Modern management of congenital diaphragmatic hernia

Congenital diaphragmatic hernia (DH) is a life-threatening malformation (incidence 1 in 2,000-5,000 live births). The diaphragmatic defect (80% are left-sided) is of varying size through which abdominal viscera including liver, spleen, stomach and intestine can herniate into the chest from about the tenth week of gestation. Lung growth and development are impaired through limitation of space, reduced fetal breathing movements and loss of fetal lung liquid, leading to variable degrees of pulmonary hypoplasia. The combination of pulmonary hypoplasia and pulmonary hypertension (PHT) is the main determinant of postnatal survival. Over the last two decades there has been an improvement in survival, predominantly through advances in neonatal care with ventilation strategies to avoid lung injury, and targeted therapy for pulmonary hypertension1.

The following article outlines the strategies used in Glasgow for the management of infants born with DH at the severe end of the clinical spectrum.

### Presentation and indicators of severity

**Antenatal diagnosis and fetal medicine**

DH may be diagnosed antenatally with an overall detection rate of around 60% in regions where routine scanning is offered, although the presence of multiple malformations, karyotype anomalies or syndromes improves detection rates2. All newly diagnosed cases of DH should be offered referral to a Regional Fetal Medicine Service for further evaluation and counselling by a multi-disciplinary team (fetal medicine, neonatal surgery, neonatology) to ensure consistent, accurate information is given.

A reliable method of antenatally predicting the severity of the DH would be invaluable to guide decision making and to counsel families accordingly but, until recently, no one method had been validated in multicentre studies. Most methods aim to determine the degree of pulmonary hypoplasia. The most widely quoted method is the lung/head ratio (LHR) measured by ultrasound. A reliable method of antenatally predicting the severity of the DH would be invaluable to guide decision making and to counsel families accordingly but, until recently, no one method had been validated in multicentre studies. Most methods aim to determine the degree of pulmonary hypoplasia. The most widely quoted method is the lung/head ratio (LHR) measured by ultrasound.

### Keywords

- congenital diaphragmatic hernia
- pulmonary hypertension
- follow-up
- pulmonary hypoplasia

### Key points


1. Antenatally measured indicators help identify high risk diaphragmatic hernia (DH) cases and aid counselling and planning.

2. Postnatal management targeting pulmonary hypertension with lung protective ventilation strategies, including extracorporeal life support in selective cases, is essential for optimal outcome.

3. Structured multidisciplinary long-term follow-up for all DH survivors is critical to identify and proactively manage comorbidities.
ultrasound (FIGURE 1). The contralateral lung is visualised on a transverse view of a four-chamber view of the heart. Two dimensional cross-sectional area is calculated by multiplying the longest measurements taken perpendicular to each other. This value is divided by the largest measured head circumference to give LHR.

As the LHR varies throughout gestation, making the prognostic significance less robust, the more recent refinement of using LHR values from normal fetuses to calculate the observed/expected (O/E) LHR for any given gestation is a more reliable indicator of sectionality and postnatal morbidity. In Glasgow serial O/E LHR measurements are undertaken throughout pregnancy.

Total fetal lung volume (TFLV) can be evaluated on fetal MRI. In Glasgow, fetal MRI scans are offered during the second and third trimesters. Data from ultrasound and MRI scans suggest O/E LHR and O/E TFLV are reasonable antenatal indicators of fetal lung capacity and have a role when counselling prospective parents and planning appropriate antenatal and postnatal care (FIGURE 2).

Postnatal

After birth, the degree of impairment of gaseous exchange may indicate the severity of pulmonary hypoplasia. The ability to clear CO₂, rather than oxygenate may be a better indicator of total alveolar surface area. Multivariate analysis of the International CDH Registry has shown that birth weight and Apgar score at 5 minutes were predictive of survival.

Pulmonary hypertension is the inevitable consequence of pulmonary hypoplasia and newborns with DH will have elevated (above systemic) pulmonary pressures. This will be manifested clinically by a significant difference in oxygen saturations taken pre- and post-dually and should be confirmed by echocardiography. Raised pulmonary pressures lead to failure in oxygenation and ventricular dysfunction. In Glasgow serial echocardiography is advocated to delineate the fall in pulmonary pressures and assess the efficacy in therapies directed at improving systemic perfusion and reducing pulmonary pressures. Failure to respond to these manoeuvres is linked with a high mortality.

