Management of Congenital Diaphragmatic Hernia Treated With Extracorporeal Life Support: Interim Guidelines Consensus Statement From the Extracorporeal Life Support Organization

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Abstract: **The management of infants with congenital diaphragmatic hernia (CDH) receiving extracorporeal life support (ECLS) is complex. Significant variability in both practice and prevalence of ECLS use exists among centers, given the lack of evidence to guide management decisions. The purpose of this report is to review existing evidence and develop management recommendations for CDH patients treated with ECLS. This article was developed by the Extracorporeal Life Support Organization CDH interest group in cooperation with members of the CDH Study Group and the Children's Hospitals Neonatal Consortium.**

Key Words: ECMO, CDH, ECLS, anticoagulation, guidelines

Congenital diaphragmatic hernia (CDH) is the most common indication for neonates with respiratory failure receiving extracorporeal life support (ECLS).[1] ECLS is a supportive measure to allow a patient with CDH the opportunity to recover from pulmonary hypertension/pulmonary hypertensive crisis, acute respiratory deterioration, and cardiac dysfunction. Roughly half of infants undergoing ECLS for CDH do not survive.[2] Those that survive ECLS are at increased risk for long-term morbidity, including neurodevelopmental delay and chronic pulmonary hypertension. There is wide variability in institutional practice patterns including criteria for initiation, mode of support, patient/circuit bedside care strategies, timing/approach for diaphragmatic repair, and liberation from support. Given this management variability, there is clearly a need for standardization of care across centers. The purpose of this report is to provide a set of clinical guidelines derived from the best available evidence and supplemented with expert consensus, to enable broad alignment of care for these complex patients and improve outcomes.

RISK STRATIFICATION

Prenatal Risk Assessment

Prenatal imaging studies can determine CDH defect side, lung volumes, and liver position relative to the diaphragm, as well as other concomitant congenital anomalies. These assessments enhance our ability to predict the severity of lung hypoplasia and subsequent outcome in CDH patients.[3] The most widely used and validated measure of prenatal CDH severity is the observed/expected lung-to-head ratio (o/e LHR) measured using ultrasound.[4] A second important marker of severity is the location of the liver or presence of liver herniation into the thorax ("liver up").[5] Magnetic resonance imaging (MRI)-based total fetal lung volume measurements have been shown to accurately predict the need for ECLS in patients with CDH.[6] Syndromic presentation, abnormal genetic testing, and other significant anomalies including structural cardiac disease are important considerations,

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which influence postnatal management decisions including consideration of ECLS support. Major structural defects seen on fetal echocardiography may preclude ECLS candidacy.[7] In summary, higher mortality and significantly increased likelihood of ECLS need may be expected with the following prenatal assessments:

- o/e LHR: <25%
- Liver herniation: >20%
- o/e total fetal lung volume: <25%

Recommendations

- Prenatal measurements can be used for identification of concomitant anomalies, assessment of severity, counseling and preparation for optimal resources for delivery and postnatal care, including delivery at an ECLS center.

Postnatal Risk Assessment

Between 20% and 40% of infants born with CDH escape prenatal detection, and prematurity or postnatal events clearly alter the clinical course. Therefore, reassessment of CDH risk after birth is paramount. Multiple strategies for postnatal risk assessment exist.[3] The CDH Study Group score, based on birth weight (BW) and Apgar score at 5 minutes, was developed with the purpose of estimating disease severity in the first 5 minutes of life. The Brindle CDH mortality risk model is the updated version of the CDH Study Group equation and uses an integer score comprising low BW, low or missing Apgar scores, severe pulmonary hypertension by echocardiography, major cardiac anomaly, and chromosomal anomaly. The probability of ECLS use can also be estimated using early postnatal blood gases. CDH-specific ECLS mortality risk models have also been developed.[8] However, none of the risk models meet the recommended statistical parameters to be considered adequate for clinical decision making.[3]

Recommendations

- After birth, every infant must have an individualized risk assessment.
- Most postnatal risk models are best suited for nonclinical use or use for quality assessment and improvement but may supplement or confirm a prenatal risk assessment to create a risk profile.

