Congenital Diaphragmatic Hernia Management in NICU

Procedure Responsibilities and Authorisation

Department Responsible for Procedure	Newborn Intensive Care Unit
Document Facilitator Name	Dr Priyantha Dissanayaka / Dr Vinayak Kodur
Document Facilitator Title	NICU registrar & Neonatologist (SMO)
Document Owner Name	Dr Jutta van den Boom
Document Owner Title	Head of Department, NICU
Target Audience	All NICU Staff

Procedure Review History

Version	Updated by	Date Updated	Summary of Changes
3	Dr David Bourchier	25/2/16	Changes to the values in the progress graph
4	Dr David Bourchier	19/2/19	No changes
5	Dr Priyantha Dissanayaka & Dr Vinayak Kodur	July 2024	Changes to the general and specific management based on current evidence

Congenital Diaphragmatic Hernia Management in NICU

Contents

Congenital Diaphragmatic Hernia Management in NICU

1 Overview

1.1 Purpose

Management of congenital diaphragmatic hernia (CDH).

1.2 Background

Congenital Diaphragmatic Hernia (CDH) is a complex congenital malformation of the diaphragm muscle with herniation of the abdominal contents through the defect into the thorax

Key clinical implications of CDH:

- Compression of lungs by herniated abdominal organs leads to pulmonary hypoplasia with structural and functional immaturity of the lung.
- Pulmonary hypertension (PHN) due to an increased amount of smooth muscle cells in pulmonary arteries. PHN is frequently present in CDH and remains an important determinant of survival[2].
- Associated lethal anomalies also contribute to mortality[1,4].
- Hypoxaemia with difference in pre and post-ductal oxygen saturation. However, absence of a pre and post ductal gradient in oxygenation does not exclude the diagnosis of pulmonary hypertension since right to left shunting may occur through the foramen ovale.

Key management strategies include protocol based management using gentle ventilation strategies[1,2,3,4,5,6].

- Avoid high airway pressures.
- Accept low pre-ductal saturations (down to 85%).
- Allow permissive hypercapnia.

Referral to Starship for ECMO may be required in severe cases. (NOTE: At present, Starship PICU do not offer pre-surgery ECMO for CDH infants given the poor outcomes).

1.3 Staff group

Clinical staff working with neonates in NICU.

1.4 Patient / client group

Infants with congenital diaphragmatic hernias

1.5 Definitions and acronyms

ABG	Arterial Blood gas
BP	Blood Pressure
BSID	Bailey Scale Of Infant and Toddler development
CDH	Congenital Diaphragmatic Hernia
CPAP	Continues positive Airway pressure
CVAD	Central Venous Access Devise
ECLS	Extracorporeal Life support
ECMO	Extracorporeal Membrane Oxygenation
HFOV	High frequency oscillatory ventilation
I:E Ratio	Inspiration to Expiration Ratio
iNO	Inhaled Nitric Oxide
MABP	Mean Arterial Blood Pressure
MAP	Mean airway pressure
O/E LHR	Observed to Expected Lung Head Ratio
OI	Oxygenation Index
PEEP	Positive End Expiratory Pressure
PIP	Peak inspiratory pressure
PTV	Patient triggered Ventilation
SpO2	Oxygen saturation
TC CO2 monitor	Trans Cutaneous Carbon Dioxide monitor
UVC	Umbilical venous catheter
VTV	Volume targeted Ventilation

2 Clinical management

2.1 Competency required

- Registered nurse
- Neonatal Nurse Practitioner
- NICU registrar
- Clinical Nurse Specialist – Neonatology

2.2 Procedure

2.2.1 Antenatal management

Antenatal counselling

Survival primarily depends on the degree of pulmonary hypoplasia and the level of fixed pulmonary hypertension with the influence of associated anomalies being secondary. Prenatal counselling should be offered via multidisciplinary prenatal counselling (MFM team including Neonatologist & Paediatric Surgeon), Counselling should include considerations for timing & mode of delivery, prognosis, appropriateness for location of delivery and timing of postnatal surgery.

