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The Use of Extracorporeal Membrane Oxygenation in Infants with Congenital Diaphragmatic Hernia

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The use of extracorporeal membrane oxygenation (ECMO) has revolutionized the care of the critical infant born with a congenital diaphragmatic hernia (CDH). In some respects, this is surprising given our current lack of understanding regarding optimal preoperative ventilation strategy, identification of patients most likely to benefit from ECMO, and the correct timing of hernia repair for the infant treated with ECMO. Historically, repair of CDH was considered one of the few true pediatric surgical emergencies. Mortality, however, was high. In the 1970s, ECMO was first utilized as a rescue therapy following repair of CDH when conventional methods failed. In the 1980s, advancements in neonatal intensive care and an understanding of the pathophysiology of pulmonary hypertension associated with CDH led to a strategy involving preoperative stabilization and delayed surgical intervention. Historical reviews demonstrate an improvement of survival in infants treated with ECMO from 56% to 71%. This paper will outline the advances in the care of the CDH patient and the approach used for treatment with ECMO.

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Pathophysiology

Congenital diaphragmatic hernia (CDH) occurs in 1 in every 2500 live births. The most frequent posterolateral Bochdalek hernia results from a failure of closure of the pleuroperitoneal membrane noticeable during the eighth week of gestation. CDH occurs more on the left than the right, but pulmonary pathology is bilateral despite the unilateral hernia. The resultant hernia is associated with a variable amount of pulmonary hypoplasia and pulmonary hypertension. The exact mechanisms contributing to pulmonary hypertension and lung hypoplasia are not well understood. The overall surface area of the alveoli and the vascular bed in infants with CDH is reduced. These smaller vessels are more prone to developing resistance, and even subtle insults or injuries can lead to profound increases in pulmonary vascular resistance.¹ The selective activation of thromboxane synthetase pathways precipitated by CDH may in part contribute to pulmonary hypertension.² Extracorporeal membrane oxygenation (ECMO) may allow for a rest period in which homeostasis of prosta-

noids can be achieved and lead to resolution of pulmonary hypertension.

Interventions in utero aimed at addressing lung hypoplasia have not yielded satisfying results. The use of a fetal tracheal occlusion technique or in utero CDH repair have shown fetal lung enlargement, but this may be due to mucous fluid pooling or lung emphysematous changes.³ Unfortunately, these strategies have not prevented the lung pathology associated with pulmonary hypoplasia.

Evaluation

CDH can be appreciated on prenatal sonogram. Once diagnosed, a further investigation is initiated to evaluate for chromosomal, cardiac, gastrointestinal, and genitourinary anomalies. No criteria exist to confidently predict postnatal outcome, although a comparison of lung area to head circumference (Lung Head ratio) seems most reliable.

Critical infants present with respiratory distress shortly after birth. A scaphoid abdomen may provide a clue that the abdominal organs are in the chest. Immediate care includes endotracheal intubation (bag-mask ventilation leads to distension of abdominal viscera in the chest), central venous access, and gastric decompression. The diagnosis is confirmed by plain radiograph (Fig. 1, left). Ventilator strategies