INITIAL MANAGEMENT OF INFANTS WITH CDH FOR THE LIKELY ECLS CANDIDATE

Delivery Planning

Infants identified prenatally with CDH should be delivered at or adjacent to a tertiary facility with ECLS capabilities when possible, as outborn status has been shown to be an independent risk factor for mortality.[9] Infants born preterm may benefit from antenatal steroids or postnatal surfactant administration, but these medications are not indicated for routine use in full-term infants with CDH. There are few data specific to ECLS in patients with right-sided CDH, but ECLS use may be higher in these patients compared with the CDH population as a whole due to a greater frequency of large/high-risk defects.[10]

Immediate Postnatal Management

Initial postnatal management should follow Neonatal Resuscitation Program (NRP) guidelines with additional emphasis on early and protocolized endotracheal intubation and nasogastric tube decompression. Many institutions have developed clinical care guidelines for the initial management of infants born with CDH. Minimization of barotrauma/volutrauma is the goal, with recommendations to limit the PIP utilized in conventional mechanical ventilation to 25 cmH_20 and to use higher respiratory rates with shorter inspiratory times.[11] A degree of permissive hypercapnea should be tolerated, with a pH limit of 7.2 and partial pressure of CO_2 limit of 65–70 mm Hg. Oxygen should be titrated as recommended by NRP, with targeted preductal saturations of 85% (or 75%–85% in the first hours of life).[12,13]

Recommendations

- Delivery planning at or near an ECLS center
- Goal-directed management: preductal $SpO_2 > 85\%$, $pH > 7.2$, $PCO_2 < 65–70$
- Pressure-controlled/pressure-limited *conventional* ventilation and avoidance of lung injury: $PIP < 25\ cmH_20$

POSTNATAL CARE AND MANAGEMENT OF PULMONARY HYPERTENSION

Early echocardiographic assessment of cardiac anatomy, biventricular systolic, and diastolic function and evaluation for pulmonary hypertension (PH) should occur within 4–12 hours of life, particularly for high-risk infants. In severe CDH, cardiac dysfunction may be symptomatic in the delivery room. Special attention should be paid to the right and left ventricles given the fact that numerous factors can lead to diminished right ventricular (RV) and left ventricular (LV) volume/function, along with the strong association with outcome.[14] In addition to its role in assessing cardiac function, echocardiography is also critical to identify associated major congenital heart disease. Fluid overload in these patients is associated with poor outcomes, and aggressive fluid resuscitation in the setting of RV and LV dysfunction may be poorly tolerated.

Inhaled nitric oxide (iNO) is often considered for PH with close assessment of patient response, or as a bridge to ECLS; however, current literature does not show a conclusive benefit (and may be deleterious in the setting of LV dysfunction).[15] Moreover, several studies have shown neither reduction in ECLS use nor improvement in survival among CDH patients receiving iNO. Milrinone, a phosphodiesterase (PDE3) inhibitor with inotropic and lusitropic effects on the heart, which is also a pulmonary vasodilator, may be of benefit in the setting of ventricular dysfunction. However, symptomatic LV dysfunction is an indication for ECLS. Prostaglandin E1 may be used to maintain ductal patency if there is evidence of right ventricular failure.[16] If started before cannulation, many centers continue iNO through repair, but such long-term use and empiric use are not supported by evidence. Finally,

pulmonary vasodilator pharmacotherapy including phosphodiesterase five inhibitors (Sildenafil), endothelin receptor antagonists (Bosentan), and prostanoids (epoprostinol), while potentially important for mid/long-term pulmonary vessel stabilization, are not generally employed in the acute stabilization phase.[17]

Recommendations

- Early (4–12 hours of life) echocardiogram to assess cardiac anatomy and function
- Judicious fluid resuscitation and use of vasopressors for hemodynamic support
- Avoid iNO if evidence of left ventricular dysfunction with elevated left atrial pressure, and prompt discontinuation if no clinical response
- Pulmonary vascular resistance reducing agents such as sildenafil, prostacyclin, milrinone, and vasopressin may improve pulmonary hypertension but require further study

ECLS INDICATIONS AND TIMING OF ECLS INITIATION

In general terms, the initiation criteria for ECLS are the same for neonates with noncardiac respiratory failure and those with CDH. Both ELSO and the CDH Euro consortium have previously made recommendations regarding the physiologic parameters that may represent failure of conventional or other therapies.[12] Given the differences in practice patterns, there are no uniformly accepted and rigidly followed criteria for ECLS initiation for CDH.[18] ECLS may be considered for patients who have persistently labile cardiopulmonary status and low preductal saturations (<85% with markers of impaired end-organ perfusion).