Factors that can be used to guide the prognosis of neonates with congenital diaphragmatic hernia include:

1. The foetal Lung volume

Foetal lung volume can be estimated by the Observed to Expected Lung Head Ratio, or O/E LHR. It is a numeric estimate of size of the foetal lungs, based on measuring the amount of visible lung. The O/E LHR measured on ultrasound examination between 22 and 32 weeks gestational age is a useful predictor of subsequent survival in a foetus with CDH[3].

O/E LHR	Predicted outcome
<15%	Virtually no chance of survival
15-25%	Predicted survival ≈ 15%
26-45%	Predicted survival 30-75%
>45%	Very likely to survive provided no other major anomalies

2. The presence of other associated anomalies

- CDH is frequently associated with other anomalies. These include, chromosome anomalies (25%), defects of the heart (20%), central nervous system (CNS), kidneys and the gastrointestinal tract.
- CDH has been associated with more than 50 genetic syndromes. A comprehensive assessment includes invasive sampling for microarray.

3. Liver position

Infants with the liver in the chest have a more severe form of CDH and a lower survival rate.

4. Site of the Diaphragmatic hernia

Presence of bilateral diaphragmatic hernia is associated with a very poor prognosis. Mortality rate of the right and left sided CDH are same. However, the long-term lung morbidity rate is higher for right CDH [14].

2.3 Timing and Mode of Delivery

The optimal timing and mode of delivery remains controversial. Studies have shown significant decrease in neonatal and infant mortality with advancing gestational age and decrease in need for ECMO. Other studies have found no differences when dividing gestational age at delivery categorically as under 37 weeks, 37–38 weeks and 39. There does not appear to be a difference in mortality between vaginal and caesarean birth.

Recommendations:

- Discussion between neonatal and obstetric team in all cases to facilitate optimal care
- Delivery should be planned around 39 weeks in a tertiary centre
- In the case of preterm labour prior to 34 weeks of gestation, antenatal steroids should be given.

2.4 Considerations for location of delivery

An early fetal MRI and ultrasound guided O/E LHR, liver herniation and knowledge of additional abnormalities can help in the parent's decision on possible future care options, including referral and/or second opinion to a centre that offers ECMO in severe cases (Starship, Auckland).

Refer for antenatal consult in a centre with ECMO capabilities (Starship, Auckland) for all cases with < 45% expected lung volume. This does not automatically mean they should be delivered at Starship, Auckland.

3 Postnatal management

- Every known case of CDH must have in attendance neonatal personnel capable of intubation.
- Avoid bag and mask ventilation and continuous positive airway pressure (CPAP).
- Electively intubate – avoid hyperinflation at all times by restricting peak inspiratory pressure (PIP) to 26 cm or less. Rarely, some of the infants with O/E LHR > 50% with other favourable prognosticating factors can be managed without ventilation.
- Place saturation probe on right hand. Target pre ductal saturation between 80% - 95%.
- Decompress the stomach with 8Fr orogastric or nasogastric tube. Continuous free drainage with 4-hourly aspiration, in order to prevent gastric and bowel distension and further lung compression.
- There is no evidence for routine use of surfactant in infants with CDH.

3.1 General management

- Minimal handling, reduce noise, avoid direct light in the face
- Maintain normothermia
- Monitor Pre and Post ductal saturation levels
- Invasive blood pressure monitoring (right radial artery preferred)
- Strict fluid balance monitoring (consider placement of an indwelling urinary catheter)
- Type of Blood sampling and frequency should be determined by the cardiorespiratory status of the infant as well as previous results. A plan for frequency of blood sampling should be clarified at each ward round.
- Oxygenation index must be calculated with each arterial blood gases.
- Oxygenation index = $\frac{\text{Mean Airway pressure x FiO2}}{\text{Pa O2}}$
- $TcCO_2$ monitoring
- Chest X-ray and Abdominal X-ray
- Early cardiac ultrasound to assess cardiac function and shunts

Other investigations

- Microarray
- Cranial and renal ultrasound

3.2 Central Venous access and Arterial access

- A double lumen UVC is preferable. A CVAD can be considered at day 5-7 of UVC. (Consider a double lumen CVAD if ongoing requirement or anticipation of inotropes requirement).
- To allow assessment of pre-ductal blood gases and saturations, right radial arterial catheterisation is desirable. If this is not possible, a post-ductal arterial line (e.g. umbilical arterial catheter) and pre-ductal saturation monitoring is acceptable.