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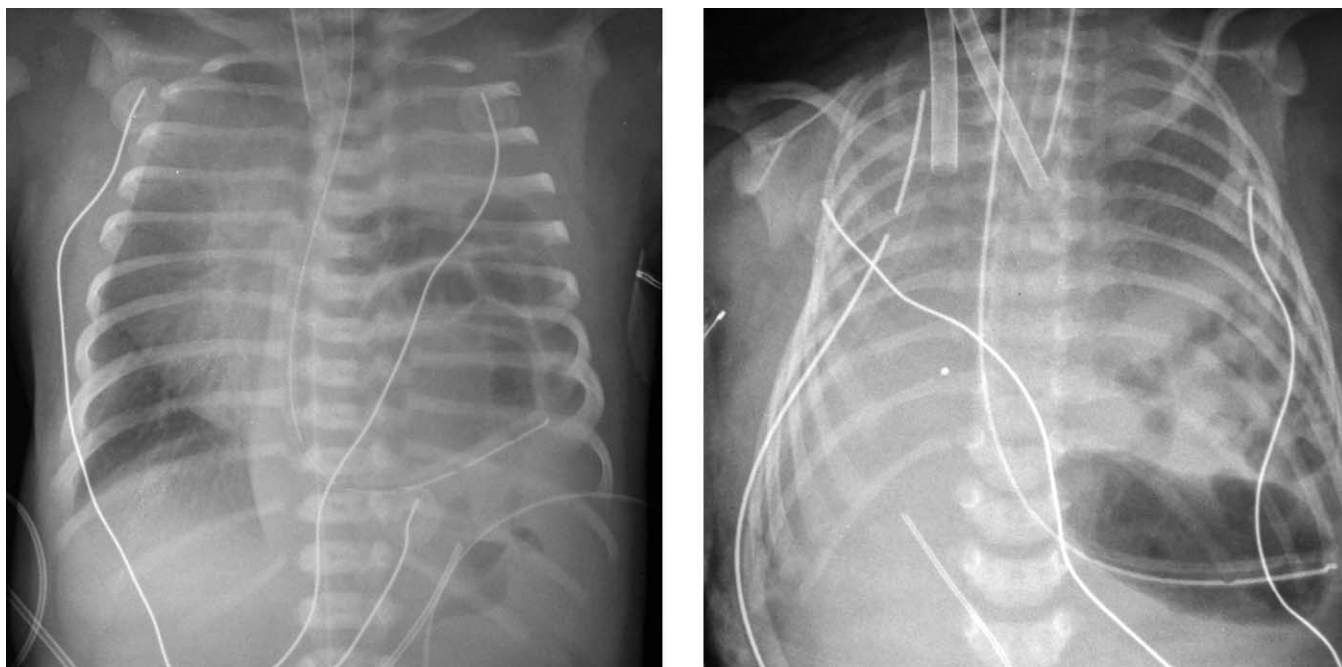


Figure 1 (Left) Radiograph findings seen in a typical left diaphragmatic hernia patient. Note that the nasogastric tube is in the left chest. (Right) The typical picture of a patient with congenital diaphragmatic hernia on VA ECMO. The ECMO cannulae are shifted to the right, indicating the shift of the heart into the right chest.

that reduce barotrauma to the fragile lungs should be undertaken immediately. Vasopressors should be used cautiously as these may increase cardiac output and systemic vascular resistance and exacerbate or initiate pulmonary hypertension. An echocardiogram should be performed shortly after diagnosis to evaluate for any cardiac anomalies as these may limit potential ECMO therapy.

Indications for ECMO

For an infant with a pre- or postnatal diagnosis of CDH, no criteria are absolutely predictive of a poor outcome. Infants who have CDH repair and do not require ECMO have near 100% survival.⁴ An analysis of the Extracorporeal Life Support Organization database failed to identify reliable predictors of mortality in CDH patients requiring ECMO. There was a trend toward improved survival in patients who tolerated medical management for greater than 18 hours, had an older gestational age, had a birth weight greater than 3.5 kg, a pre-ECMO pH greater than 7.4, or a P_aCO_2 less than 49.⁵⁻⁹ Although the following issues are consistently recognized in the literature, it remains difficult to predict which infants will do well with ECMO.¹⁰

The most often-sited indication for ECMO in CDH patients is a “failure of conventional medical management.” Traditional medical management strategies consist of mechanical ventilatory and vasopressor hemodynamic support and sedation in an effort to control pulmonary hypertension by hyperventilation and maintaining postductal oxygen saturations greater than 90%.¹¹ Achieving these goals required high respiratory rates and peak inspiratory pressures resulting in pulmonary barotrauma. The lung injury resulting from

this approach was clearly responsible for much of the historic morbidity of CDH infants. Modern strategies incorporating new intensive care technologies emphasize lower inspiratory pressures, permissive hypercapnea, and spontaneous respirations in attempts to minimize barotrauma.¹²⁻¹⁴ High frequency oscillatory ventilators (HFOV) have been used as rescue therapy for children failing conventional ventilator management in the preoperative management of CDH.