Delay in initiation of ECLS may occur secondary to a belief in reversibility of the respiratory failure, which could lead to barotrauma from prolonged, higher-pressure ventilation. There are no data that suggest a specific number of pre-ECLS ventilator days that exclude neonates with CDH from being candidates for ECLS, and clinicians should use their judgement based on the circumstances of each patient. Current clinical practice recommendations support the concept of minimizing barotrauma through limitations on peak airway pressure.[12] Consensus indications based on expert opinion are summarized in Table 1.

Table 1. Indications for Initiation of ECLS for CDH

ECLS Indications	Considerations
Hypoxic/hypercapnic respiratory failure	1. CMV settings PIP > 26–28 cm H_2O, PEEP > 6 cm H_2O, RR > 50 2. HFOV settings MAP > 14, frequency <7 Hz, amplitude >40 3. Inability to achieve or maintain preductal SpO_2 > 85% 4. Persistent severe respiratory acidosis (PCO_2 > 70 mm Hg) with pH < 7.20
Circulatory failure	1. Inadequate oxygen delivery (DO_2) with metabolic acidosis 2. Inadequate end-organ perfusion, lactate >3, oliguria 3. Refractory systemic hypotension nonresponsive to fluid and vasoactive medications 4. Pulmonary hypertension ± right ventricular dysfunction 5. Left ventricular failure
Acute clinical deterioration	1. Preductal desaturation <70% with inability to recover with ventilator optimization 2. Hemodynamic instability recalcitrant to inotrope and chronotrope initiation/titration

ECLS CONTRAINDICATIONS

The most common relative contraindications to ECLS support are low birthweight (BW), low gestational age (GA), grade III–IV intracranial hemorrhage, significant coagulopathy, or uncontrolled bleeding. Patients with CDH who have additional major anomalies, chromosomal aberrations, or syndromes have significantly lower survival than infants with isolated CDH. In these cases, if there is a predicted high risk of mortality, increased risk of ECLS complications, and anticipated poor outcomes, clinicians, and families may reasonably choose not to proceed with ECLS.

Broadly accepted patient selection criteria for ECLS are GA 34 weeks or greater and BW greater than 2 kg. There have been neonates below the accepted weight and GA criteria who have been treated with ECLS reported from the ELSO registry, and it is possible to lower these previously accepted limits to 32 weeks for gestational age and 1.7–2 kg for weight.[19,20]

Short-term survival is possible in patients with both CDH and congenital heart disease treated with ECLS.[21] Pulmonary hypertension, as classically seen in CDH patients, may serve as a contraindication to palliative congenital heart surgery; as such, these children may not be considered ECLS candidates. It has been shown that operative mortality for index cardiac operations is greater in patients with CDH and congenital heart disease.[22] Therefore, use of ECLS in the setting of concomitant congenital heart disease and CDH should be considered on a case-by-case basis and at centers with significant experience.

Recommendations

- GA ≤ 32 weeks and weight ≤ 1.7–2 kg should be considered relative contraindications
- Concomitant severe congenital heart disease and CDH may be considered a contraindication for ECLS based on severity of the cardiac defect; multidisciplinary communication is mandatory in such patients
- Major genetic abnormalities or syndromes are commonly considered relative contraindications for ECLS

MODE OF SUPPORT

The choice of ECLS mode for CDH patients is an area where there is considerable controversy. Proponents of venovenous (VV) ECLS point toward a potential benefit to the delivery of oxygenated blood to the pulmonary arterial system, as well as the potential for decreased acute neurologic complications during ECLS; proponents of venoarterial (VA) ECLS cite a proposed benefit of both offloading the RV and decreasing pulmonary blood flow in the setting of pulmonary hypertension. Previous studies have shown that patients with CDH can be effectively treated with VV

ECLS but have also not shown a survival benefit.[23] Nevertheless, the most recent ELSO analysis suggested a survival difference with VA in the subset of neonates who required ECLS after CDH repair (pre-ECLS repair), which may be due to the small sample size of the pre-ECLS repair group.[24] There is some evidence of decreased neurologic complications for CDH patients treated with VV when compared with VA, which parallels data on post-ECLS MRI for neonatal respiratory patients.[23,25] The most recent ELSO analysis did not identify any differences in rates of acute, severe neurologic events between VA and VV.[24] Despite having equivalent outcomes, VV cannulation is not always anatomically possible, as the diameter of the jugular vein may be too narrow to allow the smallest possible VV cannula to be used safely. Further, venous cannulation may be technically difficult with the mediastinal shift typically seen in CDH.

