ERS TASK FORCE REPORT

Congenital diaphragmatic hernia

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ABSTRACT: Infants with congenital diaphragmatic hernia (CDH) have significant mortality and long-term morbidity. Only 60–70% survive and usually those in high-volume centres. The current Task Force, therefore, has convened experts to evaluate the current literature and make recommendations on both the antenatal and post-natal management of CDH. The incidence of CDH varies from 1.7 to 5.7 per 10,000 live-born infants depending on the study population. Antenatal ultrasound scanning is routine and increasingly complemented by the use of magnetic resonance imaging. For isolated CDH, antenatal interventions should be considered, but the techniques need vigorous evaluation. After birth, management protocols are often used and have improved outcome in nonrandomised studies, but immediate intubation at birth and gentle ventilation are important. Pulmonary hypertension is common and its optimal management is crucial as its severity predicts the outcome. Usually, surgery is delayed to allow optimal medical stabilisation. The role of minimal invasive post-natal surgery remains to be further defined. There are differences in opinion about whether extracorporeal membrane oxygenation improves outcome. Survivors of CDH can have a high incidence of comorbidities; thus, multidisciplinary follow-up is recommended. Multicentre international trials are necessary to optimise the antenatal and post-natal management of CDH patients.

KEYWORDS: Antenatal ultrasound, congenital diaphragmatic hernia, congenital lung malformation

Congenital diaphragmatic hernia (CDH) is an uncommon congenital malformation of the lung, but one with important implications for diagnosis, management and prognosis. It is associated with high mortality and although improvements in medical and surgical management have improved the outlook, survival remains at 60–70% [1–6]. Newer modalities, including antenatal screening and intervention, are available but are often introduced without formal evaluation. The current Task Force has convened experts in neonatal and paediatric respiratory medicine, paediatric pathology, fetal medicine, and paediatric surgery to evaluate the current literature and make recommendations for the management of CDH.

EPIDEMIOLOGY OF CDH

To provide population-based incidence of congenital anomalies, the European Union's European Surveillance of Congenital Anomalies (EUROCAT) collects data from 43 European registries in 20 European countries, capturing ~29% of Europe's birth population [7]. The reported incidence of CDH in 2008 for all pregnancies from 20 weeks onwards from EUROCAT was 2.62 per 10,000 [7] and 1.76 per 10,000 for live-born infants compared to 1.7–5.7 per 10,000 reported by other studies [3, 8–10].

PATHOLOGY OF CDH

The diaphragm is complete by 8 weeks of gestation from its components including the septum transversum and the pleuroperitoneal membranes. In CDH, the defect forms during the embryonic phase of lung development, usually on the left side (85–90%), but can occur on the right or bilaterally and may be associated with other anomalies. The commonest (70%) defect involves the posterolateral (Bochdalek) region of the diaphragm (fig. 1) but the anterior (Morgagni; 25–30%) or central regions (2–5%) can also be affected [11]. Airway generations and terminal bronchioles are markedly decreased, alveolar