3.3 Sedation and analgesia

- Sedate lightly, allowing the babies to breathe spontaneously
- Neonates with severe pulmonary hypertension will require more analgesia and sedation to facilitate optimal ventilation
- Pain score must be recorded according to the protocol
- Use paralysis sparingly and only if the infant is showing signs of dyssnchrony with the ventilator and all other means to achieve control of oxygenation and ventilation have exhausted.

3.4 Ventilator support

- In preparation for admission, the ventilator should be set up ready for use with inhaled nitric oxide set up and available for immediate use.
- Monitor pre-ductal and post-ductal SpO2
- Set up for $TcCO_2$ monitoring
- Ventilator induced lung injury has a significant negative impact on outcomes of infants with CDH. Follow a lung protective strategy approach as outlined below.

3.4.1 Lung protective strategy

- Titrate oxygen (FiO_2) to achieve pre-ductal SpO_2 of between 85%-95%
- Accept pre-ductal SpO_2 levels > 70% in the initial period of stabilisation (1-2 postnatal hours) without escalating ventilation settings provided pH >7.2 and $PaCO_2$ < 8.7 kPa
- Target pH of 7.25 - 7.4 and $PaCO_2$ between 6 – 8 kPa
- The preferred ventilation mode is PTV (SLE6000), with volume targeting – i.e. PTV + VTV up to maximum of 5ml/kg
- Initial ventilatory settings:

Ventilator parameter	Recommendation	Reason
Peak inspiratory pressure (PIP)	Target PIP ≤ 26 cm H2O	Minimize Ventilator Induced Lung Injury
Positive end Expiratory pressure (PEEP)	Use a PEEP of 5 cm H2O (Lower PEEP can be used depending on the lung inflation)	To improve the lung compliance + To prevent gas trapping +To improve the preload
Ventilator Rate	40-60 /Min (back-up rate)	
Tidal volume	Starting VTV 4ml/kg. Limit to maximum of 5 ml/kg.	Due to pulmonary hypoplasia (restrictive lung disease)

- High frequency oscillatory ventilation (HFOV) should be used if the PIP required to achieve target $PaCO_2$ is >26cm H2O, or the required VTV to achieve adequate MV for target $PaCO_2$ is greater than 5ml/kg.

HFOV settings:

Mean Airway Pressure (MAP)	Commence with a MAP 2cm above what was required on conventional ventilation – **Limit MAP <17**
Frequency (Hz)	Usually set at 8-14 Hz
Amplitude (Delta P)	Consider starting with an amplitude approximately 1.5 to two times the set MAP
I:E ratio	1:2

- Obtain a CXR within an hour of commencement of HFOV to determine adequate lung distension. Adjust MAP as necessary with consideration to maximum MAP limit.
- Switch back to conventional ventilator when stable and arterial blood gases (ABGs) show improvement

.

3.4.2 Oxygenation targets

- Aim should be to maintain acceptable saturation levels that improve the pulmonary hypertension and organ transfusion while preventing hyperoxia

Target pre-ductal saturation levels	>85% - 95%
Target post-ductal saturation levels	>70%

3.5 Hemodynamic support

- Haemodynamic management should be aimed at achieving appropriate end organ perfusion.
- The assessment of the circulatory adequacy and the decisions and interventions for that should be dependent on the multidimensional parameters.
- These should include blood pressure, heart rate, acid-base status, arterial lactate, urine output, and capillary refilling time and echocardiography findings.

