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Review Article

Biologic versus synthetic patches: A systematic review and comparative meta-analysis of repair strategies for neonatal congenital diaphragmatic hernia

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ABSTRACT

Background: Congenital diaphragmatic hernia (CDH) is a severe neonatal condition frequently requiring patch repair, yet the optimal prosthetic material remains contested. Synthetic patches offer structural durability but are associated with foreign body reactions, while biologic patches may promote tissue integration but raise concerns regarding long-term recurrence.

Methods: We conducted a systematic review and meta-analysis of observational studies comparing biologic versus synthetic patch repair in neonates with CDH. Databases were searched through May 2025 per PRISMA guidelines. The primary outcome was hernia recurrence. Secondary outcomes were small bowel obstruction (SBO), mortality, extracorporeal membrane oxygenation (ECMO), length of hospital stay (LOS), and duration of mechanical ventilation. Not all studies reported every secondary outcome; therefore, the number of studies contributing to each pooled analysis varied. Pooled odds ratios (ORs) and mean differences (MDs) were calculated using random-effects models. Risk of bias was assessed via ROBINS-I.

Results: Seventeen studies comprising 608 neonates (biologic: n = 249; synthetic: n = 359) met inclusion criteria. No statistically significant differences were observed in recurrence (OR 2.17, 95 % CI: 0.95–4.96), SBO (OR 2.29, 95 % CI: 0.74–7.05), mortality (OR 1.26, 95 % CI: 0.57–2.79), ECMO use (OR 0.86, 95 % CI: 0.16–4.65), LOS (MD −7.75 days, 95 % CI: −22.68 to 7.18), or ventilation days (MD −5.46, 95 % CI: −19.55 to 8.62).

Conclusions: Biologic and synthetic patches demonstrate comparable short- and mid-term outcomes following neonatal CDH repair. In the absence of clear clinical superiority, prosthesis selection should be individualized based on defect characteristics and perioperative context. High-quality, prospective, multicenter studies are warranted to inform material-specific recommendations.

HIGHLIGHTS

- Seventeen studies including 608 neonates were analyzed (biologic patches: 249; synthetic patches: 359).
- Primary outcome (hernia recurrence) showed no significant difference between biologic and synthetic patches (OR 2.17; 95 % CI: 0.95–4.96).
- Secondary outcomes—mortality, small bowel obstruction (SBO), length of hospital stay (LOS), extracorporeal membrane oxygenation (ECMO) requirement, and duration of mechanical ventilation—also showed no significant differences.
- Most included studies carried a moderate risk of bias, mainly due to confounding and incomplete data.
- Findings suggest patch material alone does not determine outcomes in neonatal CDH repair.
- Supports individualized, patient-specific selection of prosthetic material rather than reliance on assumptions of material superiority.

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1. Introduction

Congenital diaphragmatic hernia (CDH) is a developmental anomaly characterized by failed diaphragmatic formation or fusion during embryogenesis, which allows abdominal viscera to occupy the thoracic cavity. The associated pulmonary hypoplasia and pulmonary hypertension [1] arise from disrupted fetal lung development rather than from post-herniation compression. Despite improvements in prenatal diagnosis, neonatal intensive care and surgical management, CDH remains associated with significant morbidity and mortality, especially in patients with large defects that require patch repair [2,3].

When primary closure is not feasible, surgeons typically use either synthetic materials, such as polytetrafluoroethylene (PTFE) or polypropylene, or biological patches derived from human or animal tissues, such as acellular dermal matrices or small intestinal submucosa [4]. The ideal patch should be durable, biocompatible, resistant to infection, and capable of integrating with native tissue while minimizing the risk of hernia recurrence and other postoperative complications [5].

Synthetic patches offer mechanical strength and wide availability, but have been associated with a higher risk of infection, seroma formation, foreign body reactions, and poor integration with native tissue [6]. Conversely, biological patches are thought to promote remodeling and host tissue ingrowth, potentially reducing infection and promoting long-term integration; however, concerns persist regarding their long-term durability and risk of reherniation [7].

The decision between synthetic and biologic materials remains controversial, as studies comparing their outcomes have yielded inconsistent results, often limited by small sample sizes and heterogeneous methodologies [8,9]. As the selection of prosthetic material may significantly influence both short- and long-term outcomes, a comprehensive synthesis of current evidence is essential to clarify potential differences between materials and support more standardized, data-driven surgical approaches [10].

This systematic review and meta-analysis aims to synthesize the available evidence comparing outcomes between synthetic and biological patches in children undergoing CDH repair. Our objective is to evaluate differences in reherniation rates, postoperative complications, length of hospital stay, and long-term outcomes, thereby guiding evidence-based surgical practice in this high-risk population.

2. Materials and methods

2.1. Search strategy and data extraction

A systematic literature search was conducted in the PubMed and Scopus databases from inception through May 2025, with the following search terms: “neonate”, “congenital diaphragmatic hernia”, “Bochdalek”, “repair”, “patch”, “mesh”, “prosthetic”, “biologic”, “natural”, “absorbable”, “synthetic”, “nonabosrbable”. Additionally, reference lists of included articles and relevant reviews were screened to identify further eligible studies. Two reviewers (ALAM and IEVS) independently screened studies and extracted data using predefined eligibility and data extraction criteria. Discrepancies were resolved by consensus.

2.2. Eligibility criteria

Inclusion in this meta-analysis was restricted to studies that met all the following eligibility criteria: (1) retrospective or prospective cohort design; (2) included neonatal patients undergoing surgical repair for congenital diaphragmatic hernia; (3) compared biologic patch versus synthetic patch repair; (4) reported at least one postoperative outcome of interest; (5) were published in English or Spanish. Studies were excluded based on the following: (1) were case reports; (2) did not include any patients who underwent patch repair; (3) did not specify the type of patch used; (4) lacked reporting of postoperative outcomes; (5) had an overlapping population.

