Guidelines for Extracorporeal Membrane Oxygenation (ECMO) in Congenital Diaphragmatic Hernia (CDH)

Introduction and Aims

The benefit of ECMO in the treatment of infants with CDH remains unclear. The Extracorporeal Life Support Organization (ELSO) registry showed a survival rate of 51% of patients with CDH who required ECMO.

Decision for ECMO in patients with CDH should preferably be discussed early with the ECMO team to establish indications and goals of management.

This guideline aims to streamline the management of neonates and infants with CDH who may require ECMO and to standardize subsequent management on ECMO where possible.

Indications for ECMO

The following table is adapted from the ELSO CDH guidelines (2021) and CDH EURO Consortium Consensus 2015 Update

Indications for ECMO	Considerations
1. Persistent hypoxic/hypercapnic respiratory failure despite optimal ventilatory management • Goal of ventilation for neonates with CDH should be to optimize lung recruitment and avoid ventilator associated lung injury (VALI)	• Inability to maintain pre-ductal SpO2 > 85% • OI ≥ 40 for ≥ 3 hours • Severe respiratory acidosis (pH <7.2 and pCO2 >70 mmHg) • PIP> 28 cm H2O or MAP > 17cm H_2O required to achieve saturation > 85%
2. Circulatory failure	• Metabolic acidosis with pH <7.2 and inadequate end-organ perfusion with lactate ⩾ 5 mmol/L, oliguria (urine output <0.5ml/kg/hr) • Refractory hypotension resistant to fluid and inotropic therapy • Severe pulmonary hypertension with evidence of right ventricular and/or left ventricular dysfunction.

Acute clinical deterioration resulting from respiratory or haemodynamic instability, despite optimization, may also warrant an urgent discussion for consideration of ECMO.

Relative contraindications in ECMO in CDH

1. Significant congenital anomalies – including (and not limited to) severe congenital heart disease, lethal chromosomal abnormalities or other lethal malformations. Multidisciplinary communication is mandatory in such patients.
2. Grade III/IV intracranial haemorrhage
3. Weight less than 2kg
4. Gestational age less than 35 weeks
5. Uncontrolled bleeding

All other contraindications and relative contraindications for neonatal ECMO as specified in the ECMO PnP apply to CDH infants.

Special considerations for ECMO in neonates with CDH

The most reliable antenatal predictors of mortality for neonates diagnosed with CDH include:

1. The degree of pulmonary hypoplasia,
2. Presence of liver in the thorax.

Severity of pulmonary hypoplasia may be defined by lung to head ratio (LHR) and the observed to expected LHR (O/E LHR). The lung to head ratio is a sonographic measure used to prognosticate CDH in the foetus. The lung area contralateral to the CDH is obtained by tracing the limits of the lung and this is divided by the head circumference. The observed/expected lung to head ratio may be expressed as a percentage of the expected mean for gestational age.

Prenatal assessment needs to include identification of concomitant anomalies. Assessment of severity, counselling and preparation for delivery should be done with both the obstetrics and neonatal teams. In cases where antenatal prognosis is poor, referral to the Peri-Pal team should be considered.

Predictors of Likelihood of ECMO on antenatal assessment

1. LHR > 1.4 suggests low probability of pulmonary hypoplasia with favourable prognosis, LHR < 1.4 suggests a high probability of need for ECMO and LHR < 1.0 suggests a high probability of pulmonary hypoplasia
2. Observed/ Expected LHR: <25% indicates a poor prognosis
3. Presence of Liver herniation

Post-natal risk assessment

After birth, every infant must have an individualized risk assessment. Most postnatal risk models are best suited for nonclinical use or quality improvement but may be useful to supplement or confirm a prenatal risk assessment to create a risk profile for a patient. It is worth noting the following risk factors:

- Hemodynamically significant congenital heart disease (CHD) is present in 10–15% of infants with CDH, and is independently associated with mortality (survival with CDH with CHD 41% vs. without CHD 70%)
- Prematurity is associated with survival of 31–50%.