Inhaled nitric oxide (NO) therapy has been successful in managing pulmonary hypertension in CDH patients. NO is a potent vasodilator derived from endothelial cells. In this setting, NO exerts its effects on the pulmonary vasculature and is rapidly metabolized before reaching the systemic circulation.¹⁵⁻¹⁷ Unfortunately, in a randomized trial, the National Inhaled Nitric Oxide Study Group (NINOS) did not find any benefit for CDH patients treated with NO in terms of need for ECMO or mortality.¹⁸ The NO therapy was used in conjunction with HFOV in 50% of the patients in that trial. The success rate of NO therapy in CDH patients is disappointing compared with other causes of pulmonary hypertension. In addition to the pulmonary hypoplasia and hypertension noted in the CDH patients, some studies have documented lung immaturity. Administration of surfactant in a fetal lamb model of CDH has been associated with an improvement in lung compliance, pulmonary vascular resistance, and gas exchange.¹⁹ Unfortunately, surfactant therapy shows no benefit in CDH patients in terms of survival, need for ECMO, or development of chronic lung disease.²⁰ Classical objective criteria for the need for institution of ECMO therapy include alveolar–arterial oxygen gradient of greater than 600 mm Hg for 4 hours, oxygenation index greater than 40, $P_aO_2 < 40$ mm Hg, or pH < 7.15 for 2 hours.

Exclusion Criteria

Available cannula sizes limit ECMO therapy to CDH infants weighing at least 2 kg. With the systemic anticoagulation required for ECMO bypass, an increased risk of intracranial hemorrhage (ICH) in premature infants limits eligible patients to a gestational age greater than 34 weeks.^{11,21} Similarly, due to concerns for rebleeding, a child who has already suffered an ICH greater than grade II is generally excluded from ECMO. Infants with evidence of ongoing bleeding and coagulopathy are rarely considered for ECMO therapy. CDH is frequently associated with other anomalies including congenital heart disease. Neonates with concomitant lethal anomalies are not considered for ECMO. The initial investigation of all children with CDH should include an echocardiogram to evaluate for anatomic cardiac defects.

Technical Considerations

Because venoarterial (VA) ECMO offers the added advantage of circulatory support, it has been the standard ECMO modality for rescue of the CDH patient. Recent studies, however, show that venovenous (VV) ECMO is as efficient in supporting CDH patients as VA ECMO.²²⁻²⁶ Compared with the VA ECMO, VV ECMO is associated with fewer cerebral infarcts and seizures, maintenance of pulsatile oxygenated blood flow through the lungs inducing production of endogenous nitric oxide, improved coronary blood flow, and avoidance of increased left ventricular afterload, thereby decreasing the incidence of cardiac stun and decreased entrapment of particulate matter from the ECMO circuit in the pulmonary vasculature.

CDH patients are preferentially cannulated via the right internal jugular vein and right common carotid artery for VA ECMO and the right internal jugular vein for VV ECMO. This is usually performed via a transverse or oblique incision in the right neck, although some centers have done VV ECMO via a percutaneous approach. For VA ECMO, the tip of the venous cannula is placed in the right atrium and tip of the arterial cannula at the junction of the innominate artery and the ascending aorta. Proper cannulae position is confirmed by chest radiograph (Fig. 1, right) or echocardiography. Optimal positioning of the catheters can be difficult in patients with CDH because herniated abdominal viscera in the thorax tend to shift the mediastinum. The cannulae are sutured in place on completion of the procedure.