2.3. Outcomes of interest

The primary outcome was hernia recurrence. Secondary outcomes included length of hospital stay (LOS), small bowel obstruction (SBO), mortality, extracorporeal membrane oxygenation (ECMO), and mechanical ventilation days. Chest wall deformity and late (>1 year) recurrence were recognized as clinically meaningful postoperative outcomes. However, these variables were reported infrequently and with considerable heterogeneity in definitions across the included studies. Due to this inconsistency, they could not be reliably pooled in the quantitative meta-analysis and were therefore synthesized qualitatively to maintain methodological rigor.

2.4. Quality assessment

Risk of bias was assessed independently by two reviewers (ALAM and IEVS) using the Cochrane ROBINS-I tool for non-randomized studies. Each study was evaluated across seven domains: confounding, selection of participants, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes, and selection of the reported results. Risk was categorized as low, moderate, serious, or critical. Publication bias was evaluated through visual inspection of funnel plots for each outcome, and by Egger's test.

2.5. Statistical analysis

The systematic review and comparative meta-analysis were performed following the Cochrane Collaboration Handbook [11] and the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement guidelines [12]. All statistical analyses were conducted using RStudio (version 4.4.3; R Foundation for Statistical Computing, Vienna, Austria) [13] with the meta and metafor packages [14,15]. Random-effects model with the DerSimonian–Laird estimator was performed to account for expected clinical and methodological heterogeneity across studies. For dichotomous outcomes, including hernia recurrence, small bowel obstruction, mortality, and ECMO use, odds ratios (ORs) and 95 % confidence intervals (CIs) were calculated. For continuous outcomes, such as length of hospital stay and duration of mechanical ventilation, mean differences (MDs) and 95 % CIs were reported.

Heterogeneity was assessed using the I^2 statistic, with values of 25 %, 50 %, and 75 % considered low, moderate, and high heterogeneity, respectively. Between-study variance was estimated using the τ^2 statistic, and significance of heterogeneity was evaluated with Cochran's Q test. To further assess heterogeneity and robustness, Baujat plots were generated and leave-one-out sensitivity analyses were performed. Statistical significance was defined as a p-value <0.05.

3. Protocol registration

This systematic review was prospectively registered in the PROSPERO international database of systematic reviews under the number: CRD420251149419.

4. Results

4.1. Study selection and characteristics

The initial search strategy yielded 2806 results. After the removal of 1475 duplicate records and 1778 unrelated studies based on title and abstract screening, 113 full-text articles were assessed for eligibility (Fig. 1). Of these, 17 studies met the inclusion criteria and were included in the meta-analysis, comprising a total of 608 neonates who underwent surgical repair of congenital diaphragmatic hernia with either biological or synthetic patches. Among them, 249 patients (40.9 %) underwent repair with biological patch repair, while 359 (59 %) received synthetic patch materials.

All included studies were observational and were published between 2006 and 2021. Sample sizes varied across studies, ranging from 5 to 72 patients per cohort. The types of biological patches used included acellular dermal matrices and small intestinal submucosa, while synthetic materials predominantly consisted of polytetrafluoroethylene (PTFE) and polypropylene. Not all studies reported the specific brand or composition of the patch material.

All studies evaluated at least one of the following outcomes: hernia recurrence, small bowel obstruction, mortality, length of hospital stay, and need for extracorporeal membrane oxygenation. Follow-up durations varied considerably, from immediate postoperative periods to long-term assessments of over 12 months in some cohorts. Baseline characteristics such as defect size, associated anomalies, and preoperative ECMO use were inconsistently reported. A summary of the main characteristics of the included studies is provided in Table 1.

4.2. Meta-analysis of hernia recurrence

The incidence of hernia recurrence was reported in 16 studies [16–30] (Fig. 2). Pooled analysis showed no statistically significant difference in recurrence rates between biologic and synthetic patch repairs (OR 2.17; 95 % CI 0.95–4.96; p = 0.06), although the estimate suggested a trend toward higher recurrence in the biologic patch group. Heterogeneity was moderate (I^2 = 63.3 %). Across all included studies, the crude recurrence rate was 34.7 % in the biologic patch group and 20.1 % in the synthetic patch group. Reported follow-up duration ranged from 12 to 103.2 months (approximately 1–8.6 years), with a median follow-up of 42 months (3.5 years) across studies. There was no consistent difference in follow-up length between biologic and synthetic cohorts.

