

Early surgical complications after congenital diaphragmatic hernia repair by thoracotomy vs. laparotomy: A bicentric comparison☆

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ABSTRACT

Purpose: The surgical strategy for congenital diaphragmatic hernia (CDH) repair remains debated and mainly depends on the training and preference of the surgeon. Our aim was to evaluate the occurrence and nature of surgical reinterventions within the first year of life, following repair through thoracotomy as compared to laparotomy.

Methods: This is a retrospective bi-centric cohort study comparing postero-lateral thoracotomy (n = 55) versus subcostal laparotomy (n = 62) for CDH repair (IRB: MP001882). We included neonates with isolated, left-sided, Bochdalek-type CDH who were operated on between 2000 and 2017, and had a minimum follow-up of 1 year. Excluded were patients treated prenatally and/or had extra-corporeal membrane oxygenation. Outcomes were occurrence and nature of surgical reinterventions and mortality by 1 year of life.

Results: Both groups had comparable neonatal severity risk profiles. The overall surgical reintervention rate by 1 year of age was higher in the thoracotomy group (29.1% vs. 6.5%; p = 0.001), mainly because of a higher prevalence of acute bowel complications (18.1% vs. 3.2%; p = 0.012) requiring surgery, such as perforation, obstruction and volvulus. At 1 year of follow-up, groups were similar in terms of recurrence (5.5% vs. 1.6%; p = 0.341), surgical interventions related to severe gastroesophageal reflux disease (3.6% vs. 1.6%; p = 0.600) and mortality (5.5% vs. 6.6%; p = 1.000).

Conclusion: Postnatal CDH repair through thoracotomy was associated with a higher rate of surgical reinterventions within the first year of life, especially for severe acute gastro-intestinal complications. There seemed to be no difference in recurrence and mortality rate.

Type of Study: Retrospective Comparative Cohort Study.

Level of Evidence: Level III.

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Congenital diaphragmatic hernia (CDH) is a rare disease that is life-threatening (incidence 2.62/10,000 births; ORPHA-code: 2140), resulting from the failed closure of the pleuro-peritoneal folds and the transverse septum during the 8th to 12th gestational week, leading to a defect in the diaphragm [1]. Most hernias (90%) are Bochdalek-type, involving the posterolateral region of the diaphragm. They are most commonly left-sided (85%) [2]. The herniation of abdominal organs into the chest interferes with normal lung development eventually leading to pulmonary parenchymal and vascular hypoplasia. At birth,

this leads to variable degrees of respiratory insufficiency and pulmonary hypertension. Despite optimal neonatal care in specialized tertiary centers, mortality rates of up to 30% are still being reported [3].

Ideally, birth takes place at a specialized tertiary care center, for immediate stabilization and standardized neonatal management [4]. Once stable, surgical repair of the diaphragmatic defect can be performed by either closing the defect primarily or by means of a patch to reconstruct the diaphragm.

Although historically open surgical repair was mostly performed through thoracotomy, nowadays the majority is performed through laparotomy (95%) [5, 6]. Recently, minimally invasive approaches have been used for CDH repair with a revival of a thoracic access [7]. We wanted to determine the occurrence rate and nature of complications in an unselected population undergoing either laparotomy to thoracotomy. Theoretically, one may expect a difference in complications due to

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a different incision site, difference in visualization of the defect as well as the evaluation of the viscera prior and after reduction [8]. Such comparison may be relevant as it may determine a pattern of access-specific complications that may resurface as minimal access thoracic repair is increasingly being performed.

Such comparison may be very difficult, as most centers are traditionally choosing for one or another technique or do so based on specific patient characteristics. In order to exclude as much as possible selection bias, we embarked on a retrospective study comparing complications within 1 year of surgery, at two centers within the European Reference Network on Inherited and Congenital Anomalies of the thorax (ERNICA) [9]. During the study period these centers performed preferentially either a posterolateral thoracotomy or subcostal laparotomy for the initial neonatal repair of the defect.

