days. CDH accounts for 69% of neonatal ECMO cases lasting for more than 3 weeks. Survival rates of 56% at 2 weeks, 46% at 3 weeks, and 43% after 4 weeks of ECMO have been reported. Patients with severe CDH will take longer to wean from ECMO. After 5 weeks of ECMO, survival dropped to 15%.
- In patients who are not weaning after 1 week of ECMO support or those who show evidence of severe RV failure on VV ECMO support, begin iNO and/or sildenafil prior to weaning from ECMO.

Post operative management:
- No routine chest tube placement postoperatively
- If a chest tube is placed, it should be connected to water seal, but not to suction to prevent rapid mediastinal shift

    - Excessive mediastinal shift can result in worsening pulmonary hypertension due to excessive stretch of the contralateral lung and collapse of the ipsilateral lung.
    - Excessive mediastinal shift can on occasion result in major airway obstruction.
- Wean ventilator settings slowly since pulmonary hypertension may recur post-op and post-ECMO
- Avoid hyperoxia and hyperventilation even in the face of pulmonary hypertension.
- Continue nitric oxide and/or sildenafil in those infants that required treatment preoperatively. Wean nitric oxide first.
- Continue gastric decompression
- Provide adequate pain control using a morphine infusion and acetaminophen
- Some patients may develop severe pulmonary hypertension following repair and require a second ECMO run. Second courses are associated with poorer outcomes.

Late complications:

Pulmonary:

- Chronic pulmonary hypertension
- Bronchopulmonary dysplasia
- Pneumonia
- Obstructive airway disease
- Recurrent diaphragmatic hernia
- Patch infection
- Chest wall abnormalies: Pectus excavatum, pectus carinotum
- Scoliosis

GI:

- Gastroesophageal reflux
- Esophageal ectasia
- Failure to thrive
- GI obstruction due to strictures
- Midgut volvulus due to malfixation

Neurodevelopmental:

- Hearing loss
- Speech, vision, learning abnormalities
- Motor problems

References:

Kays DW et al. Extracorporeal life support in patients with congenital diaphragmatic hernia: how long should we treat? *J Am Coll Surg* 2014;218:808-818

Puligandla PS et al. Management of congenital diaphragmatic hernia: a systematic review from the APSA Outcomes and Evidence Based Practice Committee*; J Pediatr Surg*. 2015 Nov; 50(11):1958-70

Snoek KG, et al. Conventional mechanical ventilation versus high-frequency oscillatory ventilation for congenital diaphragmatic hernia: A Randomized Clinical Trial (The VICI-trial); *Ann Surg*. 2016; 263(5):867

Snoek KG, et al. Standardized postnatal management of infants with congenital diaphragmatic hernia in Europe: The CDH EURO consortium consensus-2015 Update; *Neonatology* 2016; 110:66-74

Weems MF, et al. Congenital diaphragmatic hernia: maximizing survival; *Neoreviews* Dec 2016, 17(12):e705-716

Wung JT, et al. Congenital diaphragmatic hernia: survival treated with very delayed surgery, spontaneous respiration, and no chest tube; *J Pediatr Surg* 1995;30(3):406