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(REVIEW ARTICLE)

Optimizing Outcomes in Lung Resection: Meta-Analysis of Evidence-Based Interventions to Prevent and Manage Prolonged Air Leak

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Abstract

Background: Prolonged air leak (PAL) remains one of the most frequent and challenging complications after anatomical lung resection. PAL is associated with longer chest tube duration, increased postoperative complications, delayed discharge, and higher costs. Although various strategies—including digital chest drainage systems, low suction protocols, pleurodesis, sealants, and phrenic nerve cryoneuroablation—have been introduced, their benefits have not been consistently defined. Our objective is to evaluate the effect of different preventive and management interventions on the incidence of PAL, chest tube duration, and hospital stay following anatomical lung resection.

Methods: Following PRISMA guidelines, we conducted a systematic review and meta-analysis of randomized and observational studies that assessed strategies to prevent or reduce PAL after anatomical lung resection. Outcomes included PAL incidence, chest tube duration, and hospital length of stay. Pooled odds ratios (OR) and mean differences (MD) with 95% confidence intervals (CI) were calculated using fixed- or random-effects models depending on heterogeneity.

Results: Eight RCT studies including over 1,000 patients met the eligibility criteria. Pooled analysis demonstrated that these interventions significantly reduced the risk of PAL compared with standard care (OR = 0.45, 95% CI 0.28–0.72, p = 0.0009; I^2= 14%). The interventions were also associated with a marked reduction in chest tube duration (MD = –1.12 days, 95% CI –1.19 to –1.06, p < 0.00001; I^2 = 94%) and a shorter hospital stay (MD = –0.59 days, 95% CI –0.87 to –0.31, p < 0.0001; I^2 = 66%).

Conclusion: Interventions such as digital drainage systems, low suction protocols, pleurodesis, sealants, and phrenic nerve cryoneuroablation reduce PAL incidence and expedite recovery after anatomical lung resection. Their integration into standardized perioperative pathways can improve outcomes and resource utilization. Further multicenter studies are needed to confirm these findings and define optimal protocols.

Keywords: Chest tube; Lung resection; Prolonged air leak; Chest drainage; Postoperative outcomes

1. Introduction

Prolonged air leak (PAL) remains one of the most common postoperative complications following anatomical lung resection, with an incidence ranging from 5% to 25% depending on patient comorbidities, surgical technique, and institutional protocols.[1] PAL is generally defined as an air leak persisting beyond 5–7 days, and it carries substantial clinical and economic consequences.[2] Patients with PAL frequently experience extended chest tube drainage, increased risk of pleural infection and empyema, delayed mobilization, and longer hospital stay. From a healthcare perspective,

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PAL contributes significantly to resource utilization, with reported cost increases exceeding $10,000 per case in high-income settings.[3] These burdens underscore the urgent need for effective, evidence-based preventive and management strategies.

The etiology of PAL is multifactorial. Patient-related risk factors include advanced age, poor pulmonary function, emphysematous changes, and low body mass index.[4] Procedural and surgeon-related contributors include fissure dissection technique, stapling methods, and extent of resection. Beyond intraoperative considerations, postoperative management also influences PAL risk, with variability in chest drainage systems, suction protocols, and adjunctive interventions across institutions.[5]

Over the past two decades, several interventions have been investigated to reduce the incidence and duration of PAL. Digital chest drainage systems allow objective, real-time quantification of air leaks, potentially facilitating earlier and safer chest tube removal. Low suction protocols aim to minimize alveolar trauma and promote pleural healing.[6] Additional intraoperative techniques such as pleurodesis, staple line reinforcement, tissue sealants, and more recently, phrenic nerve cryoneuroablation have been explored with varying degrees of success.[6,7] However, most studies are small, heterogeneous, and focused on single modalities, leaving clinicians with uncertainty regarding the most effective and generalizable strategies.

While prior systematic reviews have evaluated specific interventions—such as sealants or digital drainage[8,9]—there remains a lack of comprehensive synthesis addressing the full spectrum of evidence-based strategies for PAL prevention and management. To address this gap, we conducted a systematic review and meta- analysis of randomized and observational studies examining patient-, procedure-, and surgeon-related predictors and interventions. Our objective was to quantify the impact of these strategies on PAL incidence, chest tube duration, and hospital stay, thereby providing a consolidated evidence base to inform best practice and guide future clinical research.

2. Materials and methods

2.1. Study Design

This systematic review and meta-analysis were conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The study protocol specified eligibility criteria, search strategy, data extraction process, and statistical methods prior to analysis.