1. Material and methods

This is a bi-centric, retrospective cohort study comparing posterolateral thoracotomy (TT) as practiced in the University Hospitals Leuven, to subcostal laparotomy (LT) repair which was the standard in Great Ormond Street Hospital (GOSH), London.

Included were all patients with left-sided Bochdalek type CDH who underwent neonatal (<28d of life) surgery during a 16-years period from 2000 (GOSH) or 2001 (Leuven) onwards and in whom post-discharge follow-up was available at least until 1 year of age or had died before. Excluded were patients with Morgagni defects, right sided or bilateral defects, eventrations, patients operated on via minimally invasive approach and those with associated major structural or genetic anomalies. Conditions that independently lead to additional morbidity or mortality were considered as major anomalies. Hence, patients with smaller atrial or ventricular septum defects or patent ductus arteriosus were not excluded. Patients who underwent prenatal Fetoscopic Endoluminal Tracheal Occlusion (FETO) [10, 11] and any use of Extracorporeal Membrane Oxygenation (ECMO) were also excluded, as these potentially impact outcome independently [12]. Exclusion of these specific patients was performed to decrease heterogeneity of patient profiles between centers.

To retrospectively assess the nature case mix, patients were post hoc stratified according to the validated severity indicators proposed by the Congenital Diaphragmatic Hernia Study Group (CDHSG) [13, 14]. The CDHSG-score is a compound of the APGAR-score at 5 min, birth weight, the presence of pulmonary hypertension and association of any major cardiac or chromosomal anomalies (Fig. 1). The score subdivides patients in three severity groups; i.e. with a low (<10%), intermediate (~20%) or high mortality risk (~50%).

Neonates were operated on after initial stabilization, as suggested in the guidelines for the standardized management of CDH-patients defined by the EuroCDH-consortium [15]. During the study period, repairs were done by three thoracic surgeons with pediatric surgical expertise for this condition in the TT group (pediatric surgery is not a formally recognized discipline in Belgium), and by six pediatric surgeons in the LT group. In Leuven, the repair was performed through a low left posterolateral thoracotomy. For that, the patient was installed in contralateral decubitus position and an incision was made above the eighth or ninth rib. After manual reduction of abdominal organs, the diaphragmatic

rim (if present) was dissected and the defect closed in a tension-free fashion, either primarily using non-absorbable monofilament polypropylene suture (Prolene 4/0, Ethicon, Zaventem, Belgium) or with a Gore polytetrafluoroethylene (PTFE) dual mesh (thickness 1 mm, W.L. Gore & Associates, Flagstaff, AZ, USA), at discretion of the surgeon. In case of complete absence or insufficient tissue at the diaphragmatic rim, pericostal sutures were applied. All patients routinely had a thoracic drain (12Ch) postoperatively. In London, repair was performed through an ipsilateral subcostal laparotomy. For that, the patient was installed in the supine position and a transversal incision was made. After manual reduction of abdominal organs, the diaphragm was either primarily sutured tension-free as above, or reconstructed with a polyethylene terephthalate mesh (Dacron, Thickness, DuPont, Wilmington, DE, USA) or a PROLENE® 3D Patch polypropylene mesh (Ethicon, San Lorenzo, PR) at discretion of the surgeon. In London no thoracic drains were routinely left.

Data were collected through hand-search in individual medical records and operative notes. Data included: (1) *prenatal data*: prenatal diagnosis, (2) *neonatal data*: gender, gestational age and weight at birth, APGAR score at 5 min, occurrence of severe pulmonary hypertension at 24 h of life, as determined by cardiac ultrasound showing a predominant unidirectional right to left cardiac shunt [16], (3) *surgical data*: age at repair, type of defect according to the Congenital Diaphragmatic Hernia Study Group (CDHSG)-defect classification [17] (for patients undergoing repair before 2013, defects were graded post-hoc based on operative notes), patch-use and/or use of pericostal sutures, nature and occurrence of surgical complications during NICU-stay, (4) *follow-up* after discharge data: length of follow-up, nature and occurrence surgical reinterventions or death between initial repair and 1 year of life.