Assessed parameter	**Target value**
Mean arterial blood pressure (MABP)	>40mmHg in term neonate and equivalent to their gestational age (the 10th percentile for each gestation). This can be revised as per the findings on the cardiac scan.
Arterial Lactate concentration	≤3mmol/l
Urine output	>1ml/kg/h
Acid base status	pH 7.25 -7.4 (preferably 7.25-7.35)

- Echocardiography allows for anatomic and functional cardiac and pulmonary vascular assessment and must be performed early in the course (<24 hours after birth) for all infants with CDH.

3.6 Management of poor perfusion

- All CDH infants with poor perfusion must get a functional cardiac assessment. Please see Appendix A for the pathophysiology of cardiac dysfunction.
- Infants with biventricular dysfunction have poorer outcomes when compared with those without dysfunction.
- Treatment of poor perfusion (capillary refill > 3 s, lactate> 3 mmol/L, urine output < 1 mL/kg/h) and BP below normal values for age includes the judicious administration of crystalloid, generally sodium chloride 0.9% bolus (10 ml/kg).

- Further fluid bolus are not be given unless discussed with the neonatal consultant. See Appendix B for management of right and left cardiac dysfunction.
- The choice of inotropic and/or vasopressor support should be considered carefully according to the underlying problem and current cardiovascular status clinically and on cardiac scan.

Inotrope	Mechanism of action	Dose
Dobutamine IV for neonates (Ref. 2909)	Raises blood pressure by increasing cardiac output and decreasing peripheral vascular resistance.	5-10 (max) microgram/kg/min
Adrenaline for neonates (Ref. 0559)	At low doses of 0.01 – 0.1 microgram/kg/min, adrenaline primarily stimulates cardiac and vascular beta-1 and beta-2 receptors, leading to increased inotropy, chronotropy, conduction velocity and peripheral vasodilatation. At high doses of >0.1 microgram/kg/min, adrenaline also stimulates cardiac and vascular alpha-1 receptors, causing vasoconstriction and increased inotropy.	0.05-1 microgram/kg/min
Milrinone for neonates (Ref. 6611)	It is a PDE-3 inhibitor that inhibits degradation of cAMP. This improves cardiac contractility (which increases cardiac output) and lowers peripheral vascular resistance. Milrinone may also reduce pulmonary vascular resistance and improve right ventricular performance and oxygenation in the setting of PPHN. Avoid loading dose as it leads to systemic hypotension.	0.2 (preterm)-0.33 Term (min) to 0.75 microgram/kg/min
Vasopressin for neonates (Ref. 6612)	Can be considered in infants with right ventricular dysfunction and systemic hypotension, either instead of noradrenaline or in order to reduce tachycardia that can be induced by noradrenaline.	

- There is evidence that in the presence of pulmonary hypertension, dopamine and other adrenergic agents, in high doses, raise pulmonary pressures along with systemic pressure and are not recommended in this setting.
- Hydrocortisone may be used for the treatment of hypotension after other treatment has been ineffective. Consider hydrocortisone before adding 2nd inotrope and early in the management of the baby.

3.7 Pulmonary Hypertension

- The physiological basis for pulmonary hypertension in neonates with CDH is a decreased number of pulmonary arterial structures associated with significant adventitial and medial wall thickening, due to an increased amount of smooth muscle cells in pulmonary arteries. Appendix A.
- As a result, elevated pulmonary vascular resistance may lead to right to left ductal shunting after birth.
- Echocardiography is one of the best modalities for real time assessment of pulmonary arterial pressure and right and left heart function.
- If pre-ductal saturations fall below 85% and/or if there are signs of poor organ perfusion, with sonographic evidence of pulmonary hypertension, treatment of pulmonary hypertension should be initiated. iNO can be initiated while awaiting the cardiac assessment as per clinical status. See Appendix B for management of right and left cardiac dysfunction.
- Optimize cardiac function and blood pressure by maintaining adequate circulatory volume and judicial inotropic support.
- Inhaled NO (iNO) Nitric Oxide Usage in NICU Ref 1553 should be started if,