Antenatal therapy

Antenatal steroids

Maternal antenatal glucocorticoid administration in premature labour has beneficial effects on lung maturity and surfactant production. The structural immaturity of the lungs, and evidence of surfactant deficiency in animal models, suggested a role for antenatal steroids in fetuses with DH. Case series have reported promising results from the use of repeated dose antenatal steroids in severe congenital DH, although a randomised-controlled trial was inconclusive. However, concerns have been raised regarding possible detrimental impact on neurological development. In Glasgow two doses of maternal steroids are administered at around 34 weeks’ gestation at the time of the third trimester fetal MRI scan.

Fetal surgery

Open fetal surgery is technically achievable. However, clinical studies showed that repair of the DH was only possible in those in whom potential benefit was marginal (liver in abdomen) and not technically possible for those who might benefit most (liver in chest). Reports of pulmonary hyperplasia resulting from laryngeal atresia led to the concept of tracheal ligation to prevent the egress of fetal lung fluid from the trachea, thus promoting lung growth. This concept of ‘plugging the lung until it grows’ (PLUG) has evolved to incorporate fetoscopic placement of either a detachable balloon (FETO) in the trachea that could be ruptured prior to delivery or a biodegradable gel. This technique results in larger structurally normal lungs, although antenatal steroids should be administered to prevent abnormalities in type II pneumocyte development, impaired surfactant synthesis and poorly compliant lungs.

Clinical experience has demonstrated that the technique is feasible but preterm labour and premature delivery remain relatively common complications. The major impediment to all fetal inter-vention is the absence of definitive predictors of mortality to ensure that this potentially high-risk therapy is only offered to cases where optimal postnatal management will result in little chance of survival. A randomised controlled trial of tracheal occlusion is currently recruiting in Europe for fetuses with an O/E LHR of <25%.

Postnatal therapy

Resuscitation at delivery

Antenatal diagnosis of DH permits detailed planning of delivery and optimal perinatal medical management. Ideally, elective delivery should be near term at a centre with direct access to specialist neonatal surgical services. Normal vaginal delivery where possible is advocated with experienced medical personnel available for immediate resuscitation. The goal of newborn resuscitation in DH is to avoid air insufflation of the herniated bowel, a complication that will further compress the heart and lungs. An endotracheal tube should be inserted before the first breath and a large bore nasogastric tube placed and left on free drainage to ensure decompression of the stomach. Venous access through the umbilical vein allows sedating and paralysing drugs to be administered. An umbilical arterial line (post-dually) or right radial arterial line (pre-dually) facilitates regular blood gas analysis and invasive blood pressure monitoring. Peripheral saturation monitors should be placed on the right arm and a lower limb to monitor pre- and post-dually saturations (to identify degree of right-to-left shunting).

In cases with no antenatal diagnosis, clinical signs at birth that suggest a DH include early respiratory distress in association with a scaphoid abdomen and heart sounds shifted from the normal position (usually to the right). Standard newborn resuscitation with bag/mask ventilation will often cause deterioration as air is delivered into the herniated gut, further embarrassing cardiac and respiratory function (FIGURE 3). If DH is suspected, the DH protocol outlined above
should be followed. A chest X-ray will confirm the diagnosis.

Respiratory support

An important aspect of early management of infants with DH is the careful management of ventilatory support. Avoidance of iatrogenic ventilator trauma is key with adherence to the concept of 'gentle ventilation'. As indicated previously, the lungs in newborns with DH are small and immature so attempts to achieve normal tidal volumes can lead to lung damage, particularly pneumothorax in the acute setting. Tolerating hypercarbia, accepting pre-ductal \( \text{SaO}_2 \geq 90\% \), accepting lower post-ductal \( \text{SaO}_2 \) if blood lactate and \( [\text{H}^+] \) are satisfactory, are essential strategies to prevent ventilator-induced lung injury.