Diaphragm Repair

With the recognition that associated pulmonary hypertension and hypoplasia are the major contributors to mortality, rather than the presence of bowel in the chest (Fig. 2) leading to respiratory compromise, the timing of diaphragmatic hernia repair has shifted from emergent to delayed. ECMO support allows for time to achieve pulmonary vascular bed stabilization with subsequent surgical repair.^{4,27} Still, the optimal timing for repair with respect to the discontinuation of ECMO remains controversial. Although some still advo-

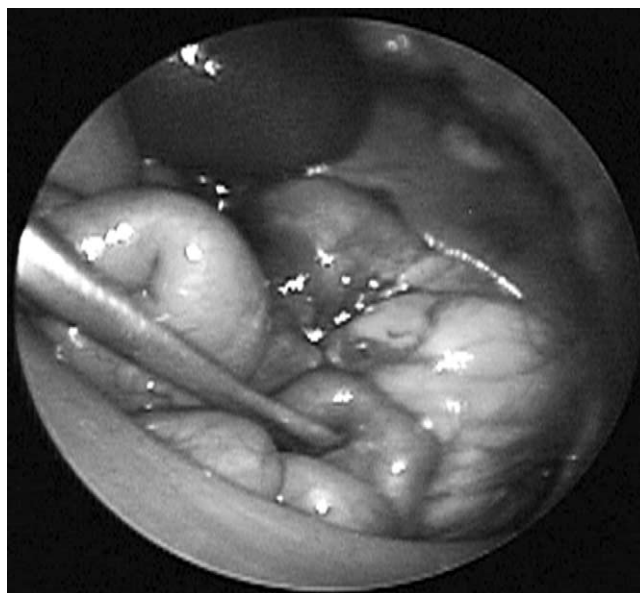


Figure 2 Thoracoscopic view of the bowel and liver in the chest of a congenital diaphragmatic hernia patient.

cate repair within the first 48 hours to achieve closure of the defect before the onset of critical pulmonary hypertension, those patients that do require ECMO after emergent repair have a marked reduction in their survival.²⁸ An alternative approach for those infants who require ECMO is to perform the repair after stabilization of pulmonary hypertension and immediately before decannulation. ECMO can then continue postoperatively if undergoing the repair leads to deterioration in the patient's condition. Repair while on ECMO is associated with an increase in bleeding complications and high mortality.^{29,30} Hemorrhagic complications can be decreased from 58% to 21% by postponing repair until pulmonary hypertension has improved enough to allow weaning off ECMO and a period of observation on conventional ventilation.²⁷ This strategy has led to survival rates in CDH patients requiring ECMO of up to 78%.^{6,12,21,27}

Outcomes

Although ECMO has contributed to improved survival in infants with CDH, it is not without complications. Careful monitoring for potential hemorrhagic and neurologic and infectious complications are required and can necessitate discontinuing ECMO and death.

The overall incidence of bleeding in patients with CDH treated with ECMO is as high as 43% and may lead to death in up to 4.8%. Sites of hemorrhage include the surgical site, if the repair is undertaken before or during ECMO, ICH (the most common cause of hemorrhage-related mortality), pulmonary, gastrointestinal, urinary, and umbilical.³¹ The use of antifibrinolytic therapies significantly reduces bleeding at the surgical site and red blood cell transfusions.²⁹ The true survival rate for patients with CDH is difficult to predict due to the unknown number of fetuses that do not survive to delivery and patients too ill to survive transport. The multiple-

institution Congenital Diaphragmatic Hernia Study Group has attempted to determine the effect of ECMO on CDH survival.³² The overall survival for CDH patients requiring ECMO was 52%. A survival rate of 38.5% was seen in patients who without ECMO would have a predicted mortality of greater than 80%. Right heart failure, hypoplastic lungs, sepsis, and intracranial hemorrhage have been identified as causes of long-term mortality.³³

Of surviving CDH patients, at least one-fifth to two-thirds will display neurodevelopmental problems.³⁴ CDH patients may be more susceptible to neurologic injury than other infants requiring ECMO.³⁴ Other long-term morbidity includes chronic lung disease, gastroesophageal reflux, and malnutrition.^{35,36}

Summary

ECMO therapy has clearly saved the lives of many infants born with CDH. As the neonatal care of infants with CDH evolves, less invasive and morbid therapies will likely decrease the need for ECMO. Until then, ECMO continues to allow successful navigation of the critical period of pulmonary hypertension.

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