  Features of pulmonary hypertension on cardiac scan

  and

  Oxygenation index (OI) > 20

  and/or

  Pre and post ductal saturation difference of >10%

- Start iNO at the rate of 20ppm and continued at least one hour to assess the response. iNO responders are defined as,

  1. a decline of 10–20% in the pre-post ductal saturation difference,
  2. Increase of 10–20% of PaO 2 or (able to maintain PaO2 > 8 kPa with reduction in FiO2),
  3. In addition, following changes may be seen:
     improvement in hemodynamic parameters meaning a 10% increase in mean blood pressure, decrease in lactate levels

- Some infants may not respond adequately, please discuss with attending SMO and check with cardiac scan findings in non-responders. In non-responders, consider stopping iNO and starting alternative medications for pulmonary vasodilation such as Sildenafil, Milrinone, or Bosentan as per the findings of the cardiac scan and algorithm in Appendix B.
- Intravenous prostaglandin E1 can be considered to reopen the ductus arteriosus in case of echocardio-graphic evidence of pulmonary hypertension with right ventricular strain to reduce the right ventricular workload.

3.8 Extra-corporeal Membrane Oxygenation (ECMO)

Initiate early discussion with PICU regarding indications for ECMO

Indications for initiating ECMO include either respiratory or circulatory parameters described below:

- Inability to maintain pre-ductal saturations >85% or post-ductal saturations >70%.
- Increased PaCO2 and respiratory acidosis with pH <7.15 despite optimization of ventilator management.
- Peak inspiratory pressure >28 cm H_2O or mean airway pressure >17 cm H2O is required to achieve saturation >85%.
- Inadequate oxygen delivery with metabolic acidosis as measured by elevated lactate ≥ 5 mmol/l and pH <7.15.
- Systemic hypotension, resistant to fluid and inotropic therapy, resulting in urine output <0.5 ml/kg/h for at least 12–24 h.
- Oxygenation index ≥ 40 present for at least 4-hours despite appropriate ventilation strategies.
- Before taking any decision to start ECMO, it is necessary to exclude any comorbidities. Absence of pre-existing major compounding factors e.g. congenital, genetic or other comorbid conditions that inform a poor prognosis, severe brain injury, or vessel size too small for cannulation.
- Before commencing ECMO, detailed discussion between neonatologists, paediatric intensivists, paediatric surgeons and neonatal transport services must take place.

3.9 Fluid management

- Once a central access is achieved, infants can be started on IV parenteral nutrition.
- Consider restricting fluids to 40 ml/kg/day (especially when infant is muscle relaxed) in first 24 hours post birth. (Exclude any fluid boluses given during this period from this volume).
- Thereafter, increase fluid and caloric intake based on clinical condition.
- OIT can be started and enteral feeding commenced postoperatively in consultation with the surgical team.
- Consider diuretics in the case of persisting positive fluid balance; aim for urine output of >1 ml/kg/h.

3.10 Surgery

Surgical repair of the diaphragmatic defect should be performed after clinical stabilization defined as,

- The baby on conventional ventilator with required PIP ≤26.
- Pre-ductal saturation levels of 85–95% with oxygen requirement < 50%.
- Lactate levels <3 mmol/L
- Urine output >1ml/kg/hr
- Minimal inotropic support to maintain normal mean arterial pressure for the gestational age.
- Weaned off inhaled Nitric oxide.
- Estimated pulmonary artery pressures less than systolic blood pressure off inhaled nitric oxide.

3.11 After care

3.11.1 Post-operative management:

- Same principles as pre-operative management.
- Start enteral feeds as soon as the post-op ileus has resolved.
- Preventive **anti-reflux therapy** should be started in combination with enteral feeding.