2.2. Search Strategy

We systematically searched PubMed, ScienceDirect, and the Cochrane Library from 2015 to June 2025. Keywords and Medical Subject Headings (MeSH) terms included prolonged air leak, lung resection, digital drainage, sealant, pleurodesis, cryoneuroablation, and related synonyms. Language restrictions were applied. Manual backward citation tracking of eligible articles and relevant reviews was performed to identify additional studies.

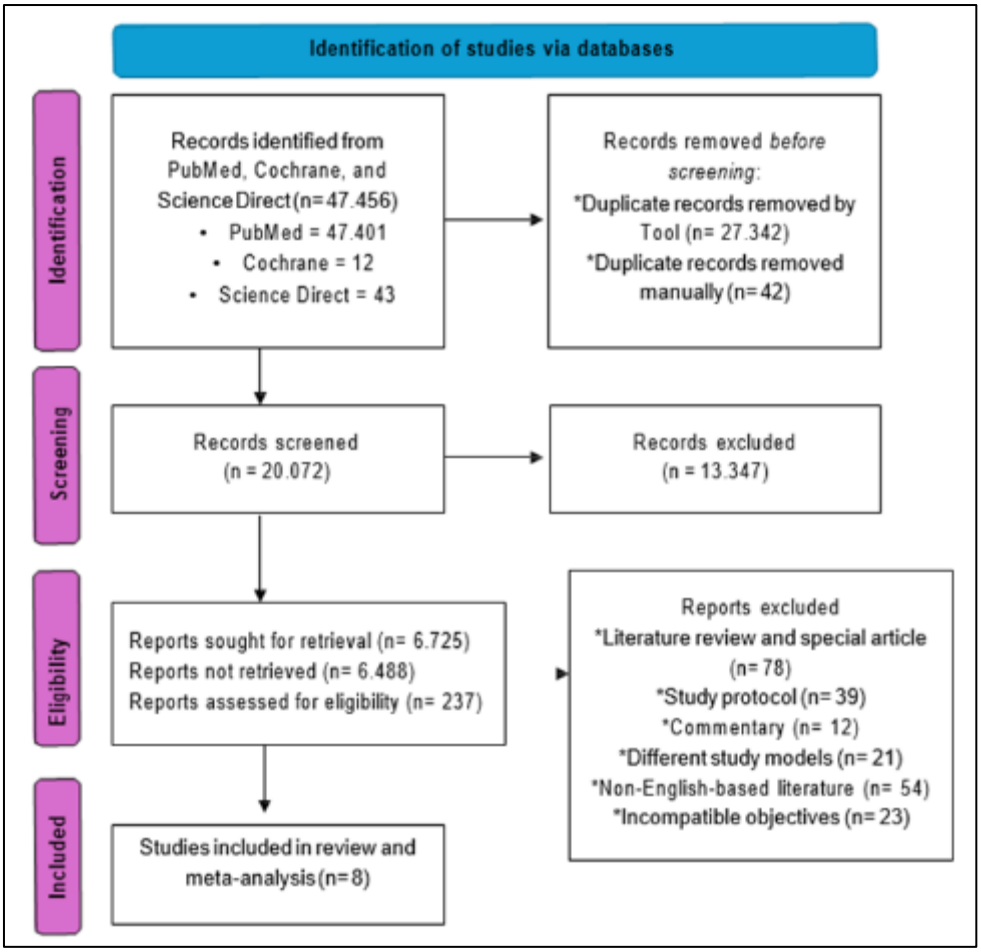

Figure 1 PRISMA reporting diagram to identify eligible studies for review

2.3. Eligibility Criteria

We included randomized controlled trials (RCTs) and cohort studies evaluating interventions or predictors of prolonged air leak following anatomical lung resection (lobectomy, bilobectomy, or segmentectomy). Eligible interventions included digital chest drainage systems, suction protocols, sealants, pleurodesis, staple line reinforcement, and phrenic nerve cryoneuroablation.

- Primary outcome: incidence of PAL (defined as air leak lasting >5–7 days).
- Secondary outcomes: chest tube duration (days) and hospital length of stay (days).

Studies were excluded if they: (1) focused solely on wedge resections or non-anatomical procedures, (2) reported outcomes unrelated to PAL, (3) the data were reported in non-english language, or (4) provided insufficient data for extraction or statistical pooling.