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septa are thickened, and there is decreased complexity of the respiratory acinus and alveolar volume [12–15]. Arterial medial wall thickness is increased and peripheral muscularisation of smaller pre-acinar arteries occurs [12, 16, 17]. Overall, the lungs are hypoplastic, with lower than normal DNA and protein content, more so in the ipsilateral than contralateral lung [18].
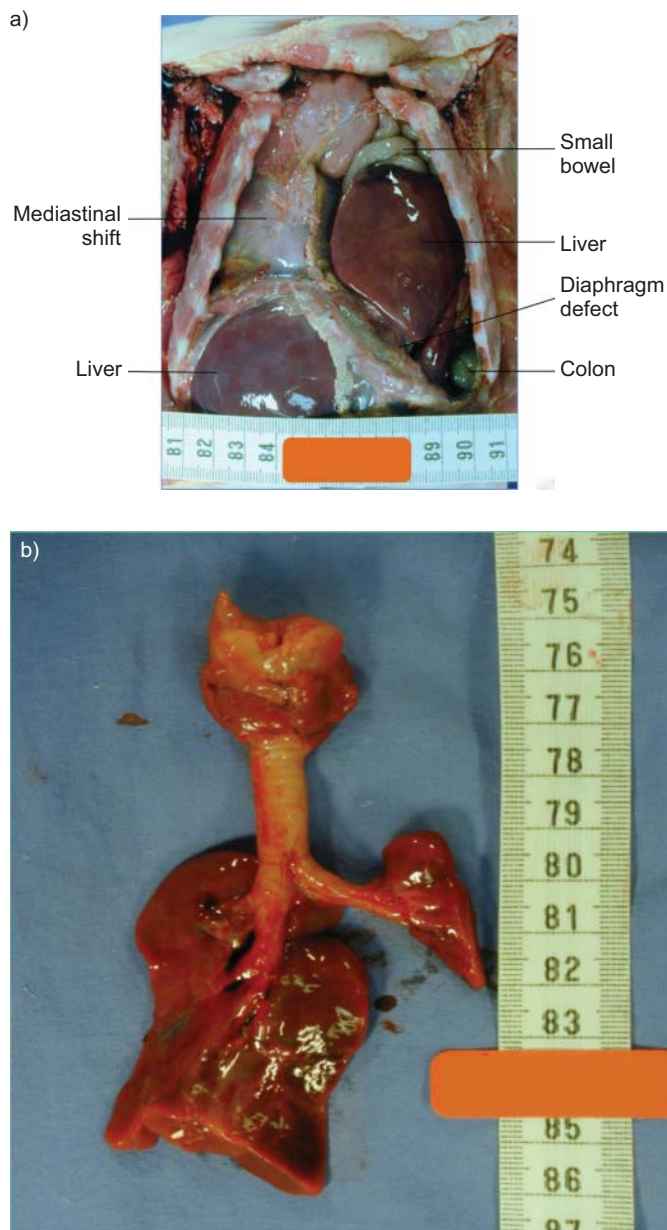

FIGURE 1. a) Only ~0.5 cm of residual diaphragm can be observed, resulting in half of the liver, all of the small bowel, the stomach, spleen and pancreas, a large part of colon, the left adrenal gland, and approximately one-third of the left kidney herniating into the left thoracic cavity. The spleen is in the right chest behind the oesophagus but in front of the aorta. b) A lung weighing 13.43 g compared with a mean±SD expected weight of 40.6±17.1 g. The lung/body ratio was 0.0045 (expected >0.01). Image kindly provided by E. Pollina (King's College Hospital, London, UK).

IMAGING MODALITIES FOR CDH
Antenatal ultrasound scanning for anomalies is routine in most industrialised countries and increasingly identifies congenital anomalies such as CDHs. Magnetic resonance imaging (MRI) is also increasingly used and should be seen to complement ultrasound scanning. Both these imaging modalities are discussed in detail in the online supplementary material. Our recommendations for antenatal management for delivery are summarised in table 1.

Antenatal presentation and imaging characteristics of CDH
Antenatal ultrasound screening identifies >70% of cases of CDH [19, 20]. Intrathoracic abdominal organs are the hallmark of CDH (fig. 2). Left-sided CDH typically presents with a mediastinal shift to the right, caused by herniation of the stomach and intestines. The viscera may show peristalsis and contrast with the more echogenic fetal lung. In right-sided CDH, part of the liver is visible in the chest. Because the liver is echogenic, it may be difficult to differentiate from the lung. Doppler studies of the umbilical vein and hepatic vessels or location of the gall bladder may be used as additional landmarks. MRI is useful to confirm the diagnosis of CDH in cases of equivocal sonographic findings, to characterise the content of the herniated tissues [21]. Diaphragmatic eventration, characterised by defective diaphragmatic muscularisation, can be challenging to differentiate from CDH antenatally. The former shows a cephalic displacement of the diaphragm and is often associated with pleural and/or pericardial effusion [22]. Pathologies associated with CDH include cardiac, renal, central nervous system and gastrointestinal anomalies [23]. Amniocentesis and genetic consultation to screen for chromosomal anomalies are advised [24].