3.11.2 Follow Up

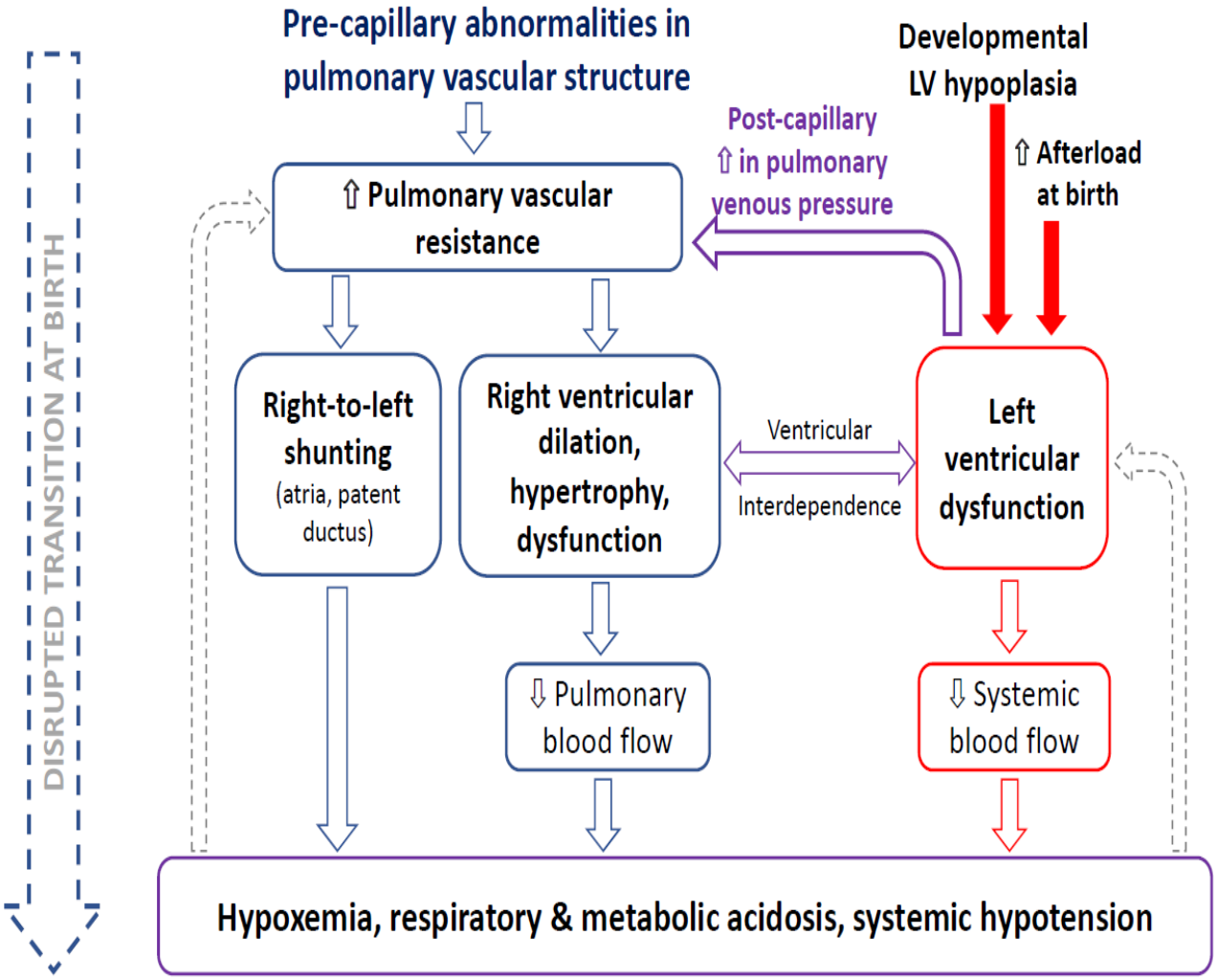
- Neonatal Community Nursing team follow-up and SMO follow-up as outpatient.
- Babies may also have an ongoing need for supplemental oxygen requiring home oxygen therapy.
- Long-term follow-up with Paediatric Surgical team.
- Consider SYNAGIS® (palivizumab) prophylaxis and influenza vaccination recommended for whole family.
- High risk hearing screening.
- GMA assessment and CDC follow-up including BSID assessment at 2 years of age.
- Long-term follow up with Paediatric respiratory team for assessment of pulmonary function.
- Clarify follow-up with Paediatric cardiology services if infant has residual pulmonary hypertension/structural heart disease.