Data on the use of VV for extracorporeal cardiopulmonary resuscitation in neonates (ECPR) is extremely limited. ECPR can be defined as VA cannulation in a patient who experienced a sudden and unexpected pulseless condition attributable to cessation of cardiac mechanical activity. Given that VV requires satisfactory cardiac output to be able to provide ECLS, in cases of extremely poor cardiac function and such as during ECPR, VA cannulation is indicated.

Recommendations

- Both venoarterial (VA) and venovenous (VV) ECLS may be used to support infants with CDH with equivalent survival
- Decision of VA *versus* VV should be based on specific clinical scenario, center experience or preference, patient/vessel size, and cannula availability

CANNULATION

Cannulation of the neonate with CDH may be more challenging given extreme changes to the thoracic and vascular anatomy as a result of the mediastinal shift and resulting changes to the vasculature. Neonates with CDH have been described to have smaller internal jugular veins.[26] In these patients, a more aggressive dissection towards the jugular vein/brachiocephalic/subclavian vein junction may be needed for cannulation.[26] Right CDH presents further anatomical challenges given the extreme changes in thoracic anatomy due to the position of intrathoracic liver.[27] Specifically, with right CDH, the venous cannula may preferentially course to the ectatic azygous vein, which may be initially difficult to recognize and difficult to correct. Confirmation of appropriate cannula position via chest radiography and echocardiography, depending upon cannula type, should occur.

Recommendations

- Cannulation in CDH carries additional risks which should be taken into account if cannulation is difficult
- Echocardiographic confirmation of cannula position may be beneficial in VA cannulation and is essential in bicaval VV cannulation

PUMP TYPE

The two most common commercially available pump types are roller and centrifugal. A recent ELSO study examined the relationship between ECLS pump type and outcomes in the CDH population, which showed no difference in mortality or severe neurologic events during ECLS between roller and centrifugal pumps; however, there was a sixfold increase in the odds of hemolysis for centrifugal pumps.[28] An alternative study from the ELSO registry of over 12,000 patients identified increased mortality (likely hemolysis-mediated) with centrifugal pumps among patients who are ≤10 kg in weight.[29] It is unknown whether some brands of centrifugal pumps are superior to others in minimizing risk of hemolysis. Hemolysis can lead to hyperbilirubinemia, acute renal failure, and other end-organ damage.[28] Some limitations of these studies include evaluating neurologic events using only head ultrasound and computed tomography (CT). There is the potential that neurologic injury was underappreciated given that MRI results were not reported.

Recommendations

- ECLS pump type has not been shown to definitively affect mortality in the CDH population
- There is an increased risk of hemolysis with centrifugal pumps among patients ≤10 kg in weight

ON-ECLS VENTILATION STRATEGIES

CDH is characterized by both bronchial and pulmonary vascular hypoplasia. Both of these conditions can contribute to the development of ventilator-induced lung injury. Such lung injury can occur even during ECLS, underscoring the importance of lung protective measures. Of the standard modes of ventilation (pressure or volume controlled, high frequency oscillatory ventilation), there is no single mode which has been demonstrated to be superior while on ECLS. Any of these modes of ventilation may be appropriate while on ECLS as long as they are undertaken with a strategy to minimize volutrauma, barotrauma, and atelectrauma. Identifying over-distention is more challenging with HFOV, while pressure volume loops may guide SIMV adjustments.