The primary outcome was the need for surgical reintervention within the first year of life, for any complication that led to reintervention under general anesthesia (Clavien-Dindo IIIb), that was life-threatening (Clavien-Dindo IV) or that caused death (Clavien-Dindo V) [18]. They were *post-hoc* categorized as either acute gastro-intestinal complications such as volvulus, intestinal perforations, bowel obstructions (irrespective of the nature or location), incisional complications, recurrences or surgical interventions for severe gastro-esophageal reflux disease (GERD). The secondary outcome measure was mortality within the first year of life.

Data are reported as percentages for categorical variables and, either as means and standard deviation or medians and quartiles (Q1,Q3) for continuous variables, depending on the normality of the distribution assessed with D'Agostino-Pearson's test. Univariate analyses (Chi-square, Fisher's exact, unpaired T- and Mann-Whitney U-test) were performed with Graphpad (Version 8.1.1, San Diego, California), and statistical significance was defined as $p < 0.05$. Post-hoc power analysis was performed using the web-based Sealed Envelope™ (Sealed Envelope Ltd. 2012) power calculator for binary outcome superiority trials [19]. Missing data were mentioned and the denominator adjusted accordingly. This study was approved by the local ethics committee in Leuven (MP001882) and it was registered in London as a clinical audit (2268). Outcomes are reported according to the STROBE guidelines for case-control studies [20].

2. Results

Fig. 2 displays the patient turnover at both centers during the study period, the number of patients included and lost to follow-up. There was no follow-up available at 1 year of age in 22 patients, hence they were excluded. Exclusion rates were comparable for both centers (6/61 vs. 16/78; $p = 0.104$). Those 22 patients had a comparable profile of CDHSG-scores as compared to the 117 patients in whom follow-up was available (55 in the TT and 62 in the LT group).

Table 1 displays patient demographics. In patients operated in the TT group, a prenatal diagnosis was made more frequently than in patients in the LT group. In both centers, weight and gestational age at delivery were similar, but the APGAR score at 5 min was lower in the TT group.

$$\begin{array}{l}
 1 \text{ (Low birth weight)} \\
 1 \text{ (Low APGAR)} \\
 2 \text{ (Missing APGAR)} \\
 2 \text{ (Severe pulmonary hypertension)} \\
 2 \text{ (Major cardiac anomaly)} \\
 1 \text{ (Chromosomal anomaly)} \\
 \hline
 + \\
 \hline
 \text{Total neonatal CDHSG score}
 \end{array}$$

Fig. 1. CDHSG score calculation by Brindle et al. [13]. Score 0: low risk group, score 1–2: intermediate risk group, score >3: high risk group.