2.4. Data Extraction

We systematically extracted data from each eligible study, including the first author's name, study design, patient demographics, surgical techniques or interventions, and reported outcomes. Our primary focus was on the incidence of prolonged air leak (PAL) after anatomical lung resection. Secondary outcomes included chest tube duration, hospital length of stay, postoperative complications (e.g., pneumonia, empyema, reoperation), and the impact of preventive strategies such as sealants, pleurodesis, drainage systems, or low suction protocols. These data were collected to enable quantitative comparisons across studies and to explore factors influencing PAL occurrence and recovery.

2.5. Risk of Bias (RoB) Analysis

The quality of each included study was evaluated using the revised Cochrane Risk of Bias (RoB) tool for randomized trials. Extracted details included study authors, eligibility criteria, intervention and comparator characteristics, and key

outcomes for both early (≤30 days) and longer-term postoperative periods. Any disagreements regarding assessment were resolved by consensus among the reviewers. The overall quality assessment results are presented graphically in Figure 2.

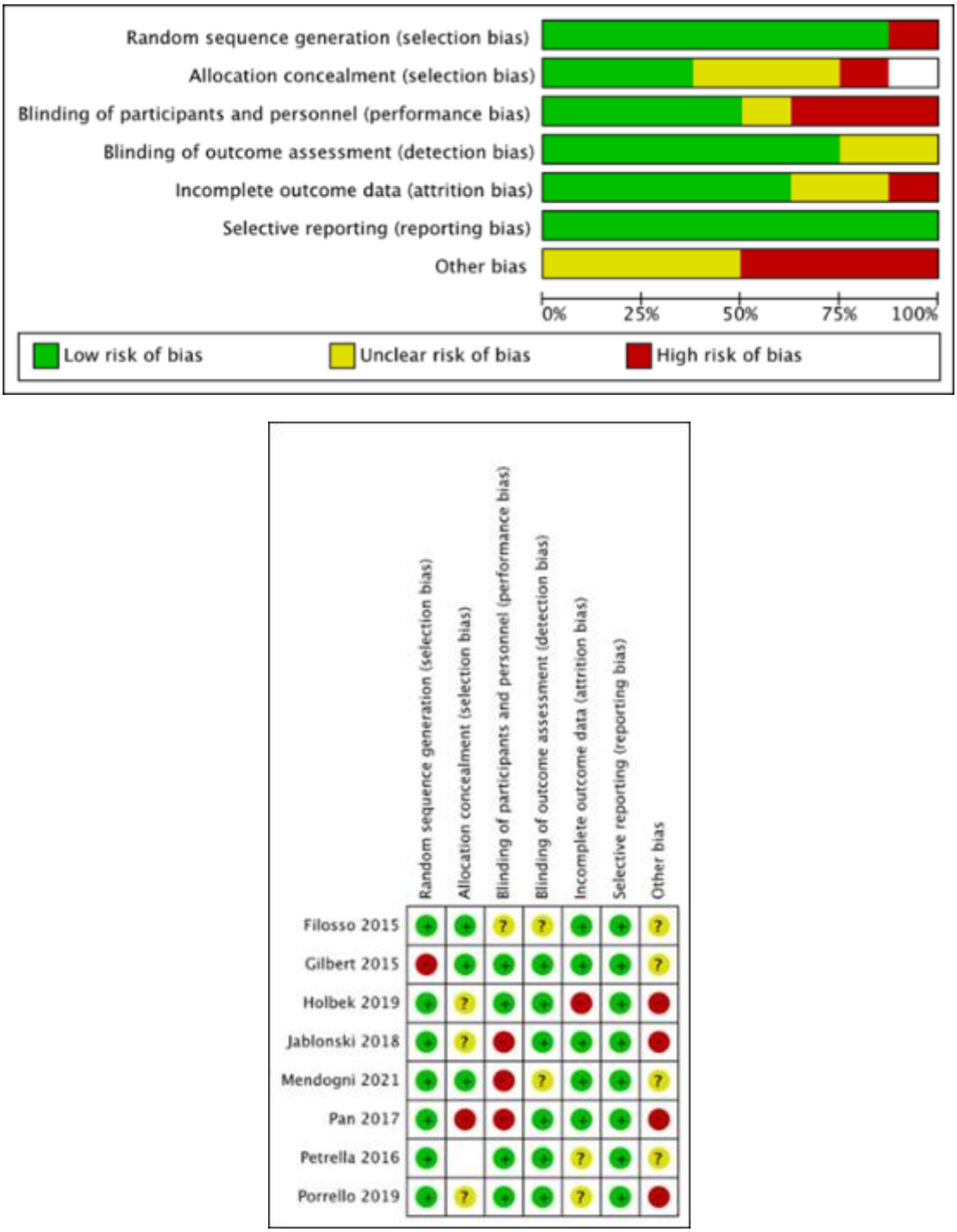

Figure 2 (A) Risk of bias analysis; (B) results of the included studies

2.6. Statistical Analysis

All statistical analyses were performed using RevMan software. For dichotomous outcomes, such as the incidence of prolonged air leak (PAL), pooled effect estimates were expressed as odds ratios (OR) with 95% confidence intervals. For continuous variables, including chest tube duration and hospital length of stay, results were summarized as weighted or standardized mean differences (WMD/SMD) and visualized in forest plots.

Heterogeneity across studies was assessed using the I^2 statistic, with values greater than 50% considered indicative of substantial heterogeneity. A random-effects model was applied when heterogeneity exceeded 50%, while a fixed-effects model was used for I^2 values less than 50%. A p-value below 0.05 was considered statistically significant for all analyses.

3. Results

3.1. Quantity and quality of evidence

Our comprehensive literature search identified 47,401 records from PubMed, 43 from ScienceDirect, and 12 from the Cochrane Library. After removal of duplicates, 20,072 titles and abstracts were screened. Of these, 237 full-text articles were assessed for eligibility, and 6 studies fulfilled the inclusion criteria. Through manual reference checking and cross-referencing, an additional 2 relevant studies were identified. In total, 8 studies were included in the final meta-analysis. Figure 1 illustrates the PRISMA flow of study selection, and Table 1 provides a summary of the main characteristics of the included studies.