Minimizing ventilator-induced injury is an essential component of using a lung-protective strategy during EMCO. Once on ECLS, the respiratory rate can be significantly reduced, allowing CO_2 removal by ECLS sweep flow. A high fraction of inspired oxygen (FiO_2) in lung areas with a low ventilation–perfusion ratio might alone cause reabsorption atelectasis and oxygen toxicity. Thus, we recommend minimizing ventilator FiO_2 to 0.21–0.40 once on ECLS. Patient blood gases and saturations, as well as mixed venous saturation on VA ECLS, will guide ECLS flow settings.[11] For lung protection during ECLS, a reduction of the tidal volume to a maximum of 4–5 ml/kg, a strategy that reduces the tidal strain in the hypoplastic CDH lung, is recommended.[11] Second, strategies to limit the intratidal alveolar opening and closing are recommended. A consistent level of positive end expiratory pressure (PEEP) (5–10 cm H_2O) should be maintained to limit the atelectrauma and prevent worsening of pulmonary hypertension secondary to atelectasis

and parenchymal inflammation. PEEP or mean airway pressure (MAP) during high frequency ventilation should be titrated to avoid under-inflation and over-inflation, thereby optimizing cardiac output and minimizing lung injury.

Recommendations

- A strategy of lung protective mechanical ventilation for minimizing lung injury with low pressures/volumes, low respiratory rate, and low FiO_2
- Titrate PEEP or MAP with a goal of maintaining alveolar inflation and minimize hemodynamic compromise
- Maintain a target preductal Sat >85% and mixed venous oxygen >65%

TIMING OF SURGICAL REPAIR

The optimal timing for surgical repair of the diaphragmatic defect for a CDH patient who receives ECLS remains controversial, and this decision must take into consideration the myriad of challenges involved in either operating while on ECLS or attempting to delay surgery until after decannulation. The challenges of surgery on ECLS include shifts in fluid status, risk of hemorrhage while anticoagulated, and the potential inability to wean from ECLS; surgical bleeding is reported in 8%–14.7% of infants repaired on ECLS and up to 30% have hemorrhagic complications. The potential/theoretical advantages of surgery while on ECLS include avoidance of nonrepair (which has a 100% mortality), and the relief of intrathoracic compression early, allowing pulmonary parenchymal expansion, minimization of obstruction to pulmonary blood flow, stabilization of pulmonary hypertension, recovery from cardiac dysfunction, and restoration of normal anatomy. The specific approach varies by institution and ranges from early repair on ECLS, to delayed repair on ECLS, to attempting to wean off before repair and, if unsuccessful, repairing on ECLS. Among CDH neonates who receive ECLS, 10% are repaired before ECLS, 47% on ECLS, 28% after ECLS, and 15% do not receive repair.[30]

Select evidence suggests that repair *after ECLS* decannulation is associated with optimal survival. A report from the CDH Study Group reviewed CDH patients who underwent diaphragmatic repair and ECLS; repair after ECLS was associated with increased survival, compared with repair on-ECLS.[31] A retrospective study concluded that delayed repair off ECLS reduced operative morbidity and improved survival.[32] A recent ELSO study evaluating showed with propensity matching that on-ECLS repair was associated increased mortality compared with repair after ECLS, but this study could not account for those patients that died before repair.[33] In contrast to those studies, and in an attempt to address bias, the CDH study group conducted a propensity score matched comparison of on-ECLS repair to post ECLS repair, accounting for center strategy and patients who expire before repair.[34] In this study, the on-ECLS repair patients were more likely to survive.[34]

Another emerging idea in the controversy of timing of repair relative to ECLS is whether earlier repair during ECLS is more adventagous compared with mid or later during the ECLS course. Several single institution studies did suggest that early repair on ECLS may also be advantageous.[35,36] The CDH study group study also evaluated early repair on-ECMO to late-repair, using a propensity score match and center strategy analysis, and showed that early repair during ECLS was associated with improved survival.[34]

Recommendations

- For patients who can be decannulated or weaned off ECLS, there may be a benefit to delaying repair until after decannulation, at the risk of having a patient go unrepaired or requiring a late, salvage repair if weaning is unsuccessful
- For patients with a severe CDH phenotype, very early repair while on ECLS may afford a survival advantage because nonrepairs will be avoided, the complication rate may be lower than late repair on ECLS, and early correction of the mechanical contributors to pulmonary and vascular pathophysiology may facilitate subsequent weaning