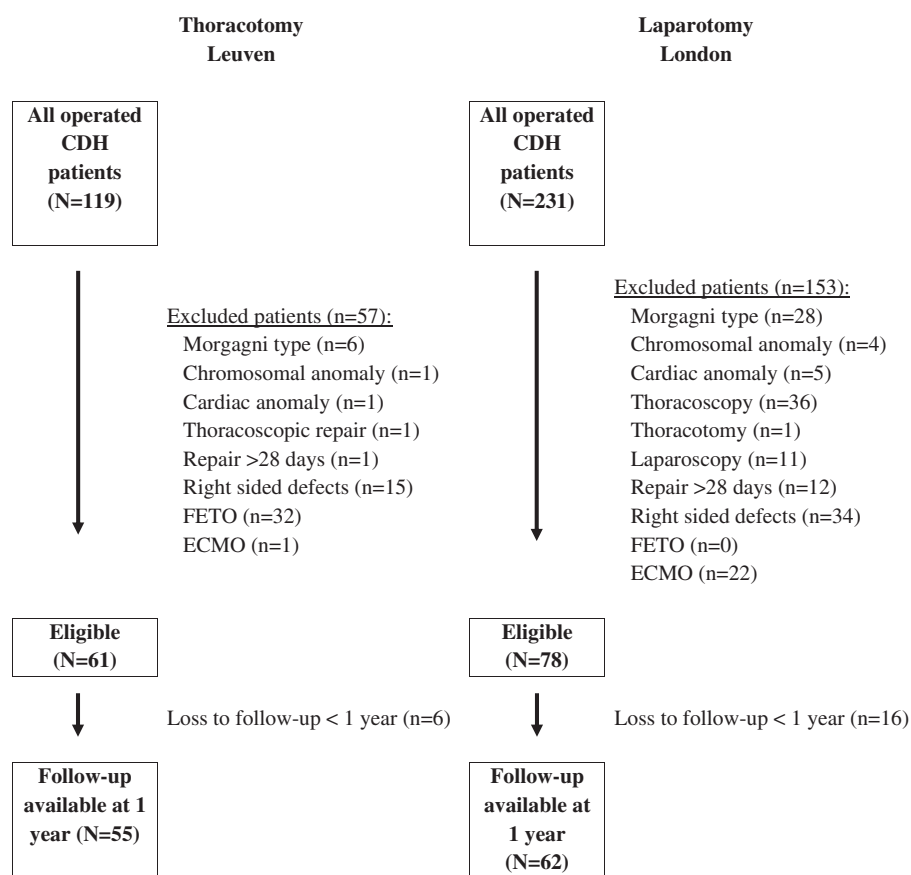


Fig. 2. Patient inclusion flow diagram.

Table 1
Demographics.

	Thoracotomy (n = 55)	Laparotomy (n = 62)	p-Value
Prenatal data			
Prenatal diagnosis	80.0% (44/55)	53.2% (33/62)	0.003
Neonatal data			
Male gender	61.8% (34/55)	66.1% (41/62)	0.701
GA at birth (weeks, median, Q1-Q3)	37.5 (34.0–38.0)	38.5 (37.0–40.0)	0.949
Birth weight (g, median, Q1-Q3)*	2830 (2250–3260)	3000 (2700–3360)	0.215
Low birth weight (<1500 g)	1.8% (1/55)	3.2% (2/59)	1.000
APGAR score at 5 min (mean, SD)**	6.3 (1.7)	8.6 (1.2)	0.0001
Low APGAR score at 5 min (<7)	41.2% (21/51)	5.4% (2/37)	0.0001
Severe pulmonary hypertension at 24 h	34.5% (19/55)	45.2% (28/62)	0.263
CDHSG-score risk groups:			
Low risk (score 0)	47.3% (26/55)	39.0% (23/59)	0.450
Intermediate risk (score 1–2)	25.5% (14/55)	35.6% (21/59)	0.310
High risk (score 3–4)	27.3% (15/55)	25.4% (15/59)	0.835
Surgical data			
Age at surgical repair (days, median, Q1-Q3)	3 (2–5)	5 (2–8)	0.001
CDHSG – defect classification§			
Type A	23.1% (12/52)	35.5% (22/62)	0.158
Type B	53.8% (28/52)	30.6% (19/62)	0.037
Type C	17.3% (9/52)	27.4% (17/62)	0.264
Type D	5.8% (3/52)	6.4% (4/62)	1.000
Patch use	67.3% (37/55)	40.3% (25/62)	0.005
Pericostal suture	56.4% (31/55)	41.9% (26/62)	0.140

Legend: Missing values: (*) Birth weight; 3 (LT), (**) APGAR scores at 5 min; 25 (LT) and 4 (TT), (§) CDHSG-defect classification; 3 (TT).

The APGAR score at 5 min in the LT group was only documented in 59.7% (vs. 92.7% in the TT group; $p = 0.0001$). Despite these differences, the frequency distribution of CDHSG-scores between groups was comparable ($\chi^2 = 1.445$, $p = 0.486$). On average, patients in the TT group were operated on 2 days earlier than in the LT group (d3 vs. d5; $p = 0.001$).

In the TT group, three patients had no reported defect classification in the operation notes. The distribution of defect types was similar, except that there were more “B” type defects in the TT group (53.8% vs. 30.6%; $p = 0.037$). Significantly more patch repairs were done in the TT group (67.3% vs. 40.3%; $p = 0.005$). Patch-use was similar per defect type for “A”, “C” and “D” types. “B” type defects however, were more often repaired with a patch in the TT group (78.6% vs. 36.8%; $p = 0.006$) (Table 2). The use of peri-costal sutures was equally frequent between groups.