4 Evidence base

4.1 Bibliography / References

1. Kitty G. Snoek, Irwin K.M. Reiss, Anne Greenough, Irma Capolupo, Berndt Urlesberger, Lucas Wessel , Laurent Storme , Jan Deprest ,Thomas Schaible Arno van Heijst , Dick Tibboel, Standardized Postnatal Management of Infants with Congenital Diaphragmatic Hernia in Europe:The CDH EURO Consortium Consensus – 2015 Update
2. Shiran S. Moore(MD), Roberta L. Keller(MD),Gabriel Altit (MD) Congenital Diaphragmatic Hernia Pulmonary Hypertension and Pulmonary Vascular Disease, https://doi.org/10.1016/j.clp.2023.10.001 perinatology.theclinics.com 0095-5108/23/ª 2023 Elsevier
3. Carla L. Avena-Zampieri, MRes, Jana Hutter, PhD,Mary Rutherford, MD, MRCPCH, Anna Milan, MD, PhD, Megan Hall, BSc(Hons), MRCOG,Alexia Egloff, MD, David F.A. Lloyd, MBChB, MRCPCH, PhD, Surabhi Nanda, MD, MDRes, Anne Greenough, MD, FRCP , Lisa Story, BMBCh, MRCOG, PhD. Assessment of the fetal lungs in utero. Am J Obstet Gynecol MFM. 2022 Sep; 4(5): 100693, Published online 2022 Sep. doi: 10.1016/j.ajogmf.2022.100693
4. Langham MR Jr et al. CDH: Epidemiology and Outcome. Clin Perinatol 1996; 23:671 – 688.
5. Dillon PW et al. The relationship of pulmonary artery pressure and survival in CDH. J Pediatr Surg 2004;p 39: 307 – 312.
6. Boloker J et al. CDH in 120 infants treated consecutively with permissive hypercapnea/spontaneous respiration/elective repair. J Pediatr Surg 2002; 37:357 – 366.
7. Downard CD et al. Analysis of improved survival rate for CDH. J Pediatr Surg 2003; 38(5):729 – 732.
8. Bagola p et al. Impact of a current treatment protocol on outcome of High-Risk CDH. J Pediatr Surg 2004; 39(3):313 -318.
9. Beca J. Outcome statistics using protocol based management in CDH. PICU Starship Children's Hospital, Auckland. Personal Communication 2007.
10. Bohn D. Congenital Diaphragmatic Hernia. Am J Respir Crit Care Med. 2002; 166:911 – 915.
11. Kays D. Wéal. Outcomes in the physiologically most severe CDH patients. J. Pediatr. Surg 2015, 50:893—97.
12. Kashyap AJ, Hodges RH, Thio M, et al. physiologically based cord clamping improves cardiopulmonary haemodynamics in lambs with a diaphragmatic hernia. Arch Dis Child Fetal Neonatal Ed 2020; 105(1):18-25
13. Snoek KG, Capolupo I, van Rosmalen J, et al, CDH EURO Consortium. Conventional mechanical ventilation versus high-frequency oscillatory ventilation for congenital diaphragmatic hernia: a randomized clinical trial (the VICI-trial). Ann Surg 2016; 263(5):867–74.
14. Schaible T., Kohl T., Reinshagen K., Brade J., Neff K.W., Stressig R., Büsing K.A. Right- versus Left-Sided Congenital Diaphragmatic Hernia: Postnatal Outcome at a Specialized Tertiary Care Center. Pediatr. Crit. Care Med. 2012; 13:66–71. doi: 10.1097/PCC.0b013e31821

Appendix A – Pathophysiology of pulmonary hypertension and cardiac dysfunction in CDH



Appendix B – Management of the right and left ventricular dysfunction