- Diaphragm agenesis, or the use of a synthetic patch or transversus abdominus flap for surgical repair, are associated with a more severe clinical course and increased risk of mortality

The CDH –CPI Score (see Table 1 below) is one such tool that may help in prognostication: it includes karyotype abnormalities, syndromic features, presence of CHD, left ventricle/right ventricle proportion, modified McGoon's index, presence of a hernia sac, presence of liver in the chest, degree of lung hypoplasia (eg. LHR etc.)

- CDH-CPI score of 8 is associated with improved survival (89% vs. 38% for infants with a score ≤8)
- 75% of those with a score of ≤5 received ECMO
- Decreased right and left ventricular function by echocardiography is also associated with an increased need for ECMO

Table 1: CDH-CPI Score

		1	0	-1
Genetics	Karyotype Syndrome	Normal No	Abnormal Yes	
Cardiac	Congenital Heart Disease LV/RV McGoon	None No ≥ 1.2	VSD/ASD/Coarctation Yes <1.2	Double outlet heart disease
Hernia	Sac Liver	Yes Down	No Up	
Lung	LHR PPLV Total lung volume	≥ 1 ≥ 15% ≥ 18mL	< 1 < 15% < 18mL	

VSD: Ventricular Septal Defect; ASD: Atrial Septal Defect; LV: Left ventricle; RV: Right ventricle
LHR: Lung Head Ratio; PPLV: Percent Predicted Lung Volume (Measured on fetal MRI)

Delivery Planning

1. Goal-directed management: pre-ductal SpO2 > 85%, pH > 7.2, PCO2 < 65 -70
2. Pressure-controlled/pressure-limited conventional ventilation and avoidance of lung injury: PIP < 25 cmH_20. A degree of permissive hypercapnia should be tolerated, with a pH limit of 7.2 and partial pressure of CO_2 limit of 65–70 mm Hg.
3. Follow Resuscitation Program (NRP) guidelines with additional emphasis on early endotracheal intubation and nasogastric tube decompression.

Post-natal care and management of pulmonary hypertension

1. Early (4-12 hours of life) echocardiogram to assess cardiac anatomy and function
2. Judicious fluid resuscitation and use of vasopressors for hemodynamic support
3. Pulmonary vascular resistance reducing agents such as inhaled nitric oxide (iNO), sildenafil or milrinone, may improve pulmonary hypertension.
4. Avoid iNO if there is evidence of left ventricular dysfunction with elevated left atrial pressure.

ECMO mode of support in CDH

Both Veno-Arterial (VA) and Veno-Venous (VV) ECLS may be used to support infants with CDH with equivalent survival. Most infants in the ELSO registry were treated with VA ECMO and local experience supports the use of VA ECMO.

Cannulation

Given neonates with CDH have changes to their thoracic and vascular anatomy as a result of the mediastinal shift and resulting changes to the vasculature, cannulation may pose several challenges, especially in right sided CDH.

Neonates with CDH have been described to have smaller internal jugular veins and face additional risks. In these patients, a more aggressive dissection towards the jugular vein/brachiocephalic/subclavian vein junction may be needed.

Ventilation strategies while on ECMO

1. A strategy of lung protective mechanical ventilation for minimizing lung injury with low pressures/volumes, low respiratory rate, and low FiO2(21%-40%).
2. Prevent atelectasis by maintaining PEEP (5 to 8 cm of H2O)
3. On HFOV, prevent under-inflation or over-inflation, optimize cardiac output and prevent lung injury

Considerations for weaning off ECMO in CDH

1. **Improved respiratory status:** Adequate lung expansion on CXR to FRC without focal areas of concern (consolidation, atelectasis, effusion)
2. **Improvement in pulmonary hypertension** as evidenced by resolution of the pre/post ductal SpO2 gradient (if ductus arteriosus is patent) or decreased (sub systemic) RV/PA pressures as evidenced by echo parameters.
3. **Haemodynamic stability** without metabolic acidosis on minimal or no inotropic/vasoactive medications, maintains adequate oxygen delivery with metabolic challenges such as with awake/crying and routine care, optimized LV function, SvO_2 spontaneously rising on VA ECMO (goal > 65%)
4. **Minimal total body edema**

Optimize medications to treat pulmonary hypertension—inhaled nitric oxide, sildenafil, prostaglandin, bosentan etc. prior to weaning trial.