The Glasgow management guideline recommends limiting peak inspiratory pressures (PIP) to \( \leq 25 \text{cmH}_2\text{O} \) for conventional ventilation. If this is not possible, early conversion to high frequency oscillatory ventilation with a low mean airway pressure strategy is considered. Many centres employ similar lung protection strategies and have reported improved results following implementation of a protocolised approach. Muscle paralysis is used to allow optimisation of ventilation and prevention of gaseous distension of the intestine in the chest.

The routine use of exogenous surfactant in infants with DH is not recommended. No randomised trials to date have shown any benefit in routine administration of exogenous surfactant and there is a risk of preferential distribution to better aerated areas of lung, causing over-distension and pneumothorax.

Cardiovascular support and therapy for pulmonary hypertension

The pulmonary hypertension (PHT) associated with DH is often resistant to conventional treatment due to the combination of the small cross-sectional area of pulmonary vessels, structural vascular remodelling and altered pulmonary vasoreactivity. Inhaled nitric oxide (iNO) has been shown to improve oxygenation but did not affect mortality. Despite this, iNO is commonly used in combination with other strategies to manipulate the cardiovascular status.

Regular echocardiography is essential for indirect measurement of pulmonary pressures (ductal flow and/or pulmonary/tricuspid valve regurgitation) and assessment of right and left ventricular function. Unexpected changes in the infant's condition may be due to cardiovascular compromise rather than being respiratory in origin, and can occur without immediately apparent alterations in peripheral or central indicators of perfusion or oxygenation. Impending right heart failure can be ameliorated through reduction of right ventricular afterload by ensuring the ductus arteriosus remains patent by infusion of prostaglandin E, (5-20 ng/kg/min). In severe cases of DH, left ventricular development can be impaired and the right ventricle represents the dominant ventricle, so ensuring right to left ductal flow allows the right ventricle to contribute to systemic perfusion in addition to improving right-sided heart failure.

If PHT is an ongoing issue, sildenafil is administered once enteral feeding is established. Non-specific intravenous pulmonary vasodilators have no place in current DH management as they impact on systemic blood pressure. Milrinone, a selective phosphodiesterase III inhibitor, which has both inotropic and lusitropic effects on the myocardium, may improve ventricular function and reduce pulmonary vascular resistance.

Nursing the infant with PHT

The aim of nursing care in a newborn with DH should follow the core principles of nursing a premature infant despite most infants being near-term. Adequate sedation should be administered and it is important to increase sedation/analgesia prior to procedures. Unlike other term surgical neonates, handling and other stressful stimuli can cause PHT episodes. These episodes are often rather dramatic with poor colour, tachycardia, hypoxia and profuse perspiration. These infants should be nursed by experienced staff that can anticipate these episodes and avoid over-reaction. A common stressful stimulus in these infants is the passage of stool and, experience in Glasgow suggests, a prompt nappy change is more effective at resolving a PHT episode than other aggressive therapies.

The issue of minimal handling needs to be explained sensitively to parents who are keen to touch and stroke their infant, although this may be best avoided initially. Initiation of oral feeding may be significantly delayed, with a number of infants requiring continuous feeds through nasogastric or nasojejunal tubes. Speech and language therapists should be involved at an early stage to introduce strategies to minimise oral aversion.

Role of extracorporeal life support (ECLS)

ECLS is an excellent rescue therapy for the infant with DH that allows optimal tissue oxygenation and provides a period of lung rest following lung injury or refractory PHT. In infants with severe pulmonary hypoplasia, where adequate gaseous exchange is impossible despite optimal treatment with lung-protective strategies, the role of ECLS is less clear. At present, there are no reliable predictors to allow accurate distinction between salvageable patients and those with inevitably fatal pulmonary hypoplasia and the authors advocate consideration and early discussion with an ECLS centre in all severe cases that do not respond to optimal support.
Surgical repair
The recognition that there is often an initial period of haemodynamic instability and that lung compliance is worsened rather than improved in the immediate postoperative period led to the concept of delayed surgical correction. Most centres now delay surgical intervention until the infant is clinically well and the PHT is controlled. For optimal timing of DH repair, the ventilation parameters (especially PIP) should be trending downwards, FiO2 requirement should be low (0.5-0.4) and there should be echocardiological evidence that PHT is being controlled. This allows some ‘wiggle room’ should there be a temporary deterioration postoperatively.