Antenatal management and prognosis of CDH
Ultrasonographic lung size assessment is best undertaken by the use of the observed/expected lung-to-head ratio (LHR; discussed in the online supplementary material) [25]. The LHR predicts survival, with a trend for better prediction at 32–33 weeks rather than 22–23 weeks, and short-term morbidity [26]. Right-sided lesions have worse outcome [27]. Three-dimensional ultrasound and MRI both permit absolute volumetry, but MRI is superior mostly because of better visualisation of the ipsilateral lung [28]. MRI can quantify the extent of liver occupying the thorax [29, 30]. Herniation of the liver is also related to survival, but it remains a matter of debate whether this is an independent predictor [26, 30, 31]. Efforts have been made to document antenatal lung vascular development, but the predictive value is still being validated. Measurements of the number of branches, vessel diameters, flow velocity or volume, and reactivity to maternal oxygen inhalation have been reported [32].

In all cases, delivery should be planned at a tertiary perinatal centre; in those with a poor prognosis (e.g. having other congenital abnormalities), termination of pregnancy may be considered. For isolated CDH, antenatal therapy is an option. In utero anatomical repair improves lung development, but requires open fetal surgery and is not currently offered if there is liver herniation [33]. Alternatively, tracheal occlusion (TO) has been used to promote lung growth [34, 35]. Antenatal TO prevents egress of lung fluid, which increases airway pressure,

TABLE 1	Recommendations for the antenatal management and delivery of congenital diaphragmatic hernia (CDH) infants
Routine antenatal ultrasound scanning for anomalies is essential in industrialised countries	
MRI is useful to confirm the diagnosis of CDH in cases of equivocal ultrasound findings	
Ultrasound lung size assessment is best determined by the use of the observed/expected LHR, which can be used to predict survival	
Herniation of the liver is related to survival, although it is debatable whether it is an independent predictor of survival and, at this stage, should not be used to inform counselling	
Antenatal counselling is essential and should be conducted by a multidisciplinary team	
Genetic consultation and amniocentesis to screen for chromosomal anomalies are advised	
In those with a poor prognosis, *e.g.* fetuses having other congenital abnormalities, termination of pregnancy should be sensitively considered	
Antenatal surgical intervention should be considered in selected cases after discussion with the parents, but going forward, this should be done in the context of randomised trials	
Delivery should be planned, wherever possible, in a tertiary perinatal centre	
Obstetric decisions should guide the mode of delivery	

MRI: magnetic resonance imaging; LHR: lung-to-head ratio.

causing cell proliferation, increased alveolar airspace and maturation of pulmonary vasculature. Sustained TO is deleterious, as it reduces type II cell numbers and surfactant expression. This can be alleviated by *in utero* release, a concept known as the "plug–unplug sequence" [36]. TO is possible by percutaneous fetoscopic endoluminal TO (FETO) *via* a 3.3-mm cannula without general anaesthesia [37]. The FETO consortium has the greatest experience in TO (n=210) [27]. When compared with the predicted survival rate after expectant management, temporary FETO in fetuses with left CDH increased survival from 24% to 49% (left-sided) and from 0% to 35% (right-sided) (both p<0.001) [27]. The procedure may cause premature rupture of membranes (17% within 3 weeks). Changes in lung volume within 2 and 7 days after FETO may be predictive of subsequent survival but the technique is currently being evaluated in a randomised trial.
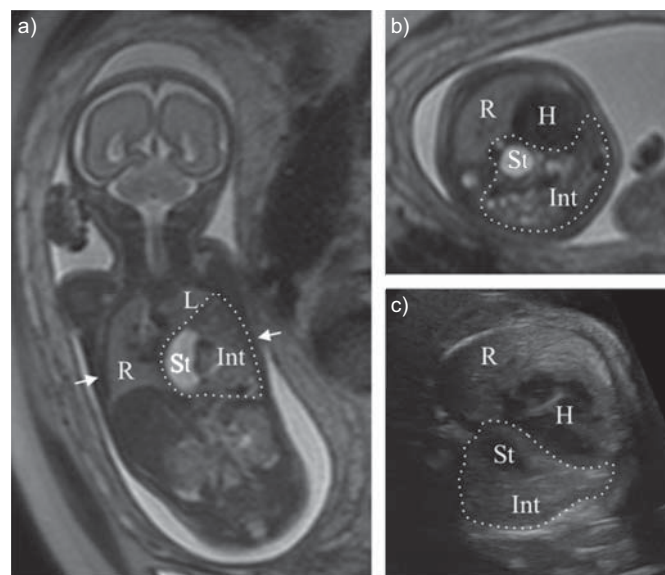