A detailed discussion prior to decannulation is recommended to discuss post-decannulation management including risk of further pulmonary hypertensive crises, re-cannulation strategy if cannulae are removed etc. If unable to meet goals for trial off, consider CDH repair on ECMO.

Timing of surgical repair of CDH and duration of ECMO

Following stabilization post cannulation on ECMO (24-48 hours), a multidisciplinary huddle (PAS, NICU, CICU, CTS, CVM, Cardiac Anesthesia) to discuss optimization of management and timing of surgery is recommended.

The optimal timing for surgical repair of the diaphragmatic defect for a CDH patient on ECMO remains controversial. Typically, the duration of ECMO support in CDH patients may vary, ranging from 1 to 4 weeks. It has been demonstrated that prolonged need for ECMO is associated with both increased morbidity and mortality.

For patients who can be decannulated or weaned off ECMO, 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 (48 to 72 hours after ECMO initiation) while on ECMO may afford a survival advantage because non-repairs will be avoided, the complication rate may be lower than late repair on ECMO, and early correction of the mechanical contributors to pulmonary and vascular pathophysiology may facilitate subsequent weaning.

In cases of weaning failure, decision to continue ECMO beyond 21 days should be evaluated based on individual patient's risk benefit assessment and with multidisciplinary input.

Repair on ECMO and anticoagulation management

1. Abdominal approach is preferred for the repair of hernia
2. Minimize the dissection of the posterior rim of the diaphragm as this is the source of ongoing post-operative hemorrhage.
3. Generous utilization of electrocautery (Argon beam coagulation)
4. Liberal use of temporary abdominal closure and routine tube thoracotomy and pledgetted sutures

Considerations during CDH repair on ECMO

Circuit	• Minimize clots within ECMO circuit, consider elective circuit change prior to surgery so as to minimize clot burden if this is a concern. • 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 - ROTEM can be used as an adjunct to evaluate the entire coagulation cascade
Anticoagulation	• Lowering anticoagulation targets during perioperative period.

	• Initiate a high-risk bleeding protocol with decreased ACT, aPTT, Anti-Xa or ROTEM goals in the post-op period. Some centers hold anticoagulation entirely till bleeding stabilizes in the post-op period.
Antifibrinolytics	• 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
Adjuncts	• Consider application of fibrin sealants 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. It also allows placement of surgical packs in case of surface oozing)

Long term follow-up of infants with CDH on ECMO

All infants with CDH on ECMO will require long term multi-disciplinary follow up (Neonatal follow up: Prof Sam, DCD, PAS, CTS, Cardiology and other subspecialties depending on other anomalies). CNS imaging (preferably MRI Brain) at or after discharge may be considered to evaluate for evidence or progression of neurologic sequelae.

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Workflow for neonates with congenital diaphragmatic hernia (CDH)

Antenatal Diagnosis of CDH

Poor prognostic factors?

- LHR < 1.4
- Observed/Expected Lung Head Ratio (LHR) < 25%
- Liver Herniation

Antenatal Counselling:

- HRC/BDC team
- Referral to PAS, Cardiology
- Genetic studies
- Parents should be counselled on prognosis and potential need for ECMO
- Consider referral to Peri-Pal team if prognosis is poor

Post-Natal Assessment

Poor prognosis?

- CDH-CPI (Composite Prognostic Index) Score ≤ 5
  Evaluation: CXR, 2D Echo, CMA/Karyotype
- Refer PAS

Is the patient a candidate for ECMO?

- MDT discussion well ahead of deterioration with (Neonatology - Consultant in charge, Prof Sam, Dr Thowfique, NICU Head), CICU, CTS, PAS, Cardiology about possible need for ECMO (Use ECMO Referral form to facilitate ECMO planning if in agreement for ECMO) followed by family conference
- Ensure adequate line placement

Once stabilized on ECMO (24-48H post cannulation)

- MDT discussion (Neonatology- Prof Sam, Dr Thowfique, NICU Head, CICU, CTS, PAS, Cardiac anaesthetist, Cardiology) should be arranged within 48 hours to discuss optimization of medical therapy, timing and suitability for weaning trial or operative repair

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