Minimally invasive versus open repair of Bochdalek hernia: a meta-analysis

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Abstract

Background: Diaphragmatic hernia can be repaired by open or minimally invasive surgery (MIS), although it is unclear which technique has better outcomes. Our objective was to compare the outcomes of these procedures in a systematic review and meta-analysis.

Methods: We sought all publications describing both techniques through MEDLINE, Embase, and CENTRAL. Our primary outcome of interest was recurrence. We conducted statistical analyses using Review Manager 5.2.

Results: We did not identify any randomized controlled trials. Our pooled estimate of results from 10 studies showed that total recurrence was higher after MIS (OR: 2.81 [1.73, 4.56], p < 0.001). Subgroup analyses indicated higher recurrence after MIS for patch repairs (OR: 4.29 [2.13, 8.67], p < 0.001), but not for primary repairs. Operative time was longer for MIS (MD: 55.25 [40.21, 70.28], p < 0.001), while postoperative ventilator time and postoperative mortality were higher after open surgery (MD: 1.33 [0.05, 2.62], p = 0.04; OR: 7.54 [3.36, 16.90], p < 0.001, respectively).

Conclusions: Recurrence rate is higher after MIS than open repair when a patch is used. Operative time is also longer with MIS. Poorer outcomes after open surgery may be a result of selection bias rather than surgical technique. Surgeons should carefully consider the potential morbidity associated with MIS when deciding on a repair method.

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1. Methods

1.1. Literature search

To identify all studies comparing MIS with open surgery for CDH repair, we conducted an electronic search of MEDLINE (1966 onwards), Embase (1980 onwards), and the Cochrane Central Register of Controlled Trials (CENTRAL). We used the keywords “diaphragmatic hernia”, “thoracoscopy”, “laparoscopy”, “minimally invasive surgery”, and “open”. We excluded any studies that did not pertain to humans and children. We also excluded editorials, case reviews, and any studies that did not compare outcomes of MIS with open surgery for Bochdalek-type hernias. Finally, we hand-searched the reference sections of all relevant articles to identify additional studies.

1.2. Quality assessment

1.2.1. Assessment tool

Methodological Index for Non-Randomized Studies (MINORS) [5]:

We used this index to assess the quality of nonrandomized studies. The MINORS criteria comprise 12 items; each item is assigned a score from 0–2, for a maximum score of 24 (comparison studies) or 16 (noncomparison studies). Higher scores are indicative of greater methodological quality.
Two researchers independently assessed each study and compared their scores for each item to reach a consensus. If an agreement could not be reached, they consulted a third researcher.

1.3. Outcomes

Our primary outcome of interest was hernia recurrence after surgery. Secondary outcomes included operative time, total length of stay (LOS), postoperative ventilator time and postoperative mortality.

1.4. Statistical analysis

We conducted our meta-analyses using Review Manager 5.2 [6]. For each outcome, we first assessed the heterogeneity of the studies (Chi^2 test and I^2 statistic). When heterogeneity was low to moderate (Q test \( P > 0.10, I^2 < 50\% \)), we used a fixed-effects model. When heterogeneity was moderate to high (Q test \( P < 0.10, I^2 > 50\% \)), we used a random-effects model [7]. We used weighted mean differences to analyze continuous data and odds ratios to analyze categorical variables.

2. Results

2.1. Study selection

Our initial search of MEDLINE, Embase and CENTRAL yielded 160 studies (Fig. 1). After applying our exclusion criteria, 9 studies remained. We identified one additional relevant study through hand-searching, thus we included 10 studies in total [8–17].

2.2. Study characteristics

We did not identify any randomized controlled trials (RCTs) as all identified studies were retrospective in nature. Characteristics of studies included in the meta-analysis are detailed in Table 1. There were 4730 patients in total (312 MIS, 4418 open surgery). The majority of these patients had undergone surgery within the neonatal period. The minimally invasive technique of choice was thoracoscopic surgery, with only 2 studies reporting laparoscopic repair [16,17].

2.3. Risk of bias in included studies

Two researchers independently assessed each study for methodological quality using MINORS. The score for each study is reported in Table 1. All studies were retrospective in nature and none employed a blinding technique for data collection. Two studies did not use an intention-to-treat analysis [10,11], and 2 studies used historical control groups [8,11]. These methodological biases are reflected in the total scores. The MINORS scores for our included studies ranged from 13 to 16, with a median score of 14.

To address the risk of publication bias, we created a funnel plot for the recurrence outcome (Fig. 2). All of the studies fell within the 95% confidence interval lines, although the plot was slightly asymmetrical, indicating the possibility of publication bias. For the secondary outcomes, there were too few studies reporting on each of these variables to accurately assess the risk of publication bias [18].