REPAIR ON-ECLS AND ANTICOAGULATION MANAGEMENT DURING SURGICAL REPAIR

For surgical repair of the CDH on ECLS, the abdominal approach may allow safe reduction of herniated contents with minimal hemorrhage risk and the ability to repair/reconstruct the defect while simultaneously controlling subtle hemorrhage. Meticulous dissection and tissue handling are paramount. Minimizing dissection of the posterior rim of diaphragm is recommended, as this is often the source of ongoing postoperative hemorrhage. Generous utilization of electrocautery and argon beam coagulation minimizes raw surface hemorrhage. Liberal use of a temporary abdominal closure (Gore-Tex patch or temporary Silastic sheet/silo), along with routine tube thoracostomy, allow the opportunity to expeditiously identify and correct hemorrhagic complications. Hemostatic agents may be used for coagulopathic hemorrhage. Pledgeted sutures may aid in hemostasis at the suture sites. These measures collectively minimize bleeding risk and maximize the opportunity to identify and manage postoperative hemorrhage early.

Optimal management of anticoagulation must occur to limit bleeding complications. There is a dearth of evidence for optimal strategies in this area, so most institutional practices are based on theory and anecdotal experience. Table 2 summarizes the general considerations that one should address when operating on ECLS, but in general, there are a range of acceptable practices that vary based on surgeon and institutional preference.

ECLS DURATION AND STRATEGIES FOR WEANING

According to ELSO data, CDH is the most common cause of prolonged neonatal ECLS runs >3 weeks.[37] Although increased ECLS length and second courses are associated with worse outcomes and increased risk of complications, more severe disease may require longer runs, and survival is possible after durations in excess of 4 weeks. Data suggest that prolonged ECLS runs beyond 4–6 weeks may be of limited benefit, although universally accepted limits on length of treatment have not been established. Kays et al described survival related to length of ECLS treatment and found survival rates of 56% after 2 weeks

Table 2. Circuit and Anticoagulation Management for On-ECLS Repair

Considerations During CDH Repair on ECLS	
Circuit	**Minimize clots within ECLS circuit.** • The circuit should be largely free from clots before surgery to limit DIC from overwhelming consumption of clotting factors by existing circuit thrombi.
Anemia	**Goal hematocrit ~35%–45%**
Platelets	**Goal platelet count >100 k**
Clotting factors	**Goals during repair** • **Fibrinogen >150mg/dL** • **≤PTT 60 sec** • **TEG™ / ROTEM™ can be used as adjuncts to evaluate the entire coagulation cascade**. Consider these adjuncts to optimize the patient preoperatively and replete specific factors postoperatively
Anticoagulation	**Lowering anticoagulation targets during perioperative period.** Many centers initiate a high risk bleeding protocol with decreased ACT, Anti-Xa, TEG/ROTEM, or aPTT goals, while some centers hold anticoagulation entirely
Antifibrinolytics	**Aminocaproic acid (Amicar) or tranexamic acid (TXA) infusion may be used to reduce bleeding risk by inhibiting fibrinolysis thus limiting clot breakdown.** • Start with a preoperative bolus, followed by an infusion that continues through the operation and up to 48 hours postoperative. • Amicar—100 mg/kg bolus 6 hours preop, then 30 mg/kg/h infusion for 24–48 hours • TXA—4–10 mg/kg bolus prep, then 1–4 mg/kg/h infusion for 24–48 hours
Adjuncts	• **Fibrin sealants**—consider application to the operative field to limit surface oozing • **Chest tube/s** • **Temporary abdominal closure** ◦ Silo or patch for skin ◦ Prevents abdominal compartment syndrome in the case of postoperative bleeding and edema ◦ Allows placement of surgical packs in case of surface oozing

of ECLS, 46% survival at 3 weeks, and 43% of patients at 4 weeks survived to discharge. After 5 weeks of ECLS, survival dropped to 15%, and after 40 days of ECLS support, there were no survivors.[38] Thus, arbitrary cutoffs of less than 4 weeks for CDH patients on ECLS may limit an opportunity for recovery and liberation from ECLS.