FIGURE 2. a) Coronal and b) axial fetal magnetic resonance images, and c) axial antenatal ultrasound of a left-sided congenital diaphragmatic hernia at gestational age 26 weeks. The level of both axial views is shown on the coronal image (arrows). The herniated tissue is outlined on the images (······). L: left lung; R: right lung; St: stomach; Int: intestines; H: heart.

CLINICAL PRESENTATION OF CDH

Clinical presentation of CDH is discussed in detail elsewhere [10, 38]. Although increasing numbers of affected infants have planned deliveries after diagnosis by antenatal scanning, undiagnosed infants usually present with acute respiratory distress in the neonatal period. Milder forms may present with later mild respiratory or gastrointestinal symptoms. Sudden onset of respiratory distress may occur later in life due to small defects.

INVESTIGATIONS FOR CDH

A chest radiograph should be performed. In infants with CDH, this will demonstrate an opacified hemithorax with a contralateral shift of the mediastinum. Bowel gas may be seen in the chest. The oesophageal portion of the nasogastric tube is deviated to the right in infants with left-sided CDH and to the left if the lesion is on the right [39]. Introduction of a radio-opaque contrast medium into the stomach and proximal gastrointestinal tract can help to distinguish between a CDH and a congenital thoracic malformation such as congenital cystic adenomatoid malformation.

Echocardiography should be undertaken to exclude congenital cardiac lesions in infants with CDH and in any infant in whom pulmonary hypertension is suspected. It is important to determine right ventricular function, as the ability of the right ventricle to function under increased afterload is an important determinant of illness severity [40].

POST-NATAL MANAGEMENT OF CDH

Venue and timing of delivery

Infants with CDH should be delivered in the hospital at which they will undergo surgical intervention. Analysis of the outcomes of 2,140 infants demonstrated infants transported for repair had a higher mortality and need for extracorporeal membrane oxygenation (ECMO) [41]. Analysis of data from 628 term infants from the CDH Study Group registry demonstrated early-term delivery by elective Caesarean section (37–38 *versus* 39–41 weeks) was associated with less use of ECMO and a trend towards greater survival later [42]. The CDH Study Group, however, found that the mode of delivery for 548 infants with CDH did not affect survival, although vaginal delivery was associated with higher use of ECMO [43], suggesting that obstetric decisions should guide mode of delivery.

Labour ward management

Infants with CDH should be immediately intubated and ventilated, and peak inspiratory pressures <25 cmH_2O employed. Face-mask and T-piece or bag and mask resuscitation should not be used, as this can cause distension of the herniated bowel, increasing respiratory embarrassment. A large-bore nasogastric tube (*e.g.* French gauge 8) should be sited to decompress the stomach and small bowel. Some advocate use of neuromuscular blocking agents to prevent swallowing and further gas distending the bowel.

MANAGEMENT IN THE NEONATAL UNIT

Standardised protocols have recently been published [44, 45] for the post-natal management of CDH with most recommending gentle ventilation and aggressive treatment of pulmonary hypertension. Both TRACY *et al.* [45] and VAN DEN HOUT *et al.* [1] have claimed improvements after introduction of standardised protocols, but their comparisons were with historical controls; thus, it is unclear whether the improvements are due to the introduction of the protocols or advances in medical care. Nevertheless, standardised protocols do ensure focus on essential aspects of management of CDH; thus, we have based our recommendations on a consensus statement (table 2) [44]. It is important to emphasise that there have been few randomised trials evaluating the management of infants with CDH and multicentre international trials are urgently required to optimise the post-natal management of CDH infants.