The number of surgical reinterventions during the first year of life was higher in the TT group (29.1% vs. 6.5%, $p = 0.001$). The nature of these complications is displayed in Table 3.

More than half of the reinterventions were due to **acute gastrointestinal complications** (Clavien-Dindo IIIb & IV) which were more often seen after thoracotomy repair (18.1% vs. 3.2%; $p = 0.012$). In the TT group there were three reoperations where the perioperative

Table 2
Patch-use per CDH defect-type.

Defect type:	Thoracotomy (n = 55)	Laparotomy (n = 62)	p-Value
A	0.0% (0/12)	0.0% (0/22)	1.000
B	78.6% (22/28)	36.8% (7/19)	0.006
C	100.0% (9/9)	82.4% (14/17)	0.529
D	100.0% (3/3)	100.0% (4/4)	1.000

Table 3

Profile of complications requiring surgery during the first year of life.

	Thoracotomy (n = 55)					Laparotomy (n = 62)					p-Value
	Proportion	Defect	Repair	Time (POD)	Details	Proportion	Defect	Repair	Time (POD)	Details	
Primary outcome:											
All surgical reinterventions	29.1% (16/55)					6.5% (4/62)					0.001
Acute gastrointestinal complications	18.1% (10/55)					3.2% (2/62)					0.012
■ Volvulus	5.5% (3/55)	A	Primary	2	Ileum	/					/
		B	Primary	3	Ileum						
		B	Patch	147	Ileum						
■ Perforation	3.6% (2/55)	B	Patch	5	Ileum	1.6% (1/62)	C	Primary	9	Duodenum	/
		C	Patch	5	Colon						
■ Obstruction	9.1% (5/55)	B	Patch	31	Colon	1.6% (1/62)	C	Patch	65	Duodenum	/
		C	Patch	45	Stomach (\$\$)						
		B	Patch	75	Stomach						
		B	Patch	113	Ileum						
		B	Patch	209	Stomach						
Recurrence	5.5% (3/55)	B	Patch	6 (\$)		1.6% (1/62)	A	Primary	179		0.341
		B	Patch	85							
		A	Primary	124							
Surgery for GERD	3.6% (2/55)	B	Patch	37	Nissen	1.6% (1/62)	B	Primary	130	Nissen	0.600
		B	Patch	44	Nissen						
Other	1.8% (1/55)	B	Primary	6	Textiloma	/					0.470
Secondary outcome:											
Postsurgical mortality within 1 year of age	5.5% (3/55)	B	Patch	5	Stroke	6.5% (4/62)	C	Primary	12	Resp. Fail.	1.000
		C	Patch	77	Resp. Fail.		B	Primary	17	Resp. Fail.	
		D	Patch	8	Resp. Fail.		D	Patch	142	Resp. Fail.	
							C	Patch	356	NA	

Legend: GERD = gastro-esophageal reflux disease, POD = postoperative day, NA = not available, Resp. Fail. = respiratory failure. (\$) Small bowel obstruction POD 147, (**) Roux-en-Y jejunostomy POD 45 and Nissen fundoplication day 363. P-value comparing proportions of two groups.

diagnosis was **volvulus** with no underlying malrotation. In two early (<d3 postoperatively) cases of midgut volvulus, bowel resection was required. In a third case, 147 days after initial repair, adhesiolysis and detorsion was performed. This did not occur in the LT group. There were in total three **perforations** within 9 days after surgery, two in the TT group (one in the jejunum, one in the colon) and one in the LT group (duodenum).