The ability to wean extracorporeal support in the CDH patient is dependent upon full recovery of bilateral ventricular function and improvement/stabilization of pulmonary hypertension. Indicators of readiness to begin weaning include: improvement in pulmonary hypertension, pulmonary recruitment on low ventilator settings, ventilator $FiO_2 < 0.4\%–0.5\%$, adequate cardiac output and heart rate with minimal to no requirement for vasoactive support, and spontaneously rising/stable mixed venous oxygen saturation near >65%–75% despite increased metabolic demand. Most CDH patients who require ECLS demonstrate suprasystemic RV pressures on echocardiography, so a decrease in these pressures to subsystemic levels before decannulation is ideal. In some cases, inhaled or systemic pulmonary vasodilator pharmacotherapy may be needed to improve RV function to either reach readiness for a trialed off or having a successful trial off. Options may include the use of Sildenafil, Bosentan, epoprostinol, and or iNO. Their availability or use may depend on institutional availability and practice patterns.

When the patient achieves adequate end organ perfusion, with adequate lung expansion, good compliance, low oxygen requirement, and minimal total body edema, the patient may be ready for a trial off ECLS support. If lung function is adequate at acceptable ventilator settings for 20–60 minutes, decannulation can be considered. The goal is to have a reasonable amount of latitude for worsening clinical condition such that increased need for ventilatory support and oxygenation can still be maintained. However, there are no restrictions on ideal ventilator type or specific settings required before decannulation. In select high-risk patients, it may be appropriate to leave the cannulas *in situ* for a brief interval following discontinuation of ECLS in the event of clinical deterioration and the need to reinstitute ECLS support or continue support for longer given the risk of thrombotic complications. See Table 3 for recommendations.

Table 3. Considerations for Weaning Off ECLS

When to trial off	**Improved respiratory status:** Adequate lung expansion on CXR to FRC without focal areas of concern (consolidation, atelectasis, effusion), FiO_2 is ≤0.4 on rest vent settings **Improvement in pulmonary hypertension** as evidenced by resolution of the pre/post ductal SpO_2 gradient (if ductus arteriosus is patent) or decreased (subsystemic) RV/PA pressures as evidenced by echo parameters. **Hemodynamic stability** without metabolic acidosis on minimal or no inotropic/vasoactive medications, maintains adequate VO_2/DO_2 with metabolic challenges such as with awake/crying and routine care. Optimized LV function. **SvO_2 spontaneously rising on VA ECLS**, with a goal >60%
If unable meet goals for trial off	**CDH repair on ECLS** **Optimize medications to treat pulmonary hypertension—**iNO, sildenafil, PGE1, bosentan, treprostinil, and others

LONG-TERM OUTCOMES

CDH is associated with significant long-term morbidities. Overall, the reported incidence of chronic lung disease in survivors of CDH is 33%–52%, with ECLS utilization associated with a ninefold increase in this complication.[39] Many survivors require long-term treatment of pulmonary hypertension. The risk of neurologic sequelae is significant in CDH survivors and those requiring ECLS are the highest risk. Predischarge MRI may identify subclinical abnormalities, allowing early diagnosis of potentially morbid neurologic sequelae. Regardless of the ultimate cause,

CDH ECLS survivors are at risk of long-term neurologic complications, and close neurodevelopmental follow-up is warranted. Given the myriad of morbidities seen in CDH survivors, long-term follow-up will help with early recognition and management of these complications. A brain MRI at or after discharge may be performed to evaluate for evidence or progression of neurologic sequalae.

Recommendations

- Long-term follow-up should occur in multidisciplinary clinics at tertiary/quaternary centers
- CNS imaging pre- and postdischarge in complex care/multidisciplinary developmental clinic may be beneficial to assess and prognosticate long-term neurodevelopmental progress

CONCLUSION

The care of infants with CDH who undergo ECLS support is extremely complex. The aforementioned guidelines summarize current multiinstitutional, international best practices based on the highest-level available evidence, institutional clinical practice guidelines, and multidisciplinary, expert opinion. Prenatal and postnatal risk assessment is critical for informed decision-making in this population. Management strategies as well as data regarding selection for ECLS, timing of cannulation and decannulation, and timing of CDH repair have all evolved considerably within the field. Despite these guidelines, care of the infant with congenital diaphragmatic hernia must be individualized. While all patients share features of pulmonary hypoplasia and pulmonary hypertension, clinicians must expect a unique clinical phenotype and response to treatment. Optimal outcomes will require a nimble, detail-oriented, knowledgeable, and multidisciplinary clinical team.

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