Respiratory support

The best outcomes for CDH infants are achieved by early medical stabilisation and delay of surgical repair until optimisation has occurred [46]. Gentle ventilation, *i.e.* avoidance of high pressures (peak pressure <25 cmH_2O and peak end-expiratory pressure <5 cmH_2O [47]) and accepting higher levels of arterial carbon dioxide tension (P_{a,CO_2}) (permissive hypercapnia up to a P_{a,CO_2} of 60–65 mmHg [48]), is preferred [49]. More than 90% of the International CDH Registry centres aimed to minimise lung injury by limiting the peak airway pressure and allowing permissive hypercapnia, rather than aiming for a low P_{a,CO_2} to reduce pulmonary vascular resistance [50]. Some centres routinely use neuromuscular blocking agents, whereas others avoid them [51], as muscle paralysis may have an adverse effect on ventilation [49]. Indications for alternative forms of support (high-frequency oscillation ventilation (HFOV), inhaled nitric oxide (iNO) and ECMO) are a pH of <7.25, P_{a,CO_2} >60 mmHg and preductal oxygen saturation less than 80–85% with an inspired oxygen concentration of 60% [52]. There is an ongoing multicentre randomised study (CDH-EURO Consortium) assessing whether elective HFOV improves survival and/or has other benefits (www.vicitrial.com); the results will be very welcome to inform the choice of respiratory support.

Analysis of data from 6,147 neonates from the Extracorporeal Life Support Organisation database (1991–2010) demonstrated an overall mortality rate of 49% for CDH infants supported by ECMO [53]. The short-term outcomes of veno-arterial and veno-venous ECMO were similar [53]. In a UK collaborative ECMO trial, there were no significant differences in survival, but only a small number of patients were recruited [54]. Meta-analysis of three randomised controlled trials (RCTs) (only 39 infants in total) indicated a reduction in early mortality with ECMO, but no long-term benefits [55]. Prediction scores may be useful to identify those at very high risk of mortality amongst infants managed with ECMO [56]. Survival appears higher if surgical repair is after ECMO, rather than when the infant is on ECMO

TABLE 2	Post-natal recommendations for the management of congenital diaphragmatic hernia (CDH) based on the consensus statement of the CDH-EURO consortium [44]
Treatment in the delivery room	No resuscitation delivered by bag and mask
	Immediate intubation
	$P_{I,max}$ <25 cmH_2O
	Nasogastric tube
Treatment in the NICU	Adapt ventilation to obtain preductal saturation between 85 and 95%
	pH >7.20, lactate 3–5 $mmol \cdot L^{-1}$
	CMV or HFOV, maximum $P_{I,max}$ 25–28 cmH_2O in CMV and $\bar{P}_{aw}$ 17 cmH_2O in HFOV
	Targeting blood pressure: normal value for gestational age
	Consider inotropic support
Pulmonary hypertension	Perform echocardiograhy
	iNO but stop if no response
	In the chronic phase: phosphodiesterase inhibitors, endothelin antagonists, tyrosine kinase inhibitors
ECMO indications	Inability to maintain preductal saturation >85%
	Respiratory acidosis
	Inadequate oxygen delivery (lactate >5 $mmol \cdot L^{-1}$)
Timing of surgical repair	F_{I,O_2} <0.5
	Mean blood pressure normal for gestational age
	Urine output >2 $mL \cdot kg^{-1} \cdot h^{-1}$
	No signs of PH

$P_{I,max}$: peak inspiratory pressure; NICU: neonatal intensive care unit; CMV: conventional mechanical ventilation; HFOV: high-frequency oscillation ventilation; $\bar{P}_{aw}$: mean airway pressure; iNO: inhaled nitric oxide; ECMO: extracorporeal membrane oxygenation; F_{I,O_2}: inspiratory oxygen fraction; PH: pulmonary hypertension.