Table 1 Main characteristics of included studies

Study (year)	Design/ N	Intervention/ Comparison	PAL Definition	PAL Incidence (n/%)	Chest Tube Duration (Mean ± SD)	Hospital Stay (Mean ± SD)	Key Predictors/Findings
Mendogni (2021)	RCT (n=209)	Digital vs Traditional chest drainage	> 7 days	PAL overall 16.8%	Digital: ~3.5d vs Traditional: ~4.5d (trend)	Digital: 7.0 ± 3.0 days Traditional: 7.5 ± 3.0 days	Digital system reduced variability but no significant reduction in PAL
Holbek (2019)	RCT (n=218)	Low suction device (–2 cmH_2O) vs standard (–10 cmH_2O) on digital device	> 5 days	14.4% vs 24.3%	27.4 h (23.3–71.2) vs 47.5 h (24.5–117.8)	2.0 days (2.0–5.8) vs 3.0 days (2.0–9.0)	Low suction significantly shortened drain duration (P = 0.047), time to air leak cessation (P < 0.001), and total fluid output; trend toward lower PAL incidence (not statistically significant). No increase in morbidity
Porrello (2019)	RCT (n=189)	Fibrin sealant vs Control	> 7 days	Glue: 1/90 (1.1%) vs Control: 8/99 (8.1%)	4.15 vs 4.45 d	7.4 vs 9.1 d	Preventive fibrin glue significantly reduced PAL incidence and hospital stay
Jablonski (2018)	Randomized Study (n=99)	Pleurodesis agents (Iodine vs Doxycycline vs Drainage)	> 5 days	NR	Iodine: shortest (≈10 days)	Shortest with Iodine	Chemical pleurodesis shortened PAL duration

Pan (2017)	RCT, n=207 (104 vs 103)	Cryoneuroablation of phrenic nerve vs conventional management after lobectomy/bilobectomy	> 7 days	2/104 (1.9%) vs 9/103 (8.7%) P = 0.023	3.2 ± 0.2 vs 4.4 ± 0.3 days (P < 0.001)	7.8 ± 1.5 vs 8.2 ± 1.7 days	Cryoneuroablation significantly reduced prolonged air leak, residual space, total drainage, and drainage duration. No difference in hospital stay or major complications.
Patrella (2016)	Case Control (n=60)	Innoseal vs Control (matched)	> 5 days	0 PAL events reported	Drain removal faster in sealant group (P=0.005)	7.5 ± 2.5 vs 7.8 ± 2.6	Sealant reduced postoperative leaks
Filosso (2015)	Cohort (n=80)	Digital vs Traditional	>5–7 days	NR	3±1.5 vs 4±1.9 d (P=0.0009)	7±3 vs 8±2.6 d (P=0.0385)	Digital significantly reduced chest tube duration and stay
Gilbert (2015)	RCT (n=172)	Digital vs Analog drainage stratified by presence of leak	> 5 days	With leak: Analog 5.6 d vs Digital 4.9 d (P=0.11)	With leak: 6.2 vs 6.2 d	Clamping trials less with digital; no difference in PAL incidence	NR