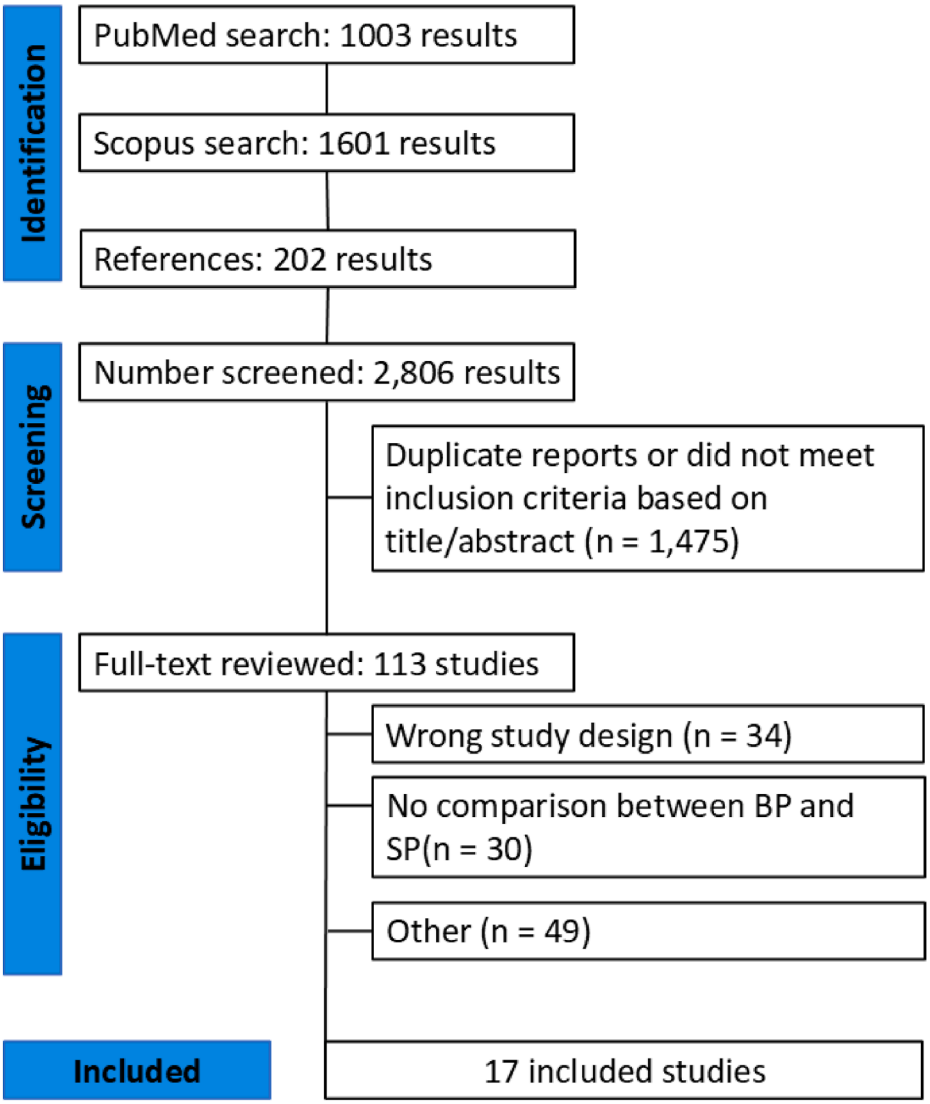


Fig. 1. PRISMA flow diagram of study screening and selection.

Table 1
Baseline characteristics of included studies.

Study	Design	Type of biologic patch	Type of synthetic patch	Patients BP/SP	Follow-up, months BP/SP	Age at surgery, days BP/SP	Left defect (%) BP/SP
Mitchell 2008	Retrospective cohort	Permacol	Gore-Tex	8/29	20 (9–33)/57 (49–73)[a]	18.2 (±54.7)/152 (±562.7)	–
Grethel 2006	Retrospective cohort	Surgisis	Gore-Tex	27/45	–	–	–
Ruhrnschopf 2021	Retrospective cohort	Surgisis	Gore-Tex	18/25	60 ± 23/26 ± 10[b]	11.7 (±5–9)/7.8 (±8.3)	13/9
Nasr 2010	Retrospective cohort	Surgisis	Gore-Tex, Marlex or SILASTIC	5/27	84[c]	–	–
Long 2019	Prospective cohort	Permacol, Tutopatch or Surgisis	Gore-Tex or Polyester	19/34	12[c]	–	–
Laituri 2010	Retrospective cohort	Surgisis or AlloDerm	Gore-Tex or Dacron	42/12	–	–	–
Jancelewicz 2013	Retrospective cohort	Surgisis	Gore-Tex	14/19	81.6 (14–144)[a,c]	–	–
Jancelewicz 2010	Retrospective cohort	Surgisis	Gore-Tex	23/16	76.8 ± 12/90 ± 36[b]	–	–
Barnhart 2012	Retrospective cohort	AlloDerm or DermaMatrix	Gore-Tex	5/5	–	–	–
De Haro 2021	Retrospective cohort	Protexa or Egis	Gore-Tex	8/25	–	–	6
Romao 2012	Retrospective cohort	Surgisis	Gore-Tex	13/9	25.5 (20–48)/38.8 (1–96)[a]	5 (±3.7)/6.8 (±3.2)	12/7
De Kort 1996	Retrospective cohort	Lyophylized dura (1)	Teflon (24) Gore-Tex (5)	1/29	60 mo (mean 70, range 6–146)	–	41/49
St Peter 2007	Retrospective cohort	Surgisis	No specified ("nonabsorbable mesh patches")	13/11	–	Median 4 (IQR 2–7)	–
Jawaid 2013	Retrospective cohort	Surgisis	Gore-Tex	2/35	Median 8.6 years (6.6–11.2)	–	25
Weaver 2016	Retrospective cohort	Surgisis (2) Alloderm (1) Permacol (10)	Gore- Tex (2)	13/2	–	–	–
Tamura 2021	Retrospective cohort	Permacol	Gore-Tex	15/20	–	–	–
Razumovskiy 2016	Comparative analysis	Permacol	Ecoflon	24/16	–	4.0 ± 1.4/2.7 ± 1.8	–

BP, biological patch; SP, synthetic patch.
[a] Median (interquartile range).
[b] Mean ± standard deviation.
[c] Both groups combined.

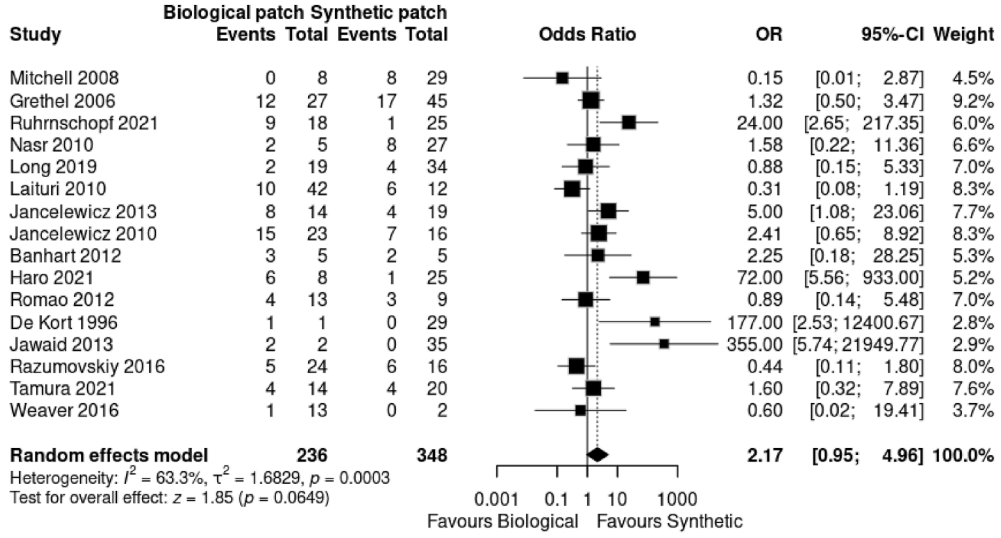


Fig. 2. Forest plot of pooled analysis of diaphragmatic hernia recurrence between the synthetic patch repair and biological patch repair groups. In this graph, squares represent point estimates for individual studies, with black horizontal lines representing 95 % confidence intervals, and diamonds represent aggregated results. The width of the diamond represents the 95 % confidence interval, and the center of the diamond represents the point estimate. It indicates no statistically significant difference between the risk of recurrence in biological patch versus synthetic patch.