[57]. Opinions differ as to whether ECMO has superior outcomes than established optimal medical management.

There is debate over whether CDH infants have evidence of surfactant insufficiency [58]. Analysis of data from the CDH Study Group failed to highlight any significant benefits of surfactant administration in >500 neonates [59].

Blood pressure support

Arterial blood pressure levels should be maintained at levels that are normal for the patient's gestational age, but if there is evidence of pulmonary hypertension, the arterial blood pressure in term-born infants should be maintained at higher levels (*i.e.* $\geqslant$50 mmHg). Echocardiography should be undertaken to determine whether volume expansion is appropriate. There are no RCTs to determine which inotropes are the most effective in infants with CDH.

Treatment of pulmonary hypertension

Pulmonary hypertension is common in infants with CDH [60]. The severity of pulmonary hypertension predicts the outcome, nonsurvivors in one series [60] having persistent systemic or suprasystemic pressures unresponsive to therapy for >3 weeks after birth. iNO improves oxygenation in up to 50% of cases [52], but the effect may be transitory and use of iNO does not influence overall outcome. No effect on mortality was seen with iNO administration in two randomised studies (rate ratio (RR) 1.20, 95% CI 0.74–1.96) [61, 62] and there was a slight increase in the requirement of ECMO (RR 1.27, 95% CI 1.00–1.92) [63]. Sildenafil, a phosphodiesterase type 5 inhibitor, has been used to improve oxygenation and cardiac output by reducing pulmonary hypertension refractory to iNO [64, 65]. It may also prevent rebound pulmonary hypertension during weaning of iNO [66]. There are only case reports of other therapies, such as endothelin antagonists and tyrosine kinase inhibitors, for pulmonary hypertension [49], and these clearly need further evaluation.

SURGICAL MANAGEMENT OF CDH

Surgical closure of the diaphragmatic defect is generally an uncomplicated procedure. Nevertheless there are some issues that are controversial. These include the timing of surgery, the nature of the repair (prosthetic patch *versus* primary repair), the need for abdominal closure and the merits of a minimally invasive approach.

Timing of surgery

The only two prospective randomised trials and one systematic review of early or delayed closure have failed to show a statistically significant difference in mortality and secondary variables (such as length of hospital stay, need for ECMO and duration of respiratory support) [67–69].

There are no universal criteria to define pre-operative stabilisation and this can occur with minimal delay in some patients, yet extend to many days in others [70]. While scientific evidence is lacking, it seems reasonable to delay surgery until medical stability has been achieved. Most surgeons now follow this protocol, as shown by the survey of 461 infants from the CDH Study Group [71]. More recent data have confirmed this trend (table 3) [72].

TABLE 3	Number of patients whose diaphragmatic defect was repaired within different time intervals after birth
	Patients n
0–24 h	185
24–48 h	376
>48 h	2607
No repair	685
Incomplete data	10
Total	3863

From January 1, 2000 to December 31, 2009, 3,863 patients were entered into the registry. 685 of these were never repaired. Data from [72].

No consensus exists on when patients being stabilised on ECMO should be operated on. Some centres prefer to decannulate the patient before surgical repair, while others prefer to repair the diaphragm early or late in the ECMO course.

Surgical technique

The standard surgical approach to repair the diaphragmatic defect consists of a subcostal incision with removal of the herniated abdominal viscera from the thorax and complete exposure of the defect. A true hernia sac is sometimes observed (<20% of cases) and, if present, should be excised. Closure of the defect can be accomplished primarily using nonabsorbable sutures or by means of a prosthetic patch (*e.g.* GORE-TEX® (W.L. Gore & Associates, Newark, DE, USA), Marlex® (Phillips Petroleum Co., Bartlesville, OK, USA) or Permacol® (Covidien Surgical, Dublin, Ireland)) if the defect is large [70, 73]. Because synthetic material lacks the capacity for growth, hernia recurrence may reach up to 50% in some series [71]. Alternatively, muscle flaps have been used or a tissue-engineered diaphragm substitute has been proposed to close very large defects or even complete agenesis of the diaphragm [74, 75]. Little attention has been paid to the size of the prosthetic patch when performing a patch repair. A large, dome-shaped patch bulging into the thorax, compared with a small, flat patch, has the theoretical advantages of increasing the abdominal volume and decreasing the risk of patch dehiscence when the child grows. However, this question has not been evaluated scientifically. Up to half of those operated on for CDH will need a patch repair (table 4).

TABLE 4	Number of patients with primary *versus* patch repair
	Patients n
Primary repair	1562
Patch repair	1598
No repair	685
Incomplete data	18
Total	3863

From January 1, 2000 to December 31, 2009, 3,863 patients were entered into the registry. 685 of these were never repaired. Data from [72].

Closure of the abdominal wall may compromise ventilation and haemodynamic stability due to the small size of the abdominal cavity. In such circumstances, coverage of the abdominal viscera may be achieved by: skin closure, leaving a fascial defect; interposition of a prosthetic patch between the fascial edges; or creation of a surgical silo (table 5). A chest tube is not usually used, the rationale being to encourage the lung to enlarge gradually, displacing fluid and air, rather than forcefully due to a negative suction pressure applied through a thoracostomy drain [73, 76].

Neonates repaired on ECMO will almost invariably need a patch repair, as there is a strong correlation between the severity of the disease and the size of the defect [77]. These patients pose some specific problems related to bleeding. Careful inspection of the operative field and meticulous haemostasis should be performed at the end of the surgical procedure. Fibrin sealants or even the use ε-aminocaproic acid have been recommended in this setting [76]. However, in one of the author's (B. Frenckner) experience, the use of ε-aminocaproic acid has led to serious clotting in the ECMO circuit in several instances. Successful repair without bleeding complications was instead achieved in 34 out of the 36 infants recently repaired on ECMO by meticulous surgical haemostasis in combination with fibrin glue in the operating field (unpublished data).

Surgical repair can be accomplished by minimally invasive techniques, although the latent cardiopulmonary instability of such neonates has made some surgeons hesitate in using this approach. Certainly, hypercarbia and acidosis are almost invariable using carbon dioxide insufflation. Nevertheless, recent reports have shown the feasibility and safety of this approach even in unselected groups of patients [78–80]. It also seems that, in contrast to the open technique, where the abdominal approach is standard, thoracoscopic repair is somewhat easier. The role of minimally invasive surgery remains to be further defined and formally evaluated.

LONG-TERM PROGNOSIS OF CDH
Infancy
Lung and vascular developmental abnormalities associated with CDH are the primary causes of morbidity and mortality in infants, which may be compounded by the secondary effects of post-natal management including hyperoxic, high-pressure mechanical ventilation. Prematurity is associated with worse

TABLE 5	Number of patients with primary closure of the abdominal wall *versus* some type of secondary closure
	Patients n
Primary closure	2595
Silo, patch, *etc.*	371
No repair	685
Incomplete data	212
Total	3863

From January 1, 2000 to December 31, 2009, 3,863 patients were entered into the registry. 685 of these were never repaired. Data from [72].

prognosis [81]. Lung hypoplasia, due to impairment of both airway branching and alveolarisation, results in markedly decreased alveolar surface area [82].

Significant advances in the post-natal management of patients with CDH have resulted in improved survival rates over the past two decades [46]. Nevertheless, most series still reported overall post-natal survival in isolated CDH around 60–70%, although some survival rates of >90% have recently been reported [83, 84]. A significant survival advantage has been suggested for infants with CDH treated in high-volume centres [85]. However, survival estimates derived from institutional or unit-based data lend themselves to multiple biases. A recent careful evaluation of survival variables comparing all institution and population data from the province of Ontario, Canada, demonstrated a clear discrepancy in institution-based reporting [86, 87]. The number of deaths reported by the institutions was found to be 32% less than that of the population data.

Late-presenting CDHs represent <3% of cases [88]. Diagnosis may be at school age, with respiratory or gastrointestinal presenting symptoms. The prognosis is excellent.

The American Academy of Pediatrics has suggested follow-up guidelines for survivors of CDH after discharge [89]. These patients have a high incidence of respiratory, nutritional, musculoskeletal, neurological and gastrointestinal morbidities [46, 90–92]. Furthermore, the recent improved survival of very sick babies is associated with increased, particularly pulmonary, morbidity among survivors [2, 46] persisting beyond the initial hospitalisation, especially in those treated with ECMO [93, 94]. SPOEL *et al.* [95] recently observed that mean maximal expiratory flows at functional residual capacity (FRC) were significantly lower than predicted values at 6 and 12 months of age in CDH survivors. Furthermore, FRC measured by plethysmography was increased especially in those patients who had received ECMO. Oxygen dependency is also common, with 50% being oxygen dependent at 28 days of age [1] and 16% requiring oxygen at the time of discharge for a mean duration of 14.5 months [93]. Up to 2% remained oxygen dependent at 2 yrs of age [94]. Bronchodilators may be needed in 40% of patients in the first year of life [93]. Angiogenesis remains defective in hypoplastic lungs [96]. Pulmonary hypertension may persist in up to 30% of patients at 2 months of age [97] and is associated with increased risk for early death [94, 97]. Pulmonary artery hypoplasia or stenosis, and pulmonary vein stenosis or delayed venous return may contribute to persistent pulmonary hypertension [98].

Childhood
Several follow-up studies have explored long-term pulmonary morbidity (table 6). These studies report catch-up of lung volumes [99–101, 103–105]. In contrast, perfusion studies have demonstrated persistent perfusion defects in the ipsilateral lung [103–105]. Reduced airflows and poor response to bronchodilator inhalation [101, 102, 105, 106] suggest increases in lung volume occur by distension rather than by alveolar number. The few lung morphometric studies following CDH repair [107, 108] all found persistent decreases in airway, alveolar and arterial numbers in both lungs, the ipsilateral lung being most affected. Nevertheless, studies evaluating the

TABLE 6	Long-term outcomes of congenital diaphragmatic hernia	
Feature	**Outcome**	**[Ref.]**
Thoracic scoliosis	~8%	[99]
Pectus excavatum	4–21%	[99, 100]
Mean TLC	89–101% pred	[99–101]
	0.16 Z-score	[102]
Mean FEV1	79–90% pred	[99–101]
	-1.45 Z-score	[102]
Mean perfusion ratio of the affected side	53–67%	[103–105]
Mean volume ratio of the affected side	82–88%	[103–105]
Wheezing ever	17–37%	[100, 101]
$V'_{O_2,max}$	95–100% control	[100, 102]

TLC: total lung capacity; FEV1: forced expiratory volume in 1 s; $V'_{O_2,max}$: maximal oxygen uptake; % pred: % predicted.

diffusion capacity of the lung for carbon monoxide and exercise capacity have found normal values when compared with controls [100–102, 106].

Because CDH is associated with long-term morbidities that affect quality of life, survival alone is no longer a sufficient parameter for successful treatment of children with CDH. Long-term follow-up by a multidisciplinary team is recommended for these children [89, 109], to detect and treat both pulmonary morbidities and other comorbidities.

CONCLUSIONS

CDH remains a challenging condition for optimal management and for optimal outcomes. Despite recent improvements in survival, the management, both ante- and post-natally, remains to be optimised, including the role of antenatal interventional management such as FETO. After birth, innovations have been made in treating both respiratory failure and pulmonary hypertension but robust assessment of newer therapies is necessary. As survival improves, further studies are required to ensure that the survivors have a high quality of life after discharge, which can only occur with regular follow-up by a multidisciplinary team.

STATEMENT OF INTEREST
A statement of interest for A. Greenough can be found at www.erj.ersjournals.com/site/misc/statements.xhtml

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