In Glasgow the practice is to move the infant to the operating room (OR) only if they are very stable. In the event of an infant being fragile, on ECLS, or still on high-frequency oscillation as the optimal ventilation mode, OR staff are brought to the NICU and undertake surgery on the open bassinette. This has been very successful with no associated complications.

Open operative repair is undertaken through a subcostal abdominal approach. The herniated viscera are reduced and the diaphragmatic defect is inspected for the presence of a sac that is excised if present (≈10% of cases). The size of the defect is graded A-D at the time of surgery (FIGURE 4) as this has been shown to be the major determinant of outcome. Diaphragmatic closure is achieved using interrupted sutures in small defects (defect A-B in FIGURE 4) but larger defects will require the use of prosthetic patches. In Glasgow as in many other centres, GoreTex™ is used as the patch material, although parents are counselled that, as the patch material will not grow with the infant, there is a high rate of late patch disruption leading to recurrent hernia and the need for further surgery. Occasionally, in large defects it may be necessary to temporarily patch the abdominal wall in the neonate to allow space for the herniated viscera in the abdomen and avoid “abdominal compartment syndrome”.

Recently, minimally invasive repair via the thoracoscopic route has been...
advocated for repair of the diaphragmatic hernia in stable infants. Early results are encouraging although there are concerns about the impact of raised PCO₂ during surgery, and a higher than expected early recurrence rate²⁷.

Mortality in severe DH
Published mortality rates are dependent on the study population and reports from surgical centres may be biased by a ‘hidden mortality’ caused by non-inclusion of infants who died in utero or in maternity units without being transferred. Mortality in patients that survive to surgery is as low as 15%, but pooled mortality figures from population-based studies, where all live-born infants are included, show a mortality rate of around 48%²⁸. Higher mortality figures are quoted when antenatally diagnosed fetuses are included⁴⁰, although termination rates will influence these figures with some fetuses having chromosomal or cardiovascular anomalies that independently predict a fatal outcome, and other potentially ‘survivable’ fetuses with isolated DH being terminated without a ‘trial of life’.

The Glasgow data, that include live-born infants in a Regional Maternity Unit, transfers from other neonatal units and direct referrals to RHSC for ECLS, show an over-all survival for all infants with a diagnosis of DH of 75%. Survival once patients reach the neonatal surgical unit is 85%.

Long-term morbidity and multidisciplinary follow-up
Active long-term follow-up of infants with severe DH who have received iNO, ECLS, and who have had patch repair of large defects is essential. It is no surprise that this complex group of patients will have significant ongoing problems encompassing developmental, musculoskeletal, nutritional and pulmonary sequelae. Careful follow-up throughout childhood and into adulthood will allow early recognition and treatment of the potential complications that can occur. The American Academy of Pediatrics (AAP) has produced a detailed paper outlining the potential areas of morbidity for these patients and their recommended schedule of follow-up has been adopted in Glasgow for the monthly multidisciplinary DH follow-up clinic (TABLE 1). The advantage of offering a multidisciplinary clinic to cover all clinical needs and avoid multiple clinic visits with potentially conflicting treatment strategies must be balanced against the long distances some families appear willing to travel.

Scottish Diaphragmatic Hernia Clinical Network
The Scottish Government National Services Division commissioned the care of Diaphragmatic Hernia as a Managed Clinical Network in April 2009 to optimise the clinical management of infants with this condition, to achieve robust data collection, and to ensure equitable access to best care throughout Scotland. The Scottish DH Clinical Network involves a multidisciplinary team that aims to produce best-practice guidelines for all aspects of management of DH and, with co-operation from parents of children with DH, produce clear up-to-date information for families covering all stages of the patient journey.

The full gambit of therapeutic options is necessary to obtain the best results for this challenging condition and careful, multidisciplinary care and long-term follow-up is required by a dedicated team throughout the clinical course.

References


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Please contact: Chrissie Israel, NICU, Southmead Hospital, Bristol, BS4 5DZ.
Tel: 0117 323 6347. Email: chrissie.israel@bristol.ac.uk

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