4.3. Meta-analysis of small bowel obstruction (SBO)

Seven studies [16–19,23,25,27] reported the incidence of small bowel obstruction (Fig. 3). Meta-analysis revealed no significant difference between biological and synthetic patches (OR 2.29; 95 % CI: 0.74–7.05; $p = 0.14$). Heterogeneity was moderate ($I^2 = 43.3$ %). Across all included studies, the crude incidence of small bowel obstruction was 20.6 % in the biologic patch group and 8.9 % in the synthetic patch group. Reported follow-up duration ranged from 1 to 8.6 years, with a median of 3.5 years across studies. There was

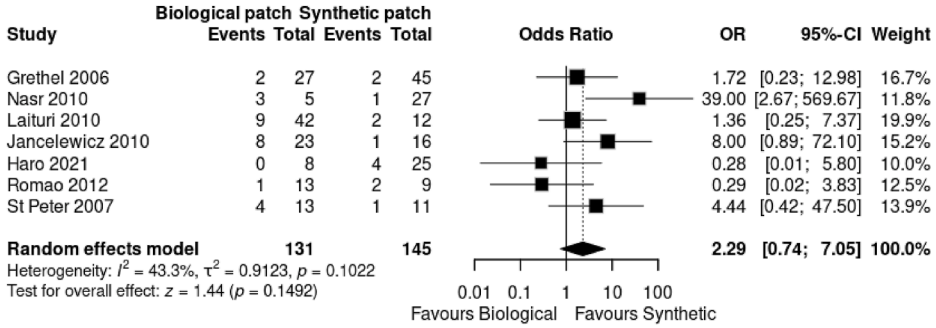


Fig. 3. Forest plot of small bowel obstruction between the synthetic patch repair and open biological patch repair groups. It indicates no statistically significant difference between the risk of small bowel obstruction in biological patch versus synthetic patch.

no consistent difference in follow-up length between biologic and synthetic cohorts.

4.4. Meta-analysis of mortality

Mortality was reported in 6 studies [17,19,21,22,26,30] (Fig. 4). No significant difference was observed between biological patch repair and synthetic patch repair (OR 1.26; 95 % CI 0.57–2.79; p = 0.56). Heterogeneity was low (I^2 = 0.0 %). Most studies did not differentiate mortality by timing (30-day, in-hospital, or late postoperative death). Only overall mortality was consistently reported, limiting the ability to evaluate early versus late deaths or to attribute mortality directly to repair versus underlying pulmonary disease. Across all included studies, the crude incidence of mortality was 20 % in the biologic patch group and 16.4 % in the synthetic patch group. Reported follow-up duration ranged from 1 to 8.6 years, with a median of 3.5 years across studies. There was no consistent difference in follow-up length between biologic and synthetic cohorts.

4.5. Meta-analysis of extracorporeal membrane oxygenation (ECMO)

Postoperative ECMO use was reported in five studies [16,18–21] (Fig. 5). Pooled results showed no significant difference between groups (OR 0.86; 95 % CI: 0.16–4.65; P = 0.85), with substantial heterogeneity observed (I^2 = 71.2 %). Across all included studies, the crude incidence of ECMO use was 28.7 % in the biologic patch group and 28.3 % in the synthetic patch group. Reported follow-up duration ranged from 1 to 8.6 years, with a median of 3.5 years across studies. There was no consistent difference in follow-up length between biologic and synthetic cohorts.

4.6. Meta-analysis of length of hospital stay

Three studies [19,21,22] reported postoperative length of hospital stay (Supplementary Fig. 1). Median LOS in the biologic patch group ranged from 13 to 18 days, compared with 9–26 days in the synthetic patch group. Pooled analysis showed no statistically

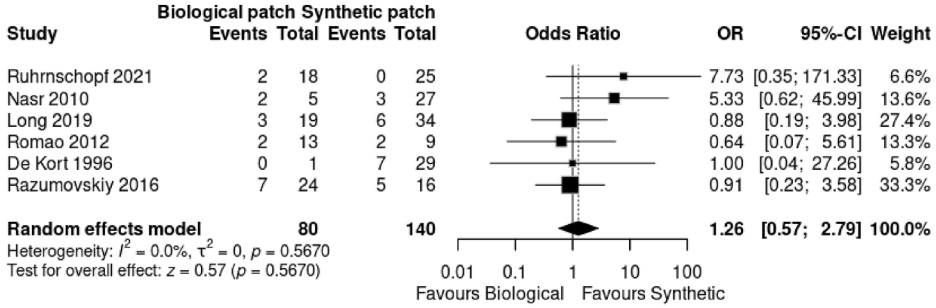


Fig. 4. Forest plot of mortality between the synthetic patch repair and open biological patch repair groups. It indicates no statistically significant difference between the risk of mortality in biological patch versus synthetic patch.