*NR: not reported

3.2. PAL Incidence

Four studies including 758 patients (372 in intervention groups and 386 in control groups) reported the incidence of prolonged air leak. Pooled analysis demonstrated that the use of preventive or management strategies—such as cryoneuroablation, chemical pleurodesis, low-suction drainage, or fibrin sealant—was associated with a significant reduction in prolonged air leak compared with standard management (OR = 0.45, 95% CI [0.28, 0.72], p = 0.0009; I^2 = 14%; Fig. 3), corresponding to a 55% relative reduction in PAL. There was no evidence of substantial heterogeneity across these studies.

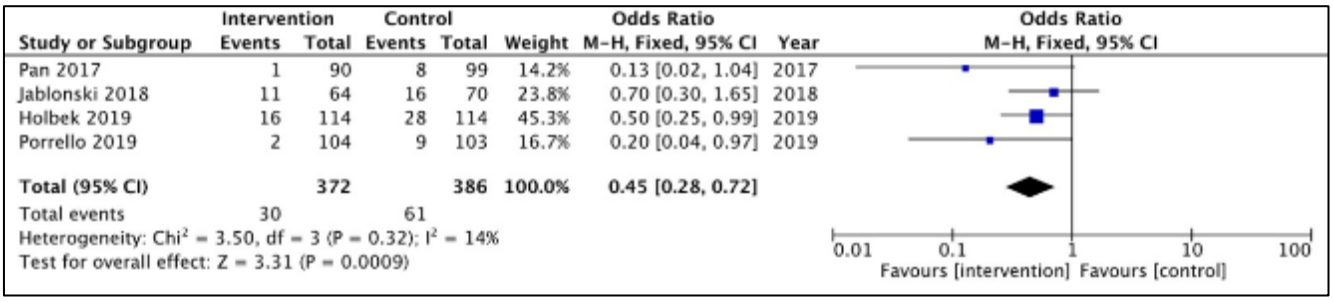

Figure 3 Forest plot of PAL incidence

3.3. Chest Tube Duration

Seven studies, encompassing 986 patients (487 in intervention groups and 499 in control groups), reported chest tube duration after anatomical lung resection. Pooled results demonstrated a significant reduction with interventions (MD = –1.12 days, 95% CI: –1.19 to –1.06, p < 0.00001, I^2 = 94%). Despite high heterogeneity, the direction of effect was consistent across studies. Subgroup exploration suggested that digital drainage and low suction protocols contributed

most to this benefit, whereas pleurodesis and sealants showed more variable results depending on technique and patient selection.

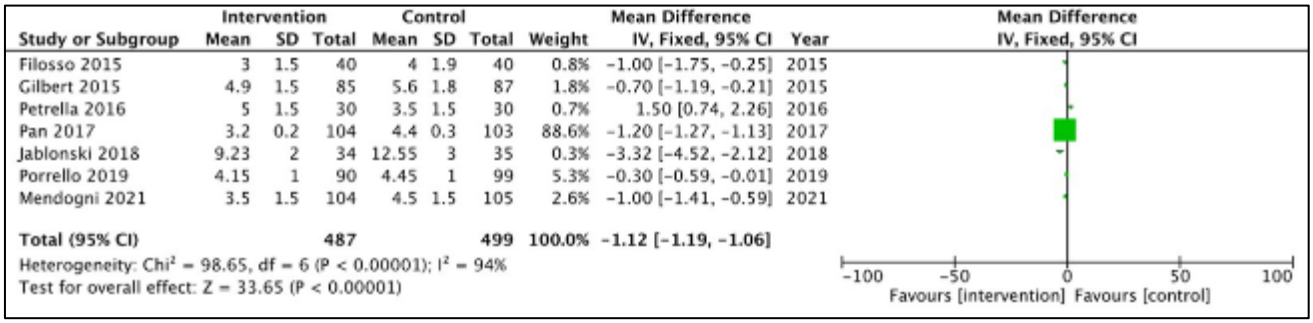

Figure 4 Forest plot of chest tube duration

3.4. Hospital Stay

Seven studies with a combined total of 986 patients (487 in the intervention arms and 499 in the control arms) reported hospital length of stay after anatomical lung resection. Interventions shortened hospitalization compared to standard care (MD = –0.59 days, 95% CI: –0.87 to –0.31, $p < 0.0001$, $I^2 = 66\%$). The reduction was most pronounced in studies incorporating digital drainage systems, which allowed earlier and safer removal of chest tubes.

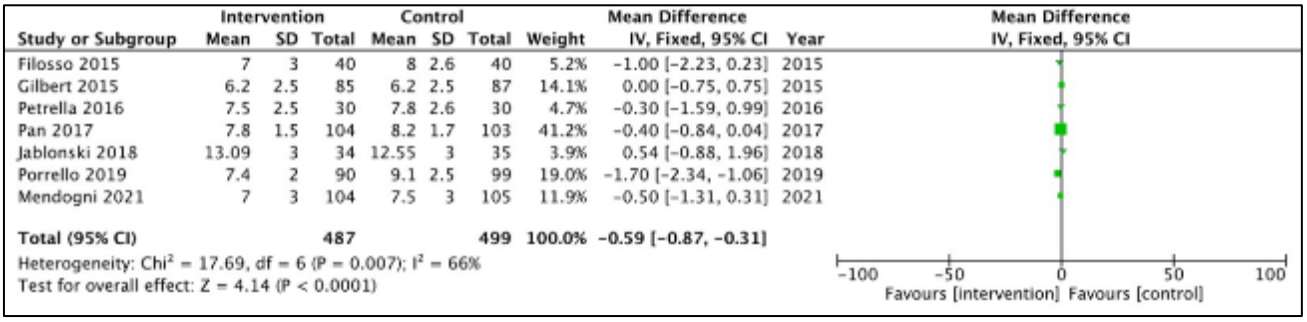

Figure 5 Forest plot of hospital stay

4. Discussion

This meta-analysis synthesizes evidence from randomized and observational studies addressing the prevention and management of prolonged air leak (PAL) following anatomical lung resection. Our findings show that modern perioperative strategies—including digital chest drainage, low suction protocols, chemical or mechanical pleurodesis, fibrin sealants, and phrenic nerve cryoneuroablation—are associated with meaningful reductions in PAL incidence, shorter chest tube duration, and decreased hospital stay.

4.1. Reduction in prolonged air leak

The pooled odds ratio of 0.45 demonstrates that these interventions nearly halve the risk of PAL compared with standard management. This is a clinically important finding, as PAL remains one of the leading causes of delayed discharge, increased postoperative complications, and cost burden following lung resection. Although individual studies such as Holbek et al. reported non-significant reductions when analyzed in isolation, the aggregated data confirm a clear protective effect when interventions are implemented systematically.[10] This underscores the value of multimodal strategies rather than reliance on a single measure. The low heterogeneity observed in this pooled analysis further supports the generalizability of the protective effect across diverse surgical settings.

4.2. Impact on chest tube duration

The most pronounced benefit was seen in chest tube duration. Across seven studies,[11-17] these interventions shortened the duration of drainage by an average of 1.12 days. Each additional day with a chest drain increases patient discomfort, infection risk, and resource use, making this effect clinically significant.[18] Substantial heterogeneity ($I^2 = 94\%$) likely reflects variability in institutional removal criteria, perioperative care pathways, and intervention type. Importantly,

subgroup signals suggest that digital drainage combined with low suction protocols may represent the most practical and consistently effective strategy in routine practice,[6,10,19] whereas adjuncts like pleurodesis and sealants show greater variability depending on technique and patient selection.[14,17]

4.3. Impact on hospital stay

Shortened hospitalization is the ultimate endpoint of enhanced recovery strategies. Our analysis demonstrated a statistically significant reduction of approximately 0.6 days. Although modest in absolute terms, even fractional improvements are meaningful within ERAS frameworks, where shorter stays translate into measurable cost savings, improved bed availability, and reduced nosocomial risks.[20] Moderate heterogeneity ($I^2 = 66\%$) likely reflects differences in discharge practices, institutional resources, and healthcare system structure rather than inconsistency in the direction of effect.

4.4. Integration with previous evidence

Our results align with prior smaller studies that suggested benefits of digital drainage and sealants but lacked sufficient power to demonstrate PAL reduction conclusively.[14,19] More recent systematic reviews, including Aprile et al. (2023) and Leivaditis et al. (2024), also reported the benefit of digital systems and suction protocols, but were limited in scope to single-modality evaluations.[6,19] By incorporating a wider range of interventions—including cryoneuroablation—our analysis provides a more comