NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of thoracoscopic repair of congenital diaphragmatic hernia in neonates

Treating hernia of the diaphragm in newborn babies with keyhole surgery through the chest

Congenital diaphragmatic hernia is a life-threatening condition caused by failure of the diaphragm to form properly during a baby's development in the womb. This results in the baby's abdominal organs moving up into the chest cavity, compressing its lungs and heart. In thoracoscopic repair, small incisions are made in the chest to insert surgical instruments, which are then used to move the abdominal organs out of the chest and repair the diaphragm.

Introduction

The National Institute for Health and Clinical Excellence (NICE) has prepared this overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in September 2010.

Procedure name

- Thoracoscopic repair of congenital diaphragmatic hernia in neonates

Specialty societies

- British Association of Paediatric Endoscopic Surgeons
- British Association of Paediatric Surgeons.

Description

Indications and current treatment

Congenital diaphragmatic hernia (CDH) results from failure of complete fusion of the developing fetal diaphragm – a process that normally occurrs between gestational weeks 6–8. The defect may be anterior (Morgagni's hernia) or posterolateral (Bochdalek hernia). Migration of abdominal organs into the thoracic cavity, pulmonary hypoplasia and respiratory failure at birth can occur.

Current standard management of CDH in newborn babies usually involves initial ventilatory support and supportive care, to allow labile cardiopulmonary physiology to improve. This is followed by surgical reduction of the hernia, usually through an abdominal approach, and repair of the diaphragmatic defect.

What the procedure involves

The procedure aims to surgically reduce the herniated abdominal organs and repair the diaphragmatric defect, but with less postoperative morbidity and shorter hospitalisation compared with open approaches. It is normally carried out for posterolateral Bochdalek defects. Thoracoscopic CDH repair can allow hernia reduction with no or less surgical manipulation, as the positive intrathoracic pressure exerted by insufflated CO_2 could push herniated organs into the abdomen. However, there are theoretical concerns about the adequacy of ventilatory support (because of the partial lung compression that is usually required) and the development of hypercapnia (because of CO_2 absorption) during the thoracoscopic procedure. In addition, it is not possible to thoracoscopically repair intestinal malrotation, which is sometimes present concomitantly.

Thoracoscopic congenital diaphragmatic hernia is performed with the patient under general anaesthesia and in the lateral decubitus position. Between 2 and 4 trocars can be used, with CO_2 insufflation of the pleural space to partially collapse the lung sufficiently to achieve good exposure of the defect and to recuce the herniated viscera within the abdomen. Following the reduction of the herniated content, the diaphragm is repaired using non-absorbable interrupted sutures (for small defects) or patches (if defects are relatively large). Where technically possible, posterolateral diaphragm stitches are passed around the posterolateral ribs and tied extracorporeally. Patients usually require temporary chest drain insertion and ventilatory support.

Although diaphragmatic hernia repair can be performed later in life, depending on the clinical presentation, this overview is only concerned with the repair of symptomatic congenital diaphragmatic hernias in neonates.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to thoracoscopic repair of congenital diaphragmatic hernia in neonates. Searches were conducted of the following databases, covering the period from their commencement to 18 March 2010 and updated 30 September 2010: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Newborn patients with congenital diaphragmatic hernia.
Intervention/test	Thoracoscopic repair.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on 328 patients from 1 meta-analysis[1], 6 non-randomised comparative studies[2,3,4,5,6,7] and 3 case series[8,9,10]. Patients aged over 12 months at the time of hernia repair were excluded from this overview.

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on thoracoscopic repair of congenital diaphragmatic hernia in neonates

Abbreviations used: CDH, congenital diaphragmatic hernia; CI, confidence interval; ECMO, extracorporeal membrane oxygenation; $EtCO_2$, end-tidal carbon dioxide level; N/A, not applicable; NR, not reported; ; NS, not significant; $PaCO_2$, partial pressure of carbon dioxide in the blood; PIP, peak inspiratory pressure; PRISMA, Preferred reporting items for systematic reviews and meta-analyses; VATS, video-assisted thoracic surgery

Study details	Key efficacy findings	Key safety findings	Comments
Lansdale N (2010)[1] **Meta-analysis of non-randomised comparative studies** International Recruitment period: studies up to 1 October 2009 Includes: Cho 2009, Giacomello 2009 (unpublished) and Gourlay 2009 (all non-randomised comparative studies) Study population: neonatal patients with CDH n = **143 (62 vs 81) [3 studies]** Age: neonates Sex: not reported Patient selection criteria: studies selected if they directly compared open and endosurgical CDH repair in the newborn infant and included date regarding survival, CDH recurrence, prosthetic patch use and operative time. Studies excluded if patients operated on outside the neonatal period or did not provide sufficient demographic or outcome data. No language or publication date exclusions. Technique: thoracoscopic repair vs open repair Follow-up: **not reported** Conflict of interest/source of funding: one author has a – Wellcome Trust Research Training Clinical Fellowship.	Number of patients analysed: **143 (62 vs 81)** [3 studies] <u>Recurrence (3 studies):</u> Thoracscopic group: 16.1% (10/62) Open group: 4.9% (4/81) Risk ratio: 3.21 (95% CI 1.11 to 9.29) This indicates significantly higher risk of recurrence in the thoracoscopic group. No evidence of heterogeneity in the results. <u>Patch usage (3 studies):</u> Thoracscopic group: 40.3% (25/62) Open group: 51.9% (42/81) Risk ratio: 1.01 (95% CI 10.01 (0.67 to 1.50) This indicates no significant difference in patch useage between the thoracoscopic and open groups (risk ratio includes 1). Some evidence of heterogeneity in the results (I^2 = 41%). However, heterogeneity only considered to be of significance if $I^2 \geq 50\%$. <u>Operative time (3 studies):</u> Thoracoscopic group: 176.1 minutes (mean) Open group: 126.4 minutes (mean) Weighted mean difference: 50.38 minutes (95% CI 31.79 to 68.97 minutes) This indicates a significantly longer operative time in the thoracoscopic group. No evidence of heterogeneity in the results.	<u>Mortality (3 studies):</u> Thoracscopic group: 3.2% (2/62) Open group: 12.3% (10/81) Risk ratio: 0.33 (95% CI 0.01 to 1.13) This indicates no statistically significant difference in risk of death between the groups (risk ratio includes 1). No evidence of heterogeneity in the results Other adverse events are not reported in this paper.	**Follow-up issues**: • Completeness of follow-up is not reported. • The duration of follow-up was longer in the open group in all 3 studies. **Study design issues**: • Thorough search (includes Medline, Embase and Cochrane Cotrolled Trials Register). • 2 independent reviewers assessed all abstracts. • Includes unpublished data – quality is uncertain. • Authors report on the limitation of the meta-analysis due to lack of double-blind randomised controlled trials. Each outcome could be affected by bias due to study design. • Intention to treat analysis. • Reported in accordance with preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines. **Study population issues**: • No statistically significant differences in proportion of males, mean birth weight, proportion of left-sided CDH, or proportion of cases with significant associated anomalies between thoracoscopic and open groups.

Abbreviations used: CDH, congenital diaphragmatic hernia; CI, confidence interval; ECMO, extracorporeal membrane oxygenation; $EtCO_2$, end-tidal carbon dioxide level; N/A, not applicable; NR, not reported; ; NS, not significant; $PaCO_2$, partial pressure of carbon dioxide in the blood; PIP, peak inspiratory pressure; PRISMA, Preferred reporting items for systematic reviews and meta-analyses; VATS, video-assisted thoracic surgery

Study details

Cho SD (2009)[2]

Non-randomised comparative study

USA

Recruitment period: thoracoscopic group: 2004–2007, open group: 2001–2004
Study population: neonatal patients with CDH of Bochdalek

n = **57 (29 vs 28)**

Age: all patients underwent repair within the first 30 days of life
Sex: thoracoscopic group: 48.3% (14/29) female, open group: 42.9% (12/28) female
Patient selection criteria: see above

Technique: thoracoscopic repair (CO_2 insufflation to 3 mmHg, defects closed with either Gore-Tex® patch or mesh hernia plugs) vs open repair of CDH (defect closed with either permanent suture or Gore-Tex® patch). The open technique is not clearly described.

Follow-up: **thoracoscopic group: 11.2 months (mean), open group: 8.1 months (mean)**

Conflict of interest/source of funding: not reported.

Key efficacy findings

Number of patients analysed: **57 (29 vs 28)**

	Thoracoscopic group (n = 29)	Open group (n = 28)	p value
Recurrence	20.7% (6/29)	7.1% (2/28)	0.25
Additional subsequent related operative procedures	34.5% (10/29)	42.9% (12/28)	0.59
Use of prosthetic patch	51.7% (15/29)	42.8% (12/28)	0.60
Median length of operating time (minutes)	179.8±1.6	116.5±7.8	<0.001
Median length of postoperative ventilator time (days)	5	5	0.56
Median postoperative time to feed (days)	6	6	0.85
Median length of stay (days)	34	24	0.11

Conversion to open procedure in the thoracoscopic group: 3.4% (1/29) due to inability to reduce the liver into the abdomen thoracoscopically.

[Chest radiographs at 2 weeks, 1 month and every 3–6 months until aged 2 years and selectively thereafter although authors do not explicitly report a successful repair rate in each group]

Key safety findings

Timing and treatment of complications is not reported unless other wise stated

	Thoracoscopic group (n = 29)	Open group (n = 28)	p value
Postoperative mortality	6.9% (2/29)	21.4% (6/28)	0.14
Any complication	55.2% (16/29)	71.5% (20/28)	0.28
Postoperative bleeding	6.9% (2/29)	14.3% (4/28)	0.42
Major infection (abscess, systemic sepsis or abdominal wall patch infection)	17.2% (5/29)	3.6% (1/28)	0.19
Wound infection	6.9% (2/29)	0	N/A
Pleural effusion / chylothorax	10.3% (2/29)	10.7% (3/28)	N/A
Pneumothorax / air leak	6.9% (2/29)	7.1% (2/28)	N/A
Bowel obstruction	6.9% (2/29)	10.7% (3/28)	N/A
Gastrointestinal perforation	6.9% (2/29)	7.1% (2/28)	N/A
Solid organ laceration	0	7.1% (2/28)	N/A
Silo creation (that is, repair patch herniates into thoracic cavity)	6.9% (2/29)	0	N/A
Other	6.9% (2/29)	10.7% (3/28)	N/A

Comments

This paper is included in Lansdale 2010

Follow-up issues:
- Complete follow-up in 100% thoracoscopic group and 64% open group ($p < 0.01$).
- An additional 15 infants with CDH died before any corrective procedure could be preformed.

Study design issues:
- Prospective thoracoscopic cohort compared with a historical open cohort of patients.
- Single site study.

Study population issues:
- Demographic characteristics similar between the two groups.
- ECMO used more frequently in the open group ($p < 0.04$).

Other issues:
- 'Other' complications include one case of superior vena cava thrombosis, 2 seizures, 1 early gastroesophageal reflux and 1 malpositioned enteral feeding tube.
- All recurrences in the thoracoscopic group were successfully treated with laparoscopic / thoracoscopic repair. Patient had a second recurrence.

Abbreviations used: CDH, congenital diaphragmatic hernia; CI, confidence interval; ECMO, extracorporeal membrane oxygenation; $EtCO_2$, end-tidal carbon dioxide level; N/A, not applicable; NR, not reported; ; NS, not significant; $PaCO_2$, partial pressure of carbon dioxide in the blood; PIP, peak inspiratory pressure; PRISMA, Preferred reporting items for systematic reviews and meta-analyses; VATS, video-assisted thoracic surgery

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>McHoney M (2010)[3]

Non-randomised comparative study

UK

Recruitment period: thoracoscopic group: 2007–2008, open group: 2003–2008
Study population: patients with CDH

n = 48 (13 vs 35)

Age: thoracoscopic group: 12.5 days (median), open group: 11.7 days (median)
Sex: not reported

Patient selection criteria: patients who did not have antenatal diagnosis of CDH or respiratory distress at birth (late diagnosis) and patients with Morgagni hernia were excluded.

Technique: thoracoscopic repair (using upper transverse abdominal incision, CO_2 insufflation at 5–8 mmHg) vs open repair of CDH. No patient received inhaled nitric oxide at time of procedure. Interrupted non-absorbable sutures or Dacron patch used to close the defect in both procedures.

Follow-up: thoracoscopic group: 15 months (median), open abdominal repair group:</td>
<td>Number of patients analysed: 48 (13 vs 35)

Conversion to open procedure in the thoracoscopic group: 38.5% (5/13). Reasons:
• 4 due to surgical difficulties
• 1 due to intraoperative O_2 desaturation

2 of the patients who converted to the open procedure also had a Ladd procedure for intestinal malrotation performed adjunctively. 5 patients in the open abdominal repair group also had an adjunctive Ladd procedure.

<table>
<tr><th></th><th>Thoracoscopic group (n = 13)</th><th>Open abdominal group (n = 35)</th><th>p value</th></tr>
<tr><td>Recurrence*</td><td>25% (2/8) [1 occurred after patch repair]</td><td>7.5% (3/40) [1 occurred after patch repair]</td><td>0.19</td></tr>
<tr><td>Patch repair used</td><td>46.2% (6/13)</td><td>34.3% (12/35)</td><td>NR</td></tr>
<tr><td>Mean duration of procedure excluding anaesthesia (hours)</td><td>3.3 ± 0.4</td><td>2.0 ± 0.1</td><td><0.01</td></tr>
</table>
* Recurrence is presented by type of procedure used to complete the repair.

Intraoperative ventilation/oxygenation measures:</td>
<td>Presumed adhesive intestinal obstruction (at mean 3 months):
Thoracoscopic group: none
Open group: 3 patients (unclear if this included people who converted to open procedure)

Postoperative mortality is not reported

Timing and treatment of complications is not reported unless other wise stated</td>
<td>This paper is included in Lansdale 2010 (same patients as Giacomello 2009 [unpublished paper])

Follow-up issues:
• Completeness of follow-up is not reported.

Study design issues:
• Retrospective comparative study of 2 historical cohorts.
• Single site study (Great Ormond Street Hospital).
• No report of chest X-ray or clinical examination follow-up to confirm success of procedure.

Study population issues:
• Patients in the thoracoscopic group were significantly heavier than patients in the open group (4.2 kg vs 3.6 kg, p = 0.05). Use of preoperative ECMO, age proportion with major cardiac defects and inotropic use at operation were similar between the two groups.</td>
</tr>
</table>

Abbreviations used: CDH, congenital diaphragmatic hernia; CI, confidence interval; ECMO, extracorporeal membrane oxygenation; $EtCO_2$, end-tidal carbon dioxide level; N/A, not applicable; NR, not reported; ; NS, not significant; $PaCO_2$, partial pressure of carbon dioxide in the blood; PIP, peak inspiratory pressure; PRISMA, Preferred reporting items for systematic reviews and meta-analyses; VATS, video-assisted thoracic surgery

Study details	Key efficacy findings	Key safety findings	Comments
31 months (median). Conflict of interest/source of funding: supported by the Mittal Foundation	See table below		

	Thoracoscopic group (n = 13)	Open abdominal group (n = 35)	p value
Intra-operative mean maximum $EtCO_2$ (kPa)	8.38 ± 0.3	6.55 ± 0.49	0.003
Intra-operative mean $EtCO_2$ (kPa)	7.05 ± 0.48	5.67 ± 0.23	0.006
Intra-operative lowest pH	7.16 ± 0.06	7.14 ± 0.03	0.89
Intra-operative mean pH	7.21 ± 0.04	7.2 ± 0.03	0.66
Intra-operative mean maximum $PaCO_2$ (kPa)	10.53 ± 1.16	10.94 ± 0.07	0.65
Intra-operative mean $PaCO_2$ (kPa)	9.94 ± 0.97	9.76 ± 0.57	0.88

Abbreviations used: CDH, congenital diaphragmatic hernia; CI, confidence interval; ECMO, extracorporeal membrane oxygenation; $EtCO_2$, end-tidal carbon dioxide level; N/A, not applicable; NR, not reported; ; NS, not significant; $PaCO_2$, partial pressure of carbon dioxide in the blood; PIP, peak inspiratory pressure; PRISMA, Preferred reporting items for systematic reviews and meta-analyses; VATS, video-assisted thoracic surgery

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Gourlay DM (2009)[4]

Non-randomised comparative study

USA

Recruitment period: thoracoscopic group: 2004–2007, open group: 1999–2003

Study population: neonates (age <30 days) with CDH

n = 73 (33 vs 40)

Age: neonates (all except one patient admitted at birth, the other at 28 days)

Sex: not reported

Patient selection criteria: no predetermined inclusion / exclusion criteria

Technique: thoracoscopic repair vs open repair of CDH

Follow-up: thoracoscopic group: 14.5 months (median), open (laparotomy) group: 37 months (median)</td>
<td>Overall success rate for hernia repair for all patients treated during study period in the thoracoscopic group:30.6% (20/33)

Number of patients analysed: 38 (20 vs 18)

<table>
<tr><th></th><th>Thoracoscopic group (n = 20)</th><th>Open (laparotoy) group (n = 18)</th><th>p value</th></tr>
<tr><td>Recurrence</td><td>1</td><td>0</td><td>NR</td></tr>
<tr><td>Patch repair used</td><td>20%</td><td>44%</td><td>0.11</td></tr>
<tr><td>Incorporated a rib in the repair</td><td>55%</td><td>39%</td><td>0.32</td></tr>
<tr><td>Mean operative time (mins)</td><td>163.8</td><td>117.4</td><td>0.01</td></tr>
<tr><td>Median number of postoperative days on ventilator</td><td>2</td><td>4</td><td>0.04</td></tr>
<tr><td>Median postoperative days requiring narcotics</td><td>5</td><td>7</td><td>0.08</td></tr>
<tr><td>Median postoperative days until tolerating full enteral feeds</td><td>8</td><td>14</td><td>0.006</td></tr>
<tr><td>Median total length of stay (days)</td><td>21</td><td>26</td><td>0.23</td></tr>
</table>

Authors also report that an additional patient in the thoracoscopic group was converted to the open procedure because the patient was unable to tolerate</td>
<td>
<table>
<tr><th></th><th>Thoracoscopic group</th><th>Open group</th></tr>
<tr><td>Death</td><td>0</td><td>1 (haemorrhage)</td></tr>
<tr><td>Complication rate</td><td>20%</td><td>27%</td></tr>
<tr><td>Minor wound infections requiring only reopening the wound</td><td>2</td><td>0</td></tr>
<tr><td>Bowel obstruction requiring laparotomy</td><td>1</td><td>3 (also required enterolysis)</td></tr>
<tr><td>Ladd procedure for intolerance to feeds</td><td>1</td><td>2 (combined with laparotomy)</td></tr>
<tr><td>Line sepsis requiring IV antibiotics and prolonged hospitalisation</td><td>0</td><td>2</td></tr>
</table>
NB: no denominator reported for safety outcomes

Timing and treatment of complications is not reported unless other wise stated.</td>
<td>This paper is included in Lansdale 2010.

Follow-up issues:
• Completeness of follow-up is not reported.

Study design issues:
• Retrospective comparative study of 2 historical cohorts.
• Single site study.
• Efficacy and safety data only reported on successful thoracoscopic repairs of CDH and controls selected from open repairs.
• Parents were preferentially offered thoracoscopic repair after June 2004 if the child was thought to be able to withstand the additional respiratory compromise associated with thoracoscopic repair.
• Patients reported in the open group were chosen to be comparable with cases of thoracoscopic repair in terms of absence of significant congenital anomaly, no need for preoperative ECMO, PIP ≤26 on day of surgery and OI ≤5 on day of surgery. The authors identified these to be features of successful thoracoscopic repair.
• No report of chest X-ray or clinical examination at longer term follow-up to confirm success of procedure</td>
</tr>
</table>

Abbreviations used: CDH, congenital diaphragmatic hernia; CI, confidence interval; ECMO, extracorporeal membrane oxygenation; $EtCO_2$, end-tidal carbon dioxide level; N/A, not applicable; NR, not reported; ; NS, not significant; $PaCO_2$, partial pressure of carbon dioxide in the blood; PIP, peak inspiratory pressure; PRISMA, Preferred reporting items for systematic reviews and meta-analyses; VATS, video-assisted thoracic surgery			
Conflict of interest/source of funding: not reported.	insufflation of the ipsilateral hemithorax to 3 mmHg. A Ladd procedure was performed (as an adjunctive procedure to the hernia reduction and diaphragm repair) in 41% (no number reported) of patients in the open group.		**Other issues:** • Study does not provide outcome data on unsuccessful thoracoscopic procedures.

Abbreviations used: CDH, congenital diaphragmatic hernia; CI, confidence interval; ECMO, extracorporeal membrane oxygenation; $EtCO_2$, end-tidal carbon dioxide level; N/A, not applicable; NR, not reported; NS, not significant; $PaCO_2$, partial pressure of carbon dioxide in the blood; PIP, peak inspiratory pressure; PRISMA, Preferred reporting items for systematic reviews and meta-analyses; VATS, video-assisted thoracic surgery

Study details

Keijzer R (2010)[5]

Non-randomised comparative study

Netherlands

Recruitment period: 2006–2008

Study population: children with posterolateral CDH

n = **46 (23 vs 23)**

Age: thoracoscopic group: 3 days (mean), open group: 4.1 days (mean)

Sex: thoracoscopic group: 43.5% (10/23) female, open group: 39.1% (9/23)

Patient selection criteria: see above

Technique: thoracoscopic repair of CDH (no description provided) vs open repair

Follow-up: **1 year**

Conflict of interest/source of funding: none.

Key efficacy findings

Number of patients analysed: **46 (23 vs 23)**

	Thoracoscopic group (n = 23)	Open group (n = 23)	p value
Survival	96% (22/23)	78% (18/23)	NS
Conversion to open procedure	26.1% (6/23)	-	-
Recurrence	17.4% (4/23) [reported as 15% in the paper]	13% (3/23)	NR
Defect closed with a patch	47.1% (8/17) [only reported numbers for those who did not convert to open procedure]	87% (20/23)	NR
Median duration of hospital stay	20 days	35 days	

Open group recurrences: 2 or the 3 recurrences in the open group were treat thoracoscopically.
Thoracoscopic group recurrences: all 4 recurrences were treated thoracoscopically.

Reasons for conversion in thoracoscopic group:

- Inability to reduce the intrathoracic abdominal organs: 4 patients

Key safety findings

	Thoracoscopic group (n = 23)	Open group (n = 23)
Mortality	1	5
Chylothorax	1	3
Haemothorax	1	3
Cerebral infarction	1	1
Pulmonary hypertension	1	5

All deaths were due to therapy-resistant pulmonary hypertension.

Timing and treatment of complications is not reported unless otherwise stated.

Comments

Study added from updated literature search during the consultation period.

Follow-up issues:

- Paper reports 49 patients with CDH were admitted. 3 patients were not treated due to associated anomalies.
- Completeness of follow-up not reported.

Study design issues:

- Retrospective single centre study.
- Unclear how diagnosis was confirmed.
- Treatment (thoracoscopic vs open) at the discretion fo the attending sugeon.

Study population issues:

- Mean weight at birth: thoracoscopic group: 3139 g, open group: 3396g

Abbreviations used: CDH, congenital diaphragmatic hernia; CI, confidence interval; ECMO, extracorporeal membrane oxygenation; $EtCO_2$, end-tidal carbon dioxide level; N/A, not applicable; NR, not reported; NS, not significant; $PaCO_2$, partial pressure of carbon dioxide in the blood; PIP, peak inspiratory pressure; PRISMA, Preferred reporting items for systematic reviews and meta-analyses; VATS, video-assisted thoracic surgery

Lao OB (2010)[6]

Non-randomised comparative study

USA
Recruitment period: 2004–2008

Study population: infants with CDH (with ICD-9 code 756.6)

n = **31 (14 vs 17)**

Age: thoracoscopic group: 3 days (median), open group: 3 days (median)
Sex: thoracoscopic group: 14.3% (2/14) female, open group: 41.2% (7/17)

Patient selection criteria: patients excluded if any of following applied: they had a repair after 50 weeks postconception, the hernia was recurrent, they had congenital cardiac abnormalities nt including consitions such as patent arteriosus or foramen ovale, they had a orgagni hernia or had ECO support during hospitalization.

Technique: thoracoscopic repair of CDH (using CO_2 insufflation up to 4 mmHg) vs open repair (5 laparotomy and 12 thoracotomy)

Follow-up: **346 days (mean)**

Conflict of interest/source of funding: none.

Number of patients analysed: **31 (14 vs 17)**

	Thoracoscopic group (n = 14)	**Open group (n = 17)**	**p value**
Conversion to open procedure	21.4% (3/14)	-	-
Median postoperative ICU length of stay	7 days	7 days	0.889
Median postoperative days on ventitlation	4 days	4 days	0.705
Median duration of hospital stay	21 days	24 days	0.662

No recurrences reported in either group during follow-up.

Reasons for conversion in thoracoscopic group: large defect requiring a patch repair was identified in all 3 cases.

	Thoracoscopic group (n = 14)	**Open group (n = 17)**
Supraventricular tachycardia (either reolved or well managed with medication at follow-up)	0	3
Pectus excavatum at 16 months	0	1
Scoliosis at 10 months (45° apex right thoracic curve treated with Lycra body suit and orthopaedic surgery) (patient treaed with anticoagulation; no adverse sequelae)	1	0
Inferior vena cava thrombus	1	0
Total complications	14.3% (2/14)	23.5% (4/17)

No in-hospital deaths reported.

Timing and treatment of complications not reported unless otherwise stated.

Study added from updated literature search during the consultation period.

Follow-up issues:
- 47.4% (27/57) children with CDH excluded due to patient selection criteria given.
- Completeness of follow-up not reported.

Study design issues:
- Retrospective single centre study.
- Unclear how diagnosis was confirmed
- Treatment (thoracoscopic vs open) at the discretion of the surgeon.

Study population issues:
- Median weight at birth: thoracoscopic group: 2.9kg open group: 3.2kg

Abbreviations used: CDH, congenital diaphragmatic hernia; CI, confidence interval; ECMO, extracorporeal membrane oxygenation; $EtCO_2$, end-tidal carbon dioxide level; N/A, not applicable; NR, not reported; NS, not significant; $PaCO_2$, partial pressure of carbon dioxide in the blood; PIP, peak inspiratory pressure; PRISMA, Preferred reporting items for systematic reviews and meta-analyses; VATS, video-assisted thoracic surgery

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Gomes FC (2009)[7]

Non-randomised comparative study

International

Recruitment period: 2003 onwards

Study population: neonates with CDH

n = 30 (18 vs 12)

Age: 4.33 days (mean)

Sex: 46.7% (14/30) female

Patient selection criteria: patients in a stable respiratory and cardiovascular condition for 24 hours, oxygen saturation > 90% with peak inspiratory pressure lower than 24 cmH_20, fraction of inspired oxygen < 40% and if required a maximum peak end-expiratory pressure of 3–4 cmH_20. Patients with high partial pressure of CO_2 (>60mmHg), acidosis (pH <7.25), persistent pulmonary hypertension, severe associated malformations and large defect requiring patch closure were considered for conventional open procedures.

Technique: thoracoscopic repair of CDH (CO_2 insufflation at 4-6 mmHg and non-absorbable sutures, Gore-Tex patch or Mersilene meshes used to close defect) vs laparoscopic repair (CO_2 insufflation at 6–8 mmHg)

Follow-up: not reported

Conflict of interest/source of funding: not reported.</td>
<td>Number of patients analysed: 30 (18 vs 12)

<table>
<tr><th></th><th>Thoracoscopic group (n = 18)</th><th>Laparoscopic group (n = 12)</th></tr>
<tr><td>Recurrence</td><td>11.1% (2/18) *</td><td>0</td></tr>
<tr><td>Easy reduction</td><td>83.3% (15/18)</td><td>41.7% (5/12)</td></tr>
<tr><td>Difficult reduction</td><td>11.1% (2/18)</td><td>33.3% (4/12)</td></tr>
<tr><td>Impossible reduction</td><td>5.6% (1/18)</td><td>25% (3/12)</td></tr>
<tr><td>Conversion to thoracotomy (open procedure)</td><td>16.7% (3/18)</td><td>0</td></tr>
<tr><td>Conversion to laparotomy (open procedure)</td><td>5.6% (1/18)</td><td>41.7% (5/12)</td></tr>
<tr><td>Conversion to VATS (video camera is inserted through a separate incision)</td><td>5.6% (1/18)</td><td>0</td></tr>
<tr><td>Total conversion rate</td><td>27.8% (5/18)</td><td>41.7% (5/12)</td></tr>
</table>

*1 partial recurrence at 1 month which was successfully closed used a thoracoscopic approach; 1 recurrence at 1 year repaired initially by thoracoscopic approach but converted to open procedure because it was not possible to reduce the stomach thoracoscopically.

Reasons for conversion in thoracoscopic group:
• Reduction difficult and insertion of patch
• Patch insertion required a 2 cm thoracotomy (using VATS)
• Reduction impossible and insertion of patch
• Insertion of patch
• Respiratory distress before insufflations.

Reasons for conversion in laparoscopic group:
• Reduction of herniated liver impossible thoracoscopically (2 patients)
• Associated bowel malrotation requiring abdominal access / surgery.
• Insertion of patch and lack of visibility
• Restricted working space after reduction.</td>
<td>Postoperative mortality is not reported

Immediate postoperative course reported as simple in 88.9% (16/18) in thoracoscopic group and 100% (12/12) of laparoscopic group

Complications in thoracoscopic group:
Peritonitis: 5.6% (1/18) at day 10, laparotomy revealed perforation of Mickel’s diverticulum

Small bowel obstruction: 5.6% (1/18) at day 8, resolved conservatively

Laparoscopic group:
No complications reported.

Timing and treatment of complications is not reported unless otherwise stated.</td>
<td>Follow-up issues:
• Completeness of follow-up not reported.

Study design issues:
• Multicentre (9 centres) study.
• All patients had a thoracoabdominal X-ray to confirm diagnosis.
• Unclear how patients were selected into each group.
• No report of chest X-ray or clinical examination at longer term follow-up to confirm success of procedure

Study population issues:
• Mean weight at birth: 2879 g
• 10 preterm newborns (gestational age: 32–36 weeks)
• Intubated at birth: 60% (18/30)
• Size of defect: total = 16.7% (5/30), large = 63.3% (19/30) and small = 20% (6/30)
• Use of patch: thoracoscopic group: 22.2% (4/18), laparoscopic group: 8.3% (1/12).</td>
</tr>
</table>

Abbreviations used: CDH, congenital diaphragmatic hernia; CI, confidence interval; ECMO, extracorporeal membrane oxygenation; $EtCO_2$, end-tidal carbon dioxide level; N/A, not applicable; NR, not reported; NS, not significant; $PaCO_2$, partial pressure of carbon dioxide in the blood; PIP, peak inspiratory pressure; PRISMA, Preferred reporting items for systematic reviews and meta-analyses; VATS, video-assisted thoracic surgery

Study details	Key efficacy findings	Key safety findings	Comments
Liem NT (2006)[8] **Case series** Vietnam Recruitment period: 2001–2005 Study population: children with CDH n = **45** Age: 28.9% (13/45) <7 days old, 13.3% (6/45) 7-30 days old, 57.8% (26/45) >30 days old. Sex: 35.6% (16/45) female Patient selection criteria: patients whose disorder of blood gas was not improved with conventional ventilator were excluded from thoracoscopic repair. Technique: thoracoscopic repair of CDH (1 optical trocar and 2 operating trocars; pleural insufflation with CO_2 at 2-4 mmHg and non-absorbable sutures used to close defect) Follow-up: **3–39 months** Conflict of interest/source of funding: not reported	Number of patients analysed: **45** Authors report that reduction of hernia contents was easily accomplished in 66.7% (30/45) [also states that it was difficult in 6 cases but this takes the total of cases above 46 – IP analyst] Recurrence: 1 patient at 10 months requiring reoperation (approach used is unclear) Conversion to open (abdominal repair) procedure: 8.9% (4/45) Of these, 3 were due to difficulty in reducing the hernia content down into the abdominal cavity and 1 due to decrease in oxygen saturation. Mean operative time: 54 minutes (excluding conversions) Mean duration of postoperative ventilation (excluding patients who died): 3.3 days (required in 30 patients) Mean duration of postoperative hospitalisation: 5.6 days.	**Mortality** Postoperative deaths: 4.4% (2/45). Both were neonates, 1 died following severe bronchopneumonia and another due to pneumothorax (timing not reported). Authors state that there were no deaths among patients older than 7 days. **Complications** Wound infection: 2 patients Pleural effusion: 2 patients (both did not require chest drain insertion and were treated by thoracocentesis). Timing and treatment of complications is not reported unless otherwise stated.	**Follow-up issues**: • Completeness of follow-up not reported. **Study design issues**: • Retrospective study. • Single site study. One surgeon performed all the procedures. • No report of chest X-ray or clinical examination at longer term follow-up to confirm success of procedure (although X-ray at 24 hours when decision to withdraw chest drain is made). **Study population issues**: • Maximum age of patients is 15 years. Unclear what proportion of children is aged ≤12 months. • Presenting symptoms included respiratory distress, bronchopneumonia and vomiting in infants and older children. • Preoperative ventilation: 15.6% (7/45) patients • Location of hernia: left side = 82.2% (37/45) and right side = 17.8% (8/45) • Presence of hernia sac: 64.4% (29/45) • Contents of hernia: intestine = 86.7% (39/45), stomach = 17.8% (8/45), spleen = 26.7% (12/45) and liver = 17.8% (8/45). • Postoperative chest drain: 95.6% (43/45).

Abbreviations used: CDH, congenital diaphragmatic hernia; CI, confidence interval; ECMO, extracorporeal membrane oxygenation; $EtCO_2$, end-tidal carbon dioxide level; N/A, not applicable; NR, not reported; NS, not significant; $PaCO_2$, partial pressure of carbon dioxide in the blood; PIP, peak inspiratory pressure; PRISMA, Preferred reporting items for systematic reviews and meta-analyses; VATS, video-assisted thoracic surgery

Study details	Key efficacy findings	Key safety findings	Comments
Shalaby R (2008)[9] **Case series** Egypt Recruitment period: 2005–2007 Study population: children with symptomatic CDH n = **18** Age: 1.58 months (mean) Sex: 33.3% (6/18) female Patient selection criteria: patients assigned to elective thoracoscopic repair (unclear how assignment determined) Technique: thoracoscopic repair of CDH using CO_2 insufflation at max 6 mmHg and mattress sutures using Reverdin needle used to close defect. All patients treated by a dose of preoperative antibiotic prophylaxis. Follow-up: **1 year** Conflict of interest/source of funding: not reported.	Number of patients analysed: **18** All defects successfully closed - this was achieved easily in 94.4% (17/18) of patients and difficult in the remaining patient. Chest X-ray and clinical examination were normal in all patients at 3 months and there were practically no visible scars at 1-year follow-up. No recurrences. Conversion (not otherwise defined, e.g. whether to open thoracic or abdominal repair) to an open procedure with minimal blood loss: 5.6% (1/18) due to decrease in oxygen saturation. Mean operative time: 30.7 ± 1.18 minutes Mean duration of postoperative hospitalisation: 5.6 days.	Mortality: 1 death at day 10 due to persistent low oxygen saturation as a result of associated lung hypoplasia. No other intra- or postoperative complications reported.	**Follow-up issues**: • 100% follow-up. **Study design issues**: • Prospective study. • One surgeon performed all the procedures. • All patients discharged at day 3 and followed-up at 7 days, 2 weeks, 6 months and 1 year. **Study population issues**: • Location of hernia: left side = 66.7% (12/18) and right side = 33.3% (6/18). • Presence of hernia sac: 16.7% (3/18) all were excised. • Contents of hernia: intestine = 38.9% (7/18), stomach = 11.1% (2/18), spleen and intestine =27.8% (5/18) and liver = 22.2% (4/18). • No patch required in any patient to close defect. • All patients had postoperative chest drain connected to underwater seal drainage system without suction which was removed at day 2. • Postoperative ventilation: 16.7% (3/18) of patients.

Abbreviations used: CDH, congenital diaphragmatic hernia; CI, confidence interval; ECMO, extracorporeal membrane oxygenation; $EtCO_2$, end-tidal carbon dioxide level; N/A, not applicable; NR, not reported; NS, not significant; $PaCO_2$, partial pressure of carbon dioxide in the blood; PIP, peak inspiratory pressure; PRISMA, Preferred reporting items for systematic reviews and meta-analyses; VATS, video-assisted thoracic surgery

Study details

Kim AC (2009)[10]

Case series

USA

Recruitment period: 2004– 2008

Study population: full or near full term neonates with CDH

n = **15**

Age: 5.7 days (mean)

Sex: 33.3% (5/15) female

Patient selection criteria: all patients underwent repair within first 30 days of life. All patients were stabilised in terms of respiratory and cardiovascular function prior to procedure (gentle ventilation parameters). Patients had to show no signs of pulmonary hypotension or major associated anomalies to be included.

Technique: thoracoscopic repair of CDH using CO_2 insufflation at 4–7 mmHg. Interrupted Ethibond / silk sutures / patch used to close the defect.

Follow-up: **15.8 months (mean)**

Conflict of interest/source of funding: none.

Key efficacy findings

Number of patients analysed: **15**

Overall

- Successful repair: 80% (12/15)
- Conversion to open procedure: 20% (3/15) due to need for patch closure (2 patients) or intraoperative instability (dangerously high PIP levels, raising concern for barotrauma) in 1 patient.
- Mean operative time: 161 ± 19 minutes
- Mean duration of postoperative ventilation: 6.9 ± 1.0 days
- Mean time until full enteral feeding: 16.7 ± 2.25 days
- Mean duration of hospitalisation: 23.8 ± 2.73 days

Comparison of successful initial repair to those who required conversion:

	Successful initial repair (n = 12)	Required conversion (n = 3)	p value
Recurrence	16.7% (2/12) (at 215 days and the timing of the other is not reported)	0	
Mean number postoperative ventilation days	5.4 ± 0.7	13.1 ± 1.2	<0.001
Mean length of stay (days)	19.8 ± 1.3	36.3 ± 5.6	0.001
Stomach herniation on radiograph	16.7% (2/12)	100% (3/3)	NR
Received chest tube*	50% (6/12)	66.7% (2/3)	NR
Required patch repair	0	66.7% (2/3)	NR

* all chest tubes placed intraoperatively except one for postoperative pneumothorax in the successful initial repair group In the initially successful group, 1 patient required one time use of surfactant and another required a 4 day course of ECMO. In the conversion group, 1 patient required 14 days of ECMO and high-frequency oscillatory ventilation.

Key safety findings

All patients survived.

Complications:

	Successful initial repair (n = 12)	Conversion (n = 3)
Pleural effusion	0	33.3% (1/3)
Pneumonia	0	33.3% (1/3)
Pneumothorax	8.3% (1/12)	33.3% (1/3)

Timing and treatment of complications is not reported unless otherwise stated.

Comments

Follow-up issues:

- Completeness of follow-up not reported

Study design issues:

- Retrospective study.
- 7 surgeons performed the procedures.
- Prenatal diagnosis involved serial ultrasounds with calculation of lung-to-head ratio and determination of liver position.
- No report of chest X-ray or clinical examination at longer term follow-up to confirm success of procedure.

Study population issues:

- Diagnosed prenatally: 40% (6/15).
- Location of hernia: left side = 86.7% (13/15) and right side = 13.3% (2/15).
- Liver herniation (confirmed by prenatal ultrasound): 2 patients with right-sided defects.
- 1 patient also had a ventricular septal defect.
- All patients intubated shortly after birth and 13.3% (2/15) required ECMO.
- Mean weight at time of repair: 3.5 ± 0.2 kg.

Efficacy

Recurrence

A meta-anlaysis of 143 patients (62 thoracoscopic vs 81 open procedures, 3 non-randomised comparative studies) reported a recurrence rate of 16.1% (10/62) in the thoracoscopic group compared with 4.9% (4/81) in the open group (length of follow-up not reported). The study reported a recurrence risk ratio of 3.21 (95%CI 1.11 to 9.29) indicating that the risk of recurrence is significantly higher in the thoracoscopic group[1].

A non-randomised comparative study of 57 patients (29 thoracoscopic vs 28 open procedures) reported no significant difference in recurrence rates in the thoracoscopic group and the open group (21% [6/29] vs 7% [2/28], p = 0.25). The timing and treatment were not reported[2].[NB: this study is included in the meta-analysis of 143 patients].

A non-randomised comparative study of 48 patients (13 thoracoscopic vs 35 open procedures) reported a non-significant difference in recurrence rates in the thoracoscopic and open groups (25% [2/8] vs 8% [3/40], p = 0.19). Patients who were converted from thoracoscopic to the open procedure were included in the results for the open group. The timing and treatment were not reported[3]. [NB: this study is included in the meta- analysis of 143 patients].

A non-randomised comparative study of 46 patients (23 thoracoscopic vs 23 open procedures) reported recurrence rates of 17% (4/23) in the thoracoscopic group and 13% (3/23) in the open group at 1 year follow-up[5].

A non-randomised comparative study of 73 patients (33 thoracoscopic vs 40 open procedures) reported 1 recurrence in the thoracoscopic group (timing and treatment were not reported) and none in the open group[4]. [NB: this study is included in the meta- analysis of 143 patients].

A non-randomised comparative study of 31 patients (14 thoracoscopic vs 17 open procedures) reported no recurrences in either group at mean follow-up of 346 days[6].

A non-randomised comparative study of 30 patients (18 thoracoscopic vs 12 laparoscopic) reported recurrence rates of 11% (2/18) in the thoracoscopic group (1 partial recurrence at 1 month closed successfully using thoracoscopic approach and 1 recurrence at 1 year repaired with thoracoscopic approach initially but converted to open procedure when it was clear that the stomach could not be reduced thoracoscopically) and none in the laparoscopic group[7].

A case series of 45 patients reported 1 recurrence at 10 months requiring reoperation (approach used is unclear)[8].

A case series of 15 patients reported recurrence in 2 patients; 1 occurred at 215 days and the timing was not specified for the other (treatment was not reported for either)[10].

Ease of reduction

The non-randomised comparative study of 30 patients (18 thoracoscopic vs 12 laparoscopic) reported 'easy reduction' of hernia contents in 83% (15/18) of patients in the thoracoscopic group and 42% (5/12) in the laparoscopic group; 'difficult reduction' in 11% (2/18) of patients in the thoracoscopic group and 33% (4/12) in the laparoscopic group; and that it was impossible to reduce the hernia contents in 6% (1/18) of patients in the thoracoscopic group and 25% (3/12) in the laparoscopic group[7].

The case series of 45 patients reported that reduction of hernia contents was easily accomplished in 67% (30/45) of patients[8].

Conversion to an open procedure

The non-randomised comparative study of 57 patients (29 thoracoscopic vs 28 open procedures) reported conversion from a thoracoscopic procedure to an open procedure in 1 patient because the liver could not be reduced into the abdomen[2].

The non-randomised comparative study of 48 patients (13 thoracoscopic vs 35 open procedures) reported conversion to an open procedure in 38% (5/13) of patients in the thoracoscopic group due to surgical difficulties in 4 patients and intraoperative oxygen desaturation in 1 patient[3].

A non-randomised comparative study of 46 patients (23 thoracoscopic vs 23 open procedures) reported conversion to open procedure in 26% (6/23) of the thoracoscopic group. This was due to the inability to reduce the intrathoracic abdominal organs in 4 patients. No reason is given for the other 2 conversions[5].

A non-randomised comparative study of 31 patients (14 thoracoscopic vs 17 open procedures) reported conversion to open procedure in 21% (3/14) of the thoracoscopic group due to large defect requiring a patch in all cases[6].

A non-randomised comparative study of 30 patients (18 thoracoscopic vs 12 laparoscopic) reported rates of conversion to an open procedure of 28% (5/18) in the thoracoscopic group and 42% (5/12) in the laparoscopic group. The reasons for conversion in the thoracoscopic group were difficult or impossible reduction, patch repair required and respiratory distress before insufflation. Reasons for conversion in the laparoscopic group were impossible liver reduction, associated bowel malrotation, insertion of patch, lack of visibility and restricted working space after reduction[7].

The case series of 45 patients reported conversion to an open procedure in 9% (4/45) of patients. Of these, 3 were due to difficulty in reducing the hernia content into the abdominal cavity and 1 was due to a decrease in oxygen saturation[8].

A case series of 18 patients reported conversion to an open procedure with minimal blood loss in 1 patient due to a decrease in oxygen saturation[9].

The case series of 15 patients reported conversion to an open procedure in 20% (3/15) of patients due to the need for patch closure in 2 patients and intraoperative instability in 1 patient[10].

Operative time

The meta-anlaysis of 143 patients (62 thoracoscopic vs 81 open procedures, 3 studies) reported reported weighted mean difference in operative time of 51 minutes (95% CI 32 to 69 minutes) indicating that the operative time is significantly longer in the thoracoscopic group compared to the open group[1].

The non-randomised comparative study of 57 patients (29 thoracoscopic vs 28 open) reported a significantly longer median operating time in the thoracoscopic group compared to the open group (179 vs 117 minutes, $p < 0.001$)[2]. [NB: this study is included in the meta- analysis of 143 patients].

Non-randomised comparative studies of 48 patients (13 thoracoscopic vs 35 open procedures) and 73 patients (33 thoracoscopic vs 40 open) reported a significantly longer mean operating time in the thoracoscopic group in comparison to the open group (3.3 vs 2.0 hours, $p < 0.01$[3] [NB: this study is included in the meta- analysis of 143 patients] and 164 vs 117 minutes, $p = 0.01$[4] respectively).

The case series of 45 patients reported a mean operative time of 54 minutes (excluding conversion)[8].

Case series of 18 and 15 patients reported a mean operative time of 31 minutes[9] and 161 minutes[10] respectively.

Ventilation time

The non-randomised comparative study of 57 patients (29 thoracoscopic vs 28 open procedures) reported the same median length of postoperative ventilation in the thoracoscopic group and the open group (5 vs 5 days, $p = 0.56$)[2].

The non-randomised comparative study of 73 patients (33 thoracoscopic vs 40 open procedures) reported significantly shorter median length of postoperative ventilation in the thoracoscopic group compared to the open group (2 vs 4 days, $p = 0.04$)[4].

A non-randomised comparative study of 31 patients (14 thoracoscopic vs 17 open procedures) reported the same median postoperative days on ventilation in both groups (4 days, p = 0.705) at mean follow-up of 346 days[6].

The case series of 45 patients reported a mean postoperative ventilation time of 3.3 days (ventilation was required in 67% [30/45] of patients)[8].

The case series of 15 patients reported a significantly lower mean postoperative ventilation time in the patients who had successful repair with an initial thoracoscopic procedure compared with those who required conversion to an open procedure (5.4 vs 13.1 days, p < 0.001)[10].

Length of stay in hospital

The non-randomised comparative study of 57 patients (29 thoracoscopic vs 28 open) reported a non-significant difference in length of stay in hospital in the thoracoscopic group compared with the open group (34 vs 24 days, p = 0.11)[2].

The non-randomised comparative study of 73 patients (33 thoracoscopic vs 40 open) reported a similar median total length of hospital stay in the thoracoscopic group in comparison to the open group (21 vs 26 days, p = 0.23)[4].

A non-randomised comparative study of 31 patients (14 thoracoscopic vs 17 open procedures) reported similar median total length of hospital stay in the thoracoscopic group in comparison to the open group (21 vs 24 days, p = 0.662)[6].

Case series of 45 and 18 patients reported a mean duration of postoperative hospitalisation of 5.6 days in both studies[8,9].

The case series of 15 patients reported a mean duration of hospitalisation of 23.8 days[10].

Safety

Mortality

A meta-anlaysis of 143 patients (62 thoracoscopic vs 81 open procedures, 3 studies) reported a mortality rate of 3.2% (2/62) in the thoracscopic group compared to 12.3% (10/81) in the open group (length of follow-up not reported). The study reported a mortality risk ratio of 0.33 (95% CI 0.01 to 1.13) indicating that the risk of death is not statistically significantly lower in the thoracoscopic group[1].

The non-randomised comparative study of 57 patients (29 thoracoscopic vs 28 open procedures) reported no significant difference in postoperative mortality rate between the thoracoscopic group and the open group (7% [2/29] vs 21% [6/28],

[p = 0.14]). The timing and cause of death were not reported[2]. [NB: this study is included in the meta- analysis of 143 patients].

The non-randomised comparative study of 73 patients (33 thoracoscopic vs 40 open procedures) reported 1 death in the open group due to haemorrhage at a median of 37 months follow-up and no deaths in the thoracoscopic group at a median of 37 months follow-up[4]. [NB: this study is included in the meta- analysis of 143 patients].

A non-randomised comparative study of 46 patients (23 thoracoscopic vs 23 open procedures) reported 1 death in the throracoscopic group and 5 deaths in the open group. All deaths were due to therapy-resistant pulmonary hypertension at 1 year follow-up[5].

A non-randomised comparative study of 31 patients (14 thoracoscopic vs 17 open procedures) reported no in-hospital deaths in either group at mean follow-up of 346 days[6].

The case series of 45 patients reported 2 postoperative deaths. Both deaths were of neonates. One died following severe bronchopneumonia and the other due to pneumothorax (timing not reported for either death)[8].

The case series of 18 patients reported 1 death at day 10 following the procedure, due to persistent low oxygen saturation as a result of associated lung hypoplasia[9].

Infection

The non-randomised comparative study of 57 patients (29 thoracoscopic vs 28 open procedures) reported no significant difference in major infection rates (defined as abscess, systemic sepsis or abdominal wall patch infection) in the thoracoscopic group and the open group (17% (5/29) vs 4% (1/28), p = 0.19). The timing and treatment were not reported[2].

A non-randomised comparative study of 73 patients (33 thoracoscopic vs 40 open procedures) reported line sepsis in 1 patient in the thoracoscopic group and no patients in the open group. The patient required intravenous antibiotics and prolonged hospitalisation (timing not reported)[4].

Bowel obstruction

The non-randomised comparative study of 57 patients (29 thoracoscopic vs 28 open procedures) reported bowel obstruction rates of 7% (2/29) in the thoracoscopic group and 11% (3/28) in the open group. The timing and treatment were not reported[2].

The non-randomised comparative study of 73 patients (33 thoracoscopic vs 40 open procedures) reported bowel obstruction requiring laparotomy in 1 patient in

the thoracoscopic group (timing not reported) and in 3 patients in the open group (which also required enterolysis, timing not reported)[4].

The non-randomised comparative study of 30 patients (18 thoracoscopic vs 12 laparoscopic) reported obstruction of the small bowel in 1 patient in the thoracoscopic group at day 8 following the procedure, which resolved conservatively[7].

Organ laceration / perforation

A non-randomised comparative study of 57 patients (29 thoracoscopic vs 28 open procedures) reported gastrointestinal perforation rates of 7% (2/29) in the thoracoscopic group and 7% (2/28) in the open group. The same study also reported solid organ laceration in 7% (2/28) of patients in the open group compared with no patients in the thoracoscopic group. The timing and treatment were not reported[2].

Validity and generalisability of the studies

- No randomised controlled trial evidence in the published literature.
- No long-term data (i.e. over 2 years) available.
- Successful closure of the defect confirmed by chest X-ray and clinical examination at longer term follow-up is rarely reported.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

There is currently no NICE guidance related to this procedure.

Specialist Advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and does not represent the view of the society.

Mr David Crabbe and Mr Simon Clarke (British Association of Paediatric Surgeons)

- One Specialist Adviser performs this procedure regularly and the other Specialist Adviser has never performed this procedure but has extensive experience of performing open repair.
- One Specialist Adviser considers the procedure to be a significant modification of the current procedure and both Specialist Advisers state that fewer than 10% of specialists are engaged in this area of work.
- The comparator is an open upper right abdominal incision (laparotomy). Open thoracotomy can also be used but is rare.
- Theoretical adverse events: solid/hollow visceral injury, recurrence, conversion to open repair, physiological instability, and hypercarbia if not carefully insufflated.
- Efficacy outcomes: reduction in postoperative abdominal adhesions, improved postoperative pain, duration of hospital stay, resumption of enteral nutrition and cosmetic appearance.
- Training and facilities: experience in advanced minimally invasive surgery in children, in-house simulation and familiarity with small working space. One Specialist Adviser states that it is currently inconceivable that a trainee in paediatric surgery in the UK will acquire this experience during his/her training. The other Specilaist Adviser states that there is a steep learning curve for this procedure.
- Trials/registers: a voluntary international congenital diaphragmatic hernia registry was established by the congenital diaphragmatic hernia study group in the US in 1995. The only UK centre contributing data to the CDH study group is Glasgow.

Patient Commentators' opinions

NICE's Patient and Public Involvement Programme sent 2 questionnaires to for distribution to the parents of patients who had the procedure (or their carers). NICE received 0 completed questionnaires.

References

1. Lansdale N, Alam S, Losty PD et al. (2010) Neonatal endosurgical congenital diaphragmatic hernia repair: a systematic review and meta-analysis. Annals of Surgery 252: 20–6.

2. Cho SD, Krishnaswami S, Mckee JC et al. (2009) Analysis of 29 consecutive thoracoscopic repairs of congenital diaphragmatic hernia in neonates compared to historical controls. Journal of Pediatric Surgery 44: 80–6.

3. McHoney M, Giacomello L, Nah SA et al. (2010) Thoracoscopic repair of congenital diaphragmatic hernia: intraoperative ventilation and recurrence. Journal of Pediatric Surgery 45: 355–9.

4. Gourlay DM, Cassidy LD, Sato TT et al. (2009) Beyond feasibility: a comparison of newborns undergoing thoracoscopic and open repair of congenital diaphragmatic hernias. Journal of Pediatric Surgery 44: 1702–7.

5. Keijzer R, van d, V, Vlot J et al. (2010) Thoracoscopic repair in congenital diaphragmatic hernia: patching is safe and reduces the recurrence rate. Journal of Pediatric Surgery 45: 953–7.

6. Lao OB, Crouthamel MR, Goldin AB et al. (2010) Thoracoscopic repair of congenital diaphragmatic hernia in infancy. Journal of Laparoendoscopic and Advanced Surgical Techniques Part (3): 271–6.

7. Gomes FC, Reinberg O, Becmeur F et al. (2009) Neonatal minimally invasive surgery for congenital diaphragmatic hernias: a multicenter study using thoracoscopy or laparoscopy. Surgical Endoscopy 23: 1650–9.

8. Liem NT, Dung LA (2006) Thoracoscopic repair for congenital diaphragmatic hernia: lessons from 45 cases. Journal of Pediatric Surgery 41: 1713–5.

9. Shalaby R, Gabr K, Al-Saied G et al. (2008) Thoracoscopic repair of diaphragmatic hernia in neonates and children: a new simplified technique. Pediatric Surgery International 24: 543–7.

10. Kim AC, Bryner BS, Akay B et al. (2009) Thoracoscopic repair of congenital diaphragmatic hernia in neonates: lessons learned. Journal of Laparoendoscopic and Advanced Surgical Techniques Part (4): 575–80.

Appendix A: Additional papers on thoracoscopic repair of congenital diaphragmatic hernia in neonates

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Bliss D, Matar M, Krishnaswami S. (2009) Should intraoperative hypercapnea or hypercarbia raise concern in neonates undergoing thoracoscopic repair of diaphragmatic hernia of Bochdalek? Journal of Laparoendoscopic & Advanced Surgical Techniques Part:A-8.	Case series n = 31 Follow-up: not reported	CO_2 insufflation: 3 mmHg Mean highest intraoperative end-tidal CO_2: 64 ± 13 torr Mean lowest intraoperative SaO_2: 92 ± 8% Average lowest intraoperative mean arterial blood pressure: 47 ± 8 mmHg Authors report that Hypercapnea and hypercarbia are common during thoracoscopic CDH repair but result in clinically evident pulmonary hypertension, hypoxia or hypotension.	Same patients reported in Cho 2009 in Table 2
Liem NT, Dung lA, Nhat LQ et al. (2008) Thoracoscopic repair for right congenital diaphragmatic hernia. Journal of Laparoendoscopic & Advanced Surgical Techniques Part (4): 661-663.	Case series n = 16 Follow-up: 2-77 months	Mean operative time: 82 minutes Conversion to open procedure: 1 patient 1 postoperative death (bronchopneumonia and septicaemia caused by nosocomial infection) 1 recurrence at day 39 Mean length of hospitalisation: 10.2 days.	Larger studies reported in Table 2 Half of patients reported in Liem 2006 in Table 2
Guner YS, Chokshi N, Aranda A et al. (2008) Thoracoscopic repair of neonatal diaphragmatic hernia. Journal of Laparoendoscopic & Advanced Surgical Techniques Part (6): 875-880.	Case series n = 15 Follow-up: 4-40 months	5 neonates required a synthetic patch to close the defect. Mean operating time: 134 minutes Recurrence: 3 patients No postoperative deaths Postoperative pneumothorax: 1 patient (required high frequency oscillatory ventilation)	Larger studies reported in Table 2

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Shah SR, Wishnew J, Barsness K et al. (2009) Minimally invasive congenital diaphragmatic hernia repair: a 7-year review of one institution's experience. Surgical Endoscopy 23 (6): 1265-1271.	Case series n = 22 (13 thoracoscopic and aged ≤12 months) Follow-up: 1–5 years (children aged up to 9 months), 6 months – 4 years (neonates)	Neonates: 9 Bochdalek hernias repaired thoracoscopically. 1 converted to thoracotomy (absent diaphragm requiring large patch), 1 to laparotomy (oxygen desaturation), 2 required mini-thoracotomies for placement of patch or lateral stitch and 2 required small stab incisions to secure the patch anteriorly around the ribs. 2 recurrences. Children up to 12 months: 4 Bochdalek hernias repaired thoracoscopically. No complications.	Larger studies reported in Table 2
Becmeur F, Reinberg O, Dimitriu C et al. (2007) Thoracoscopic repair of congenital diaphragmatic hernia in children. Seminars in Pediatric Surgery 16 (4): 238-244.	Case series n = 17 thoracoscopic (12 aged ≤12 months) Follow-up: not reported	Includes 6 newborns: 2 required thoracotomy (1 for wide defect requiring a patch and 1 for wide defect requiring a patch and difficulties reducing the liver). Complications in 3 patients: 1 small bowel obstruction, 1 perforation of Meckel's diverticulum and 1 partial recurrence treated thoracoscopically. 6 other thoracoscopic procedures in patients aged 2-11 months: 1 required a thoractomy due to ILS and complex vascular abnormality and 1 conversion to laparoscopy because reduction was not possible thoracoscopically. These patients had no complications.	Larger studies reported in Table 2
Arca MJ, Barnhart DC, Lelli JL, Jr. et al. (2003) Early experience with minimally invasive repair of congenital diaphragmatic hernias: results and lessons learned. [Review] [25 refs]. Journal of Pediatric Surgery 38 (11): 1563-1568.	Case series n = 17 (6 thoracoscopic and aged ≤12 months) Follow-up: 2 – 31 months	One repair started laparoscopically and finished thorascopically due to difficulty moving spleen into the peritoneal cavity. Repair successful in 50% (3/6) of patients. The other 3 patients converted to open procedure due to technical obstacles and anaesthetic complications. Mean operative time: 16 minutes (includes an additional patient aged > 12 months) Complications in successful cases: 1 recurrence at 11 months	Larger studies reported in Table 2

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
		(due to hernia sac not being completely excised. Patient had a second thoracoscopic repair using a collagen patch and was asymptomatic 6 months later) 1 colon perforation (puncture repaired during procedure) Complications in unsuccessful cases: 1 death at 1 year of age (reason not reported, procedure performed at 21 days after birth. This patient had a 'prohibitively large' spleen and had a 10 day course of ECMO preoperatively)	
Liem NT. (2003) Thoracoscopic surgery for congenital diaphragmatic hernia: a report of nine cases. Asian Journal of Surgery 26 (4): 210-212.	Case series n = 9 (6 aged ≤12 months) Follow-up: 3 months	All 6 were left-sided hernia repairs. Operative time: 45–90 minutes. All patients had a normal chest X-ray and clinical examination at 3 months.	Larger studies reported in Table 2
Yang EY, Allmendinger N, Johnson SM et al. (2005) Neonatal thoracoscopic repair of congenital diaphragmatic hernia: selection criteria for successful outcome. Journal of Pediatric Surgery 40 (9): 1369-1375.	Case series / reports n = 7 Follow-up: 1 – 22 months (outpatient follow-up)	All successfully repaired. 3 patients had intraoperative respiratory acidosis which was reversed with ventilator changes. Mean operative time: 152 minutes Length of hospitalisation: 5–32 days. 1 recurrence 10 months after procedure. No other long-term complications.	Larger studies reported in Table 2
Becmeur F, Jamali RR, Moog R et al. (2001) Thoracoscopic treatment for delayed presentation of congenital diaphragmatic hernia in the infant. A report of three cases. Surgical Endoscopy 15 (10): 1163-1166.	Case report n = 3 (2 aged ≤12 months Follow-up: 19 months and 1 year	Operative time: 85 and 95 minutes. Both had a smooth and uncomplicated postoperative course. Oral intake resumed 24 hours after the procedure. Both discharged at day 5. One patient had a normal chest X-ray and clinical examination at 1 year and the other patient had normal chest X-rays and normal diaphragmatic motion (confirmed by ultrasonography at 19-month follow-up)	Larger studies reported in Table 2

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Rozmiarek A, Weinsheimer R., and Azzie G. (2005) Primary thoracoscopic repair of diaphragmatic hernia with pericostal sutures. Journal of Laparoendoscopic & Advanced Surgical Techniques Part (6): 667-669.	Case report n = 2 Follow-up: 18 months and 6 months	Both tolerated the procedure well and had uneventful postoperative recoveries. At first postoperative visit one patient had minimal costal retraction which resolved by 18-month follow-up (confirmed clinically and radiologically). Other patient had recurrence at 5 months which was repaired using an open procedure. No evidence of further recurrence 6 months after open procedure.	Larger studies reported in Table 2
Schaarschmidt K, Strauss J., Kolberg-Schwerdt A. et al. (2005) Thoracoscopic repair of congenital diaphragmatic hernia by inflation-assisted bowel reduction, in a resuscitated neonate: a better access? Pediatric Surgery International 21 (10): 806-808.	Case report n = 1 Follow-up: 22 months	Operative time: 65 mins Well tolerated procedure without perioperative deterioration. Patient well at 22 months	Larger studies reported in Table 2
Liem NT, Dien T.M., and Ung N.Q. (2010) Thoracoscopic repair in the neonatal intensive care unit for congenital diaphragmatic hernia during high-frequency oscillatory ventilation. Journal of Laparoendoscopic & Advanced Surgical Techniques Part (1): 111-114.	Case report n = 1 Follow-up: 1 month	Operative time: 60 mins Intraoperative course was uneventful Normal chest X-ray at follow-up	Larger studies reported in Table 2
Szavay PO, Drews K., and Fuchs J. (2005) Thoracoscopic repair of a right-sided congenital diaphragmatic hernia. [Review] [14 refs]. Surgical Laparoscopy, Endoscopy & Percutaneous Techniques 15 (5):	Case report n = 1 Follow-up: discharge from hospital	Right-sided hernia repair Operative time: 60 mins Uneventful procedure and postoperative course. Patient discharged at 1 week.	Larger studies reported in Table 2

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
305-307.			
Shah SR, Gittes GK, Barsness KA et al. (2009) Multimedia article. Thoracoscopic patch repair of a right-sided congenital diaphragmatic hernia in a neonate. Surgical Endoscopy 23 (1): 215.	Case report n = 1 Follow-up: not reported	Right-sided Bochdalek hernia repair Successful repair using a polytetrafluroethylene patch	Larger studies reported in Table 2 Abstract only
Liem NT, Dien TM, Ung NQ (2010) Thoracoscopic repair in the neonatal intensive care unit for congenital diaphragmatic hernia during high-frequency oscillatory ventilation. Journal of Laparoendoscopic and Advanced Surgical Techniques 20: 111-114.	Case report n = 1 Follow-up: 2 months (approx)	Successful repair of CDH. Patient had prolonged vomiting after surgery. Laproscopy at day 27 showed an adhesion between the liver and greater curve of the stomach. The adhesion was released laparoscopically and patient discharged at day 35. Patient growing and developing normally 1 month after discharge.	Larger studies reported in Table 2
Said SM, Moir CR, Ishitani MB et al. (2010) Successful thoracoscopic staged repair of bilateral congenital diaphragmatic hernia. Journal of Pediatric Surgery 45: E5-E8.	Case report n = 1 Follow-up: 12 months	Patient required 2 separate thoracoscopic repairs at 6 days and 8 days after birth. Patient discharged 5 days after last procedure and no recurrence reported within 12 months.	Larger studies reported in Table 2

Appendix B: Related NICE guidance for thoracoscopic repair of congenital diaphragmatic hernia in neonates

There is currently no NICE guidance related to this procedure.

Appendix C: Literature search for thoracoscopic repair of congenital diaphragmatic hernia in neonates

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	30/09/2010	September 2010
Database of Abstracts of Reviews of Effects – DARE (CRD website)	30/09/2010	n/a
HTA database (CRD website)	30/09/2010	n/a
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	30/09/2010	September 2010
MEDLINE (Ovid)	30/09/2010	1950 to September Week 3 2010
MEDLINE In-Process (Ovid)	30/09/2010	September 29, 2010
EMBASE (Ovid)	30/09/2010	1980 to 2010 Week 38
CINAHL (NLH Search 2.0 or EBSCOhost)	30/09/2010	n/a
Zetoc	30/09/2010	n/a

Websites searched on 23/03/2010

- National Institute for Health and Clinical Excellence (NICE)
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – surgical (ASERNIP-S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- Conference websites
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

MEDLINE search strategy

The MEDLINE search strategy was adapted for use in the other sources.

1	Hernia, Diaphragmatic/cn [Congenital]
2	(congenit* adj3 diaphra* adj3 hernia*).tw.
3	CDH.tw.
4	1 or 2 or 3
5	newborn*.tw.
6	Infant, Newborn/
7	infant/
8	Child/
9	(infant* or child* or neonat*).tw.
10	or/5-9
11	4 and 10
12	(thoracoscop* adj5 congenit* adj5 diaphragmat* adj5 hernia* adj5 repair*).tw.
13	(thoracoscop* adj3 CDH adj3 repair*).tw.
14	exp Thoracoscopy/
15	thoracoscop*.tw.
16	14 or 15
17	Hernia, Diaphragmatic/
18	(diaphragmat* adj3 hernia*).tw.
19	17 or 18
20	(thoracoscop* adj3 repair*).tw.
21	16 and 19
22	12 or 13 or 20 or 21
23	11 and 22