Six patients were operated on for **adhesive obstruction**, all between d30 and d209 postoperatively, and all repaired with a patch. Five were confined to the TT group, of which three had an obstruction at the level of the stomach, and the others either at the small bowel or colon. In all five patients the obstructed intestines were adherent to the patch. There was one patient in the LT group with obstructive peri-duodenal adhesions, with no involvement of the patch. Adhesiolysis was performed and one patient had a Roux-en-Y gastro-jejunostomy for gastric outlet syndrome (d45) and later a fundoplication (d363). In another patient, a left-behind gauze, required surgical removal on post-operative day 6.

There were four **recurrences** (Clavien-Dindo IV) (5.5% (TT) vs. 1.6% (LT); $p = 0.341$). The one patient who was operated by laparotomy, had a primarily sutured-repair of an "A" type defect, yet recurred on day 179. The other three were in the TT group. One was operated on day 6 after a patched "B"-type defect; one on day 85, also for a patched "B" type defect; and one was operated on day 124 for a primarily repaired "A" type defect. The patient with the early recurrence later had a reintervention for adhesive bowel obstruction.

Three patients were re-operated within the first year of life for **severe gastro-esophageal reflux** issues (Clavien-Dindo IIb). They had a fundoplication on day 37 and 44 (TT group), and on day 130 (LT group).

The **mortality** (Clavien-Dindo V) during the first year of life was comparable (overall it was 6%). All deaths were due to persistent pulmonary hypertension and/or respiratory failure. Massive hemorrhagic stroke led to withdrawal of care in one patient.

3. Discussion

We compared the rate of surgical reinterventions within 1 year of life in patients operated at two centers, primarily either via thoracotomy

or laparotomy. We found that infants operated via thoracotomy were more likely to be re-operated within the first year of life, mainly because of acute gastrointestinal complications.

Reportedly, only 1–5% of pediatric surgeons repair left-sided CDH via thoracotomy [6, 8, 21]. However, the thoracic approach has received renewed attention with the advent of minimally invasive techniques for CDH repair [6]. Theoretically, abdominal and thoracic access each has their advantages and disadvantages. Advocates of a **transthoracic approach** argue that the chest wall in combination with the hypoplastic lung create a natural working space, and that exposure of the ribs allows easier placement of pericostal sutures, hence strengthening patch repair [8]. The main disadvantage however is that abdominal organs are reduced blindly, which *in theory* may lead more frequently to gastrointestinal complications. However, these do not seem to be commonly featured in case of minimally invasive approach [22–24]. Increased risk for musculoskeletal deformities (scoliosis, pectus excavatum and carinatum) has also been correlated to thoracotomy in specific [25, 26]. Advantages of an **abdominal approach** are that one can inspect and reposition abdominal organs anatomically under visual control. In case of malrotation, a simultaneous Ladd's procedure can be performed [8]. Disadvantages of the abdominal approach are the long-term risk of incisional hernia and abdominal obstructions due to adhesions [27, 28].

The most frequent surgical reinterventions for acute gastrointestinal complications are volvulus, obstruction by adhesions and bowel perforation. (1) **Volvulus** occurred in three patients in the TT group, while none in the LT group. No underlying malrotation was diagnosed in these cases. Jancelewicz et al. described one volvulus case following thoracoscopic repair ($n = 28$), whereas none following repair by laparotomy ($n = 129$) [25]. Although numbers are low, both experiences may suggest that volvulus is more common after thoracic approach. Especially when volvulus presents early, it may be related to an unanatomical position of the abdominal organs, which was not diagnosed as the surgeon is blinded during reduction. (2) **Adhesiolysis for gastric, small bowel and colonic obstruction** was performed in six patients. All of them underwent patch repair for a "B" or "C"-type defect. Five (9.1%) were in the TT and one in the LT group (1.6%). In the five TT-cases, the intestines were adherent to the PTFE patch. This was not the

case in the LT group, where a Dacron patch was used. The rate of bowel obstruction in this series, is comparable to what is reported in the literature (range 2.9% to 17.6% [22, 28–32]), yet the duration of follow-up in published studies was longer (range 1.0 to 18.8 years) and the case mix different. Jancelewicz et al. found that patch repair was a predictor for bowel obstruction, which our findings confirm [31]. However, they did not observe bowel adherence to the patch, like we observed in the TT group. The type of patch may also affect the rate of post-operative bowel obstruction. The use of a variety of patches has been reported, with only absorbable ones that were associated with an increased risk of small bowel obstruction [31]. (3) **Bowel perforation** was observed in three patients, two in the TT group (3.6%) and one in the LT group (1.6%) and all presenting within 9 days. Cho et al. reported a higher perforation rate, i.e. two after open abdominal approach ($n = 28$) as well as two after thoracoscopic CDH repair ($n = 29$) [29]. **Recurrence** occurred in four patients, equally frequent after repair via thoracotomy and laparotomy (5.5% vs. 1.6%; $p = 0.341$). All four infants involved were born near term (37–40 weeks GA). Two recurrences were after patch repair, the other two after primary closure of the defect. The rate of **reinterventions for GERD** was similar for both approaches, though it may be difficult to determine whether the criteria for these procedures were similar at both centers. We did not observe any **incisional herniation**.

Post-hoc power analysis ($\alpha = 5$, Power = 90%) confirmed that the study was adequately powered for the primary outcome, however not for further sub-group analysis or mortality.

This is a retrospective study comparing two surgical techniques, performed as a primary approach by one of both centers. Even though the included patients in both centers had comparable CDHSG-scores [13, 14], there may be several center-related confounders that could influence difference in outcomes. First, there is an inherent *selection bias*. We excluded the non-Bochdalek and right-sided lesions, as well as ECMO and FETO cases. This was done in an effort to homogenize patients. However, in retrospect, the severity risk profile based on the CDHSG-score of excluded patients was different between centers. One third of TT-patients excluded had a high-risk profile and all those patients had FETO and one had ECMO. In the LT group, all exclusions were for ECMO and only 5% had a high-risk profile.

Furthermore, patients in the TT group were more likely to be diagnosed prenatally, to be repaired earlier, had smaller defects (more type “B”) and were more often repaired by means of a patch. *Prenatal diagnosis* was significantly more common in the TT group. This is usually considered as a severity indicator [33], yet in the present study, one needs to take the centers’ profile into account, i.e. one being a fetal therapy center (Leuven), the other one a postnatal referral center for ECMO therapy (London). Patients in the TT group were also *operated earlier on*. Given that the CDHSG-scores were comparable, this probably points more to local preference, rather than a difference in severity. Both centers followed the same European standardized postnatal management protocol after its publication in 2010 [15]. The *difference in defect size*, may be explained by the fact that fetuses with more severe defects were managed prenatally in one center (TT center) and therefore excluded in this series. Another reason may be that intermediate (type “B” and “C”) lesions were differently allocated, without truly being different. Indeed, the pooled number of “B” and “C” lesions was equal for both centers. Ambiguous allocation of intermediate lesions was earlier demonstrated by Hunter, whereas “A” and “D” lesions are more consistently scored [34]. Usually patch use is correlated to defect size and severity of hypoplasia [35, 36]. The *difference in patch rate* between the two groups, especially in the group with the smaller “B” type lesions, could be a further argument for different allocation of defect size by surgeons of the two centers. However, the difference in patch rate may also point to a difference in practice, or a higher need when repairing via thoracotomy. Finally, this study did not include long-term complications, such as late hernia recurrence and musculoskeletal deformities, which can be access related.

Taking into account the retrospective nature of the study and the limitations above, the authors nevertheless believe there is reason for suspicion that blind reposition of abdominal organs, inherent to the thoracic approach, may increase the risk of volvulus and that patch repair may predispose for bowel obstruction by adhesion formation to the graft.

4. Conclusion

We aimed to evaluate the occurrence and nature of surgical reinterventions within the first year of life following diaphragmatic repair through thoracotomy or laparotomy as primary approach used by two centers. There were more surgical reinterventions following repair via thoracotomy, in particular for severe acute gastro-intestinal complications such as volvulus, perforation and adhesive bowel obstruction. Recurrence, surgical treatment of gastro-intestinal reflux disease and mortality rate seemed not to be different.

Disclosures

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