2.4. Demographic variables

Within individual studies, most demographic variables did not differ between the MIS and open surgery groups. All studies reported no difference in birth weight, except Fishman et al. [9] and Tsao et al. [17], who reported higher birth weights among MIS patients. Similarly, only 2 studies reported differences in gestational age (GA). Lao et al. [13] found that the open group had a greater GA, while Tsao et al. [17] reported higher GA in the MIS group. Age at surgery was not significantly different between the groups, except in the study by Okazaki et al. [15], where patients in the open surgery group were older. There were no differences in the sex of the patients or the laterality of the hernia. Follow-up time for the MIS group ranged from 1–40 months, while that of the open group ranged from 1–84 months [8–14]. One study [17] followed patients for the initial hospitalization period only and 2 studies [15,16] did not report follow-up time.

2.5. Outcome analysis

2.5.1. Recurrence

There were 10 studies reporting recurrence rates after MIS and open surgery. Three of these studies found no difference between the
2 procedures [8,9,14], while 2 found a higher recurrence rate with MIS [10,17]. There were 4 studies that did not conduct statistical comparisons for this outcome [11,12,15,16] and one study did not find recurrences in either group [13]. In our pooled analysis, we found that recurrence was significantly more likely after MIS than open surgery (OR 2.81 [1.75, 4.56] p < 0.001, Fig. 3A). Similarly, when we performed a subgroup analysis for patch repairs only [9,10,12,14,17], we found that MIS had a significantly higher recurrence rate (OR 4.29 [2.13, 8.67] p < 0.001, Fig. 3B). However, when we examined primary repairs, we found no difference in recurrence between the techniques (OR 2.05 [0.77, 5.45] p = 0.15, Fig. 3C).

We conducted a subgroup analysis examining only patients who did not die postoperatively and obtained the same result as our initial analysis—that recurrence with MIS was significantly more likely than with open surgery (OR 2.45 [1.52, 3.96] p < 0.001, Fig. 3D). This finding was consistent even when we performed a subgroup analysis with only the studies that reported follow-up time ≥ 12 months [10–12,14] (OR 3.21 [1.12, 9.18] p = 0.03, Fig. 3E).

2.5.2. Operative time

We identified 9 studies [8–16] that compared operative time between open surgery and MIS. Individually, almost all the studies found that operative time was longer with MIS [8–14,16], with the exception of Okazaki [15], who found no difference. In our pooled analysis, we found that MIS had a significantly longer operative time than open surgery (mean difference 58.71 min [48.03, 69.39] p < 0.001, Fig. 3F).

2.5.3. Total length of stay (LOS)

We identified 5 studies [8,10–13] that compared open and MIS for total LOS. Most of these studies [8,11,13] did not find a significant difference, although Gander et al. [10] reported a longer LOS after open surgery and Keijzer et al. [12] did not conduct any comparative analyses. In our meta-analysis, we found no difference for LOS between the 2 groups (mean difference 13.82 days [−10.33, 37.96] p = 0.26, Fig. 3G).

2.5.4. Postoperative ventilator time

There were 6 studies that compared postoperative ventilator time between open surgery and MIS [8,10,11,13,16]. Four studies did not find a significant difference [8,10,13,15], while 2 reported longer ventilation time after open surgery [11,16]. Our meta-analysis indicated that open surgery was associated with significantly longer ventilator time (OR 1.33 [0.05, 2.62] p = 0.04, Fig. 3H).

2.5.5. Postoperative mortality

Seven studies compared postoperative mortality rates between the 2 surgical techniques [8–12,15,17]. Individually, 4 studies found no difference [8,10,12,15], while Tsao et al. [17] reported significantly more deaths after open surgery. Gourlay et al. [11] did not conduct statistical comparisons for this outcome and Fishman et al. [9] did not find any postoperative deaths. Our pooled analysis showed that mortality was significantly higher after open surgery than MIS (OR 7.54 [3.36, 16.90] p < 0.001, Fig. 3I).

3. Discussion

Traditionally, CDH repair was performed using an open approach, most often by laparotomy. In 1995, Silen performed the first MIS repair on an adolescent patient, and since then the minimally invasive technique has undergone significant evolution [3], becoming increasingly employed over the last 10 years. However, it is still unclear whether this procedure has better outcomes than the traditional open repair. In our review, we have attempted to answer this question by comparing perioperative and postoperative outcomes between MIS and open repair of CDH.

This is the largest systematic review and meta-analysis comparing the outcomes of MIS and open surgery for the Bochdalek-type CDH. In 2010, Lansdale et al. [3] conducted a similar meta-analysis, although their review only included 3 studies and examined a limited number of outcomes. Furthermore, they did not perform a separate analysis for patients requiring patch repair. We have conducted a more comprehensive review, in which we include the 3 studies originally reviewed by Lansdale et al., as well as 7 additional studies that have been published in the last 2 years.

We found 10 studies comparing recurrence rates between MIS and open surgery for CDH repair. Our analysis revealed that MIS was associated with a higher recurrence rate, which is consistent with the finding of Lansdale et al. [3]. It is possible that we underestimated the recurrences in the open surgery group, owing to the high postoperative mortality (i.e. infants may have died before recurrence could happen).

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**Table 1**

Studies included in meta-analysis.

<table>
<thead>
<tr>
<th>Study</th>
<th>Study period</th>
<th>Location</th>
<th>Type of hernia</th>
<th>Age group</th>
<th>Comparison</th>
<th>MINORS score</th>
</tr>
</thead>
<tbody>
<tr>
<td>McHenry et al., 2010 [14]</td>
<td>2003–2008</td>
<td>London, United Kingdom</td>
<td>Bochdalek</td>
<td>Predominantly neonate</td>
<td>TS (N = 8) vs OS (N = 40)</td>
<td>16</td>
</tr>
<tr>
<td>Okazaki et al., 2010</td>
<td>2007–2009</td>
<td>Tokyo, Japan</td>
<td>All types</td>
<td>Neonate</td>
<td>TS (N = 8) vs OS (N = 13)</td>
<td>14</td>
</tr>
<tr>
<td>Szavy et al., 2012 [16]</td>
<td>2002–2009</td>
<td>Tübingen, Germany</td>
<td>Bochdalek and</td>
<td>Neonate</td>
<td>TS (N = 17), LS (N = 4) vs</td>
<td>13</td>
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<td></td>
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<td></td>
<td>OS (N = 4239)</td>
<td></td>
</tr>
</tbody>
</table>

*Note: Neonate = <28 days old.
*Note: OS = Open surgery, TS = Thoracoscopic surgery, LS = Laparoscopic surgery.*
Fig. 3. (A–I). Forest plots comparing MIS with open surgery for Bochdalek-type hernia. Perioperative and postoperative outcomes include: A) total recurrence, B) patch recurrence, C) primary repair recurrence, D) total recurrence in survivors only, E) total recurrence in studies with follow-up ≥ 12 months, F) operative time, G) total LOS, H) postoperative ventilator time, and I) postoperative mortality. Dichotomous outcomes are reported as odds ratios and continuous outcomes as weighted mean differences. We also report heterogeneity statistics for each outcome (Chi² test and I² statistic).
However, we are confident that this is not the case, as our subgroup analysis examining only the surviving infants yielded the same results—that MIS had a higher total recurrence rate (Fig. 3D). Additionally, some of the studies in our meta-analysis did not report an adequate follow-up time (i.e., at least 12 months), but we do not believe this would have affected our findings, as our results were the same when we included only the studies with follow-up ≥ 12 months (Fig. 3E).

When we conducted a subgroup analysis to examine recurrences within different types of repair (primary and patch repair), we found that the recurrence rate was higher after MIS with patch repair only; for primary repair there was no difference between MIS and open surgery. This finding may be related to the technical difficulty of the MIS procedure. MIS for CDH is still a relatively new technique, and while primary MIS repair seems to have become as effective as open repair, the learning curve to attain technical expertise in performing the MIS patch repair may be responsible for the discrepancy in effectiveness compared to its open counterpart. A further technical limitation of MIS is that this technique may not allow for adequate mobilization of the remaining diaphragm, resulting in less secure patch placements [3]. Consequently, when surgeons are deciding on a treatment approach for CDH, the size of the defect and need for patch repair should be carefully considered. During an MIS repair, if it becomes apparent that a patch will be required, the surgeon should strongly consider converting to an open procedure, in order to minimize the potential for recurrence.

Operative time was significantly longer for MIS than for open surgery. This is consistent with the findings from Lansdale et al. [3].

![Fig. 3. (continued)](image-url)
and is likely indicative of the learning curve associated with MIS. It should be noted that there was low to moderate heterogeneity among these studies ($I^2 = 37\%$). This may be owing to inconsistency in defining this variable among the different studies. Lao et al. [13] were the only authors to give a clear definition of operative time (“time from skin incision to skin closure”); most of the other studies failed to give any definition at all. Thus, operative time in some studies may have been measured from the start of the anesthesia, or even from the time the patient entered the room. Furthermore, there may be slight differences in surgical technique among the studies, which may also account for the heterogeneity in operative time. Nevertheless, the results show that MIS is significantly longer than open surgery.

The longer operative time is highly unfavourable for neonates undergoing MIS, owing to the risk of acidosis and hypothermia from CO$_2$ insufflation [3]. It is thus advisable for surgeons to carefully assess their comfort level with this procedure, as well as the patient’s illness severity, before attempting MIS in this vulnerable population group.

Total LOS did not differ between the groups. However, for infants with CDH, LOS is primarily determined by symptom severity (i.e. pulmonary hypoplasia and persistent pulmonary hypertension) and would not likely be affected by procedure type. There was also considerable heterogeneity among the studies that reported this outcome [8,10–13] ($I^2 = 95\%$). Much of this heterogeneity appears to be owing to the results of Keijzer et al. [12], who reported a significantly longer LOS in the open group ($I^2$ decreased to 0% when this study was removed from the analysis). The increased LOS in these patients may be explained by their disease severity. Keijzer et al. reported that over 60% of the open surgery infants required extracorporeal membrane oxygenation (ECMO) for persistent pulmonary hypertension, compared with 17% and 29% of the open group in the studies by Gourlay et al. [11] and Cho et al. [8], respectively, and 0% in the other 2 studies [10,13], in which patients on ECMO were excluded from analysis.

Postoperative ventilator time and postoperative mortality were both significantly higher after open repair of CDH. This finding may, however, be owing to selection bias rather than a true difference between the operative techniques. Because of the risks associated with MIS, it seems plausible that infants with a poorer prognosis would have been assigned to undergo open repair. Selection bias has been suggested by several studies as an explanation for poorer outcomes after open repair [10,12,16,17]. This is further supported by recommendations of Yang et al. [19], in which thoracoscopic surgery should only be attempted if the patient fulfills the following 3 criteria: 1) stomach and liver in abdomen, 2) patient requires minimal ventilatory support (peak inspiratory pressure < 24 mmHg), and 3) absence of pulmonary hypertension.

### 3.1. Limitations and future directions

Our results should be interpreted with caution owing to the nature of the included studies. All were retrospective and are thus vulnerable to selection bias. As previously mentioned, surgeons may choose the type of procedure based on the patient’s clinical and physiological presentation, and there is a strong tendency to assign open surgery for infants with poorer prognoses. This selection bias may account for the poorer outcomes (i.e., longer postoperative ventilation, greater postoperative LOS, and greater postoperative mortality) in the open group. Another limitation is the heterogeneity in baseline characteristics between the studies owing to the different inclusion criteria of each study. For example, while most studies included patients regardless of whether they had received ECMO treatment, 2 studies excluded patients who had undergone ECMO [10,13], as this may serve as a confounding factor for LOS. Finally, our funnel plot (Fig. 2) indicates the possibility of publication bias. However, this plot may not be an accurate assessment of publication bias, as the number of studies is low ($N = 9$). There were 10 studies originally included in this analysis; but since Lao et al. [13] did not find any recurrences for either MIS or open surgery, we could not include their study into the funnel plot. In order to accurately assess publication bias, the Cochrane Handbook for Systematic Reviews of Interventions recommends that at least 10 studies should be included in the funnel plot [20].

Despite the growing popularity of minimally invasive techniques in pediatric surgery, research comparing MIS versus open repair of CDH is scarce. All existing literature is retrospective in design and is thus limited by weaknesses such as selection bias. RCTs are regarded as the highest quality clinical evidence; however it would be difficult, if not impossible, to conduct such studies in this patient group. At the very least, future research should consist of well-designed, prospective studies to further investigate the benefits and limitations of minimally invasive repair of CDH.

Our results indicate that recurrence of Bochdalek hernia is higher following MIS than open surgery when patch repair is performed. Furthermore, operative time is significantly longer for MIS than for open surgery, which may prove detrimental for this young patient group, owing to the risks of CO$_2$ insufflation in small infants. As such, surgeons should exercise great caution when attempting MIS for CDH repair; ideally, this procedure should be performed by experienced surgeons with a high level of comfort with MIS in this age group.

Furthermore, if it is found intraoperatively that a patch repair is required, surgeons attempting MIS are advised to convert to the open procedure, in order to minimize the risk of recurrence. Currently, our study is the largest meta-analysis comparing outcomes of MIS and open surgery for CDH, and we hope that our results can stimulate and direct further research efforts in this area.

### References