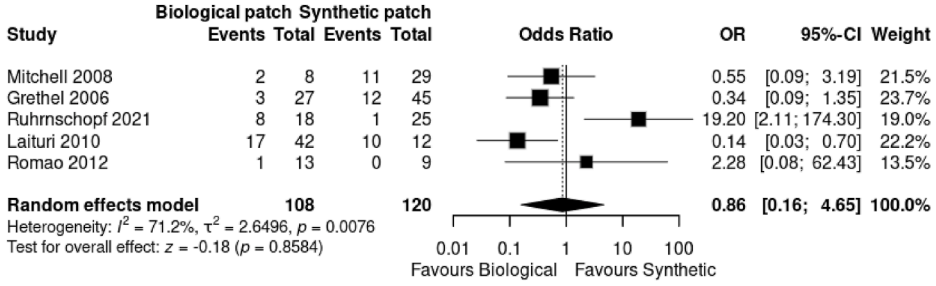


Fig. 5. Forest plot of ECMO requirement between the synthetic patch repair and open biological patch repair groups. It indicates no statistically significant difference between the risk of ECMO requirement in biological patch versus synthetic patch.

significant difference between groups (MD −7.75 days; 95 % CI −22.68 to 7.18; p = 0.31), with minimal heterogeneity (I^2 = 0 %).

4.7. Meta-analysis of mechanical ventilation days

Three studies [16,19,30] reported duration of mechanical ventilation (Supplementary Fig. 2), including 46 biologic and 70 synthetic patch repairs. Median ventilation days ranged from 8 to 24 days in the biologic cohort and 9–45 days in the synthetic cohort. Pooled analysis demonstrated no statistically significant difference between groups (MD −5.46 days; 95 % CI −19.55 to 8.62; p = 0.45), although heterogeneity was substantial (I^2 = 67.2 %).

4.8. Heterogeneity analysis

Baujat plots were generated to explore the contribution of individual studies to heterogeneity and their influence on the pooled effect estimates. For hernia recurrence, Haro 2021 exerted the greatest influence on the overall effect, while Laituri 2010 contributed most strongly to heterogeneity. In the analysis of small bowel obstruction, Nasr 2010 was both the most influential study and the major contributor to heterogeneity, followed by Romao 2012 and Haro 2021. For mortality, Nasr 2010 also emerged as the dominant study, exerting the highest influence on the pooled result and contributing substantially to heterogeneity, whereas Ruhnschopf 2021 had a moderate impact. In the ECMO use analysis, Ruhnschopf 2021 was identified as the most influential study and also accounted for the largest share of heterogeneity. For length of hospital stay, Romao 2012 exerted the greatest influence on the pooled effect, and Ruhnschopf 2021 accounted for most of the heterogeneity. Finally, in the analysis of mechanical ventilation days, Razumovskiy 2016 had the strongest influence on the pooled result, whereas Grethel 2006 was the main contributor to heterogeneity. Most of the remaining studies clustered near the origin of the plots, indicating minimal impact on both heterogeneity and the pooled results. These findings suggest that heterogeneity across outcomes was primarily driven by a limited number of studies, warranting careful consideration in sensitivity analyses. Baujat plots are provided in Supplementary Figs. S3–S8, corresponding to hernia recurrence (Fig. S3), small bowel obstruction (Fig. S4), mortality (Fig. S5), and ECMO use (Fig. S6), length of hospital stay (Fig. S7), and mechanical ventilation days (Fig. S8).

4.9. Sensitivity analysis

Leave-one-out sensitivity analyses were performed for all outcomes to assess the robustness of the pooled results. For hernia recurrence, sequential omission of individual studies did not substantially alter the direction or statistical significance of the pooled effect. Risk ratios ranged from 1.44 (95 % CI, 0.89–2.34; after omitting Jawaid 2013) to 1.89 (95 % CI, 1.03–3.47; after omitting Razumovskiy 2016), with overlapping confidence intervals. The overall heterogeneity remained moderate to high (I^2 range: 58.4 %–66.5 %) and similar to the main analysis (I^2 = 63.3 %). These findings indicate that the overall direction of the association is consistent across studies; however, given the trend toward higher recurrence with biologic patches and the observational nature of included data, these results should be interpreted cautiously.

The leave-one-out sensitivity analysis for small bowel obstruction showed that no single study had a disproportionate influence on the overall pooled estimate. The odds ratios ranged from 1.64 (95 % CI, 0.67–4.02; omitting Nasr 2010) to 3.03 (95 % CI, 1.02–8.98; omitting Romao 2012), with wide and overlapping confidence intervals. Only the exclusion of Romao 2012 resulted in a statistically significant association (OR 3.03, 95 % CI 1.02–8.98; p = 0.046). Heterogeneity was moderate, with I^2 values varying between 13.1 % and 52.4 %, similar to the overall analysis (I^2 = 43.3 %). These findings suggest that the pooled effect for SBO is generally robust, although somewhat sensitive to the omission of Romao 2012.

For mortality, the analysis confirmed the stability of the pooled effect. Excluding individual studies did not materially affect the magnitude or direction of the association, with odds ratios ranging from 1.01 (95 % CI, 0.43–2.36; omitting Nasr 2010) to 1.49 (95 % CI, 0.56–3.93; omitting Razumovskiy 2016). All confidence intervals were wide and crossed the null. Heterogeneity remained absent throughout all iterations (I^2 = 0 %), identical to the overall analysis. These findings demonstrate that the mortality outcome is highly robust and unaffected by the exclusion of any single study.

The leave-one-out sensitivity analysis for ECMO use indicated that results were generally consistent, though somewhat sensitive to the exclusion of a single study. Odds ratios ranged from 0.34 (95 % CI, 0.14–0.81; omitting Ruhrnschopf 2021) to 1.44 (95 % CI, 0.22–9.31; omitting Laituri 2010), with wide confidence intervals crossing the null in most cases. Exclusion of Ruhrnschopf 2021 reduced heterogeneity to 0 % and yielded a statistically significant protective effect of biological patches (OR 0.34, 95 % CI, 0.14–0.81; p = 0.015). In contrast, all other iterations showed substantial heterogeneity (I^2 = 69.7 %–78.4 %) similar to the overall analysis (I^2 = 71.2 %). These findings suggest that while the pooled effect for ECMO use is relatively robust, it may be influenced by the study of Ruhrnschopf 2021.

For length of hospital stay, sensitivity analysis demonstrated highly consistent results. Excluding individual studies produced mean differences ranging from −5.70 days (95 % CI, −23.26 to 11.85; omitting Romao 2012) to −9.32 days (95 % CI, −24.88 to 6.23; omitting Ruhrnschopf 2021), with all estimates overlapping the overall effect (MD −7.75 days, 95 % CI, −22.68 to 7.18). Heterogeneity was absent throughout all iterations (I^2 = 0 %), consistent with the main analysis. These findings confirm the robustness of the pooled estimate for LOS.

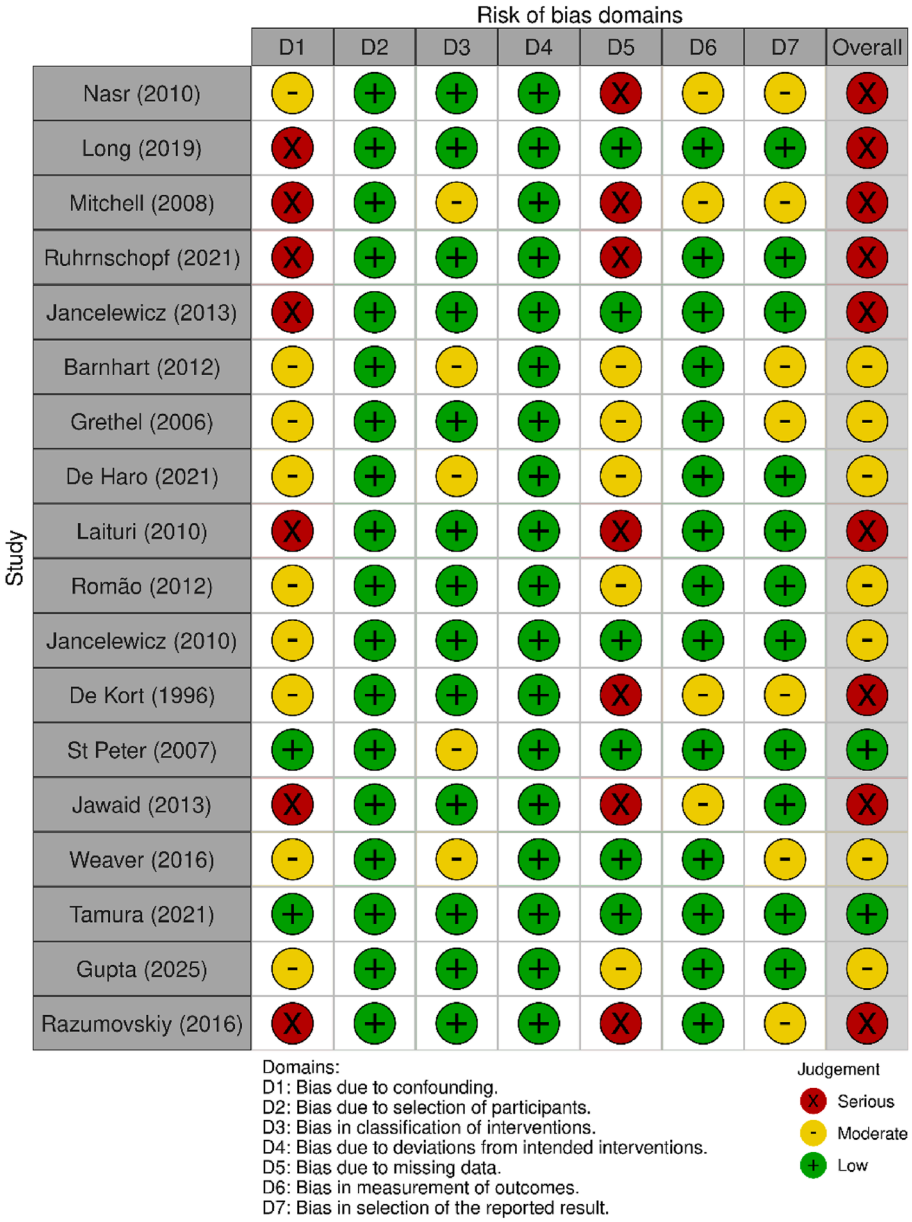
The leave-one-out sensitivity analysis for mechanical ventilation days revealed some variability across iterations. Excluding individual studies yielded mean differences ranging from 0.64 days (95 % CI, −4.21 to 5.49; omitting Grethel 2006) to −11.01 days (95 % CI, −36.48 to 14.47; omitting Razumovskiy 2016). While the overall effect size (MD −5.46 days, 95 % CI, −19.55 to 8.62) remained consistent, heterogeneity varied considerably: I^2 dropped to 0 % when Grethel 2006 was omitted but remained high (78.4 %–83.4 %) when Romao 2012 or Razumovskiy 2016 were excluded. These results indicate that the outcome for MV days is somewhat sensitive to study-level variation, particularly Grethel 2006.

Collectively, these analyses demonstrate that the pooled estimates are overall robust and not disproportionately influenced by any individual study, with minor exceptions observed for SBO, ECMO, and MV days. Leave-one-out sensitivity analysis are provided in Supplementary Figs. S9–S14, corresponding to hernia recurrence (Fig. S9), small bowel obstruction (Fig. S10), mortality (Fig. S11), and ECMO (Fig. S12), length of hospital stay (Fig. S13), and mechanical ventilation days (Fig. S14).

4.10. Quality assessment

Individual appraisal of each study included in the meta-analysis is shown in Table 2. The risk of bias for the included studies was assessed across seven domains using the Risk of Bias in Non-Randomized Studies of Interventions (ROBINS-I) tool. The

Table 2
Quality assessment of included studies.



summary table was generated using the *robvis* package in R (McGuinness & Higgins, 2020) [31]. Most studies were judged to have low to moderate risk of bias in key domains, particularly in the bias due to selection of participants (D2), classification of interventions (D3), deviations from intended interventions (D4), measurement of outcomes (D6), and selection of the reported result (D7). However, serious risk of bias due to confounding (D1) was identified in seven studies, and missing data (D5) was a common concern, leading to serious risk in seven studies. Overall, nine studies were rated as having serious risk of bias, primarily due to confounding and incomplete outcome data. Seven studies were judged as having moderate overall risk, and the remaining two studies were judged as having a low overall risk.

Funnel plots for all outcomes, including hernia recurrence, small bowel obstruction (SBO), mortality, and ECMO, did not demonstrate clear evidence of publication bias. For SBO and mortality, the plots appeared symmetrical and Egger's regression test was non-significant ($p = 0.98$ and $p = 0.30$, respectively). For hernia recurrence and ECMO, visual inspection suggested a possible tendency toward asymmetry; however, Egger's test did not reach statistical significance ($p = 0.07$ and $p = 0.27$, respectively). These findings suggest a low risk of small-study effects or selective publication, although interpretation is limited by the small number of studies included for each outcome (all with $n < 15$, and most with $n < 10$), which reduces the statistical power to detect asymmetry. The analyses for length of hospital stay and mechanical ventilation days were based on fewer than five studies each, precluding formal statistical testing; visual inspection did not reveal consistent asymmetry, although interpretation is strongly limited by the small number of available studies. Funnel plots are provided in Supplementary Figs. S15–S20, corresponding to hernia recurrence (Fig. S15), small bowel obstruction (Fig. S16),

mortality (Fig. S17), and ECMO (Fig. S18), length of hospital stay (Fig. S19), and duration of mechanical ventilation (Fig. S20).

5. Discussion

5.1. Summary of our results

In this systematic review and meta-analysis of 17 observational studies comprising 608 neonates undergoing CDH repair with either biological or synthetic patches, we found no statistically significant differences in the rates of hernia recurrence, small bowel obstruction (SBO), mortality, ECMO use, or length of hospital stay. Although synthetic materials are often preferred for their theoretical advantages in mechanical strength, our results suggest that these advantages do not translate into superior short- or mid-term clinical outcomes. These findings hold particular value for the global pediatric surgical community, as they synthesize comparative outcomes across diverse practice settings and prosthetic materials. In an era of increasing emphasis on data-driven decision-making, it is critical that studies demonstrating a lack of statistically significant differences—not only those showing superiority—receive appropriate academic consideration. Publishing high-quality analyses that reveal no significant difference helps mitigate publication bias and prevents overrepresentation of positive or exaggerated effects in the literature. Our results provide clarity in a space often dominated by anecdotal preference and institutional tradition, reinforcing the need for evidence-based individualization rather than material-based dogma. In doing so, this study contributes meaningfully to the objective, balanced evolution of CDH repair strategies worldwide. Although recurrence rates did not differ statistically between biologic and synthetic patches, the pooled estimate (OR 2.17; $p = 0.06$) suggests a trend toward higher recurrence with biologic materials. Given the modest sample sizes, heterogeneity in follow-up duration, and the observational nature of available data, this trend should be interpreted cautiously. Nonetheless, it highlights the need for adequately powered prospective studies to determine whether this apparent difference reflects a true clinical effect or residual confounding.

5.2. Description of patch types and comparison with pediatric literature

Biologic patches used in the included studies consisted primarily of acellular dermal matrices (ADMs) such as AlloDerm and DermaMatrix, and small intestinal submucosa (SIS) products like Surgisis. These materials are designed to act as scaffolds for host tissue ingrowth and neovascularization, aiming to reduce foreign body reactions and infection risk. These materials are designed to act as scaffolds for host tissue ingrowth and neovascularization, aiming to reduce foreign body reactions and infection risk [32,33]. In contrast, synthetic patches—most commonly expanded polytetrafluoroethylene (ePTFE, Gore-Tex)—offer greater mechanical stability and long-term durability, but have been traditionally associated with higher rates of adhesion formation, infection, and seroma [34–36]. Despite these theoretical distinctions, our pooled analysis showed that the choice of patch material alone does not appear to be a primary determinant of clinical outcomes.

This finding is especially relevant in the context of a long-standing mixed debate in the pediatric surgical literature. Earlier studies such as those by Grethel et al. (2006) and Nasr et al. (2010) reported higher recurrence rates associated with biologic patches, raising concerns about their durability in large or tension-prone defects [16,17]. In contrast, more recent investigations, including those by Laituri et al. (2010) and Romao et al. (2012), reported no significant difference in preventing recurrence or postoperative complications [18,19], suggesting that technical factors or patient selection may explain the earlier discrepancies. Our results align with this latter group of studies, providing further evidence that biologic patches do not offer a significant outcome advantage.

5.3. Comparison with previous pediatric meta-analyses

Our findings are consistent with and expand upon previous meta-analyses evaluating patch type in congenital diaphragmatic hernia repair. Romao et al. (2012) performed one of the earliest comparisons between PTFE and small intestinal submucosa (SIS), but their analysis was limited to fewer than 100 patients from only two institutions and did not demonstrate significant differences in recurrence or complications [10]. Lu et al. (2020) conducted a broader meta-analysis including studies up to 2018 and reported higher recurrence rates with biological patches, though their analysis was restricted by a small number of comparative studies and limited assessment of risk of bias [8]. More recently, Kamal et al. (2023) published the largest review to date, including 47 studies and nearly 1000 patients, and similarly found increased recurrence with biologic patches but higher musculoskeletal deformities with synthetic materials; however, their inclusion of case reports and non-comparative series reduced the overall quality of evidence. Our study extends this work by restricting inclusion to comparative neonatal cohorts, incorporating studies published since 2021, and evaluating additional outcomes such as ECMO use and duration of mechanical ventilation. Furthermore, we applied a rigorous methodological approach using ROBINS-I for risk-of-bias assessment and formal publication bias testing, enhancing the reliability of our findings. Taken together, while our results align with Kamal et al. in demonstrating no clear superiority of one patch type, our analysis provides a more homogeneous, neonatal-specific, and methodologically robust synthesis of the available evidence [37]. Finally, a 2024 systematic review in Annals of Surgery synthesized outcomes of patch repairs in general, without direct biological-versus-synthetic comparisons [38]. In contrast, our study focuses exclusively on comparative pediatric data, applies rigorous inclusion criteria and risk-of-bias assessment, and incorporates recent publications not available to prior reviews, thereby providing the most up-to-date and methodologically robust synthesis of outcomes between biological and synthetic patches.

Russo et al. (2021) compared infants undergoing patch repair with those receiving primary closure and demonstrated significantly worse outcomes in the patch group, highlighting the severity of disease associated with larger defects. However, this study did not evaluate differences between patch materials [9].

5.4. Comparison with other large pediatric CDH series

Several institutional series have informed of the ongoing debate on patch selection. The Toronto group has reported favorable long-term outcomes using Gore-Tex patches, although concerns persist regarding infection and seroma formation [35]. Conversely, Boston and Cincinnati centers have explored biologic matrices with encouraging early results but uncertain long-term durability in high-tension repairs [39], [40]. Although individual institutional experiences vary, our findings of comparable recurrence rates reinforce that no patch material has demonstrated consistent superiority across centers. These results support the notion that factors such as defect size, pulmonary status, and surgical technique may have a greater impact on outcomes than the specific prosthetic material chosen.

5.5. Influence of patch material on specific outcomes

The lack of statistically significant differences in outcomes such as mortality, small bowel obstruction (SBO), and ECMO use further underscores the multifactorial nature of CDH prognosis. Mortality (OR 1.26; p = 0.57) [Fig. 4] and ECMO use (OR 0.86; p = 0.85) [Fig. 5] did not differ significantly between groups, suggesting that systemic factors—such as pulmonary hypoplasia, pulmonary hypertension, and the presence of liver herniation—likely exert a stronger influence on these endpoints than the specific material used for diaphragmatic reconstruction. Similarly, no protective effect of biologic patches was observed for SBO or hospital length of stay, outcomes that may depend more on surgical technique and perioperative management than on patch type alone, as previously described in studies evaluating abdominal complications following prosthetic repair [41]. Although these variables are heavily influenced by baseline disease severity rather than the prosthetic material itself, they were included because they represent commonly reported postoperative metrics and allow consistency with prior comparative studies.

5.6. Limitations of our study

The interpretation of our findings must consider several limitations inherent to the available evidence. First, all included studies were observational, leaving results vulnerable to confounding and selection bias. Important clinical variables—such as defect size, liver position, pulmonary hypertension severity, and perioperative management—were inconsistently reported and may have differed between biologic and synthetic patch cohorts, limiting causal inference. Additionally, the risk of bias across studies—particularly in the ROBINS-I domains of confounding and missing data—constrains the internal validity of the pooled estimates. Because key prognostic factors were reported inconsistently, meaningful adjustment for baseline differences was not possible, and the observed associations should be interpreted as exploratory rather than causal.

There was also substantial heterogeneity in patch materials, surgical approaches (open vs. minimally invasive), and outcome definitions, complicating direct comparisons across studies. Subgroup analyses stratified by biologic patch subtype or operative technique were underpowered due to the small number of contributing studies and variable reporting, limiting the ability to identify material- or technique-specific effects.

Notably, chest wall deformity and late recurrence were rarely and heterogeneously reported, with variable definitions and follow-up intervals. As a result, we could not perform a robust quantitative analysis of these outcomes. This lack of standardized long-term follow-up likely underestimates the true incidence of late recurrence and musculoskeletal deformities after patch repair and represents an important gap in the existing literature. The longest follow-up among included studies (approximately 8–11 years) still reflects short-to mid-term surveillance for CDH; musculoskeletal deformities and growth-related recurrences may present during adolescence, well beyond the timelines captured in the available data. Consequently, true long-term recurrence rates remain uncertain, and existing studies likely underestimate late failures. Moreover, most reports did not distinguish early postoperative recurrence—often related to technical failure—from late recurrence arising from growth-related tension or remodeling at the patch–tissue interface. This inability to stratify early versus late recurrence further limits clinical interpretation.

Follow-up duration overall was limited and inconsistently documented, which may further underestimate long-term recurrence. Several secondary outcomes—including mortality, ECMO use, LOS, and duration of mechanical ventilation—are strongly influenced by baseline physiologic severity rather than patch material; therefore, these findings should be interpreted as exploratory endpoints rather than patch-dependent effects. Event counts were low for several outcomes, reducing statistical power and resulting in wide confidence intervals. Finally, more than half of the included studies were judged to have serious risk of bias according to ROBINS-I, raising concerns about residual confounding and selective outcome reporting. These limitations underscore the need for prospective multicenter studies with standardized outcome definitions, long-term follow-up, and adequate adjustment for baseline disease severity.

5.7. Implications for clinical practice and future research

Given the absence of clear outcome advantages, patch selection should be based on individual patient factors, including contamination or infection of the surgical site, patient's comorbid conditions, and the size of the diaphragmatic defect. Our findings suggest that both biologic and synthetic patches are acceptable options, and that other perioperative factors may be more critical in determining outcomes, rather than relying on assumptions of material superiority.

Future research should prioritize well-designed, large-scale, multicenter prospective studies with standardized definitions of outcomes and long-term follow-up. Stratification based on key variables, such as liver position, defect size, and the presence of pulmonary hypertension, will be essential to account for baseline risk differences. Finally, the development and evaluation of novel patch materials, including hybrid scaffolds combining the synthetic strength and durability with the biologic biocompatibility, represent an important frontier in improving outcomes.

6. Conclusion

In this meta-analysis of neonatal congenital diaphragmatic hernia repairs, no significant differences were observed between biological and synthetic patches in terms of hernia recurrence, small bowel obstruction, mortality, ECMO, or length of hospital stay. While synthetic patches are often preferred for their theoretical advantages in mechanical strength, potentially providing better long-term durability and reducing the risk of reherniation, current evidence does not demonstrate superior clinical outcomes over biological materials. However, the limited number of studies and heterogeneity in patient populations, surgical techniques, and follow-up periods underscore the need for well-designed prospective studies to clarify whether specific subgroups may benefit more from a particular patch type.

Conflict of interests

The authors declare no conflicts of interest related to the subject matter of this article.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jpedsurg.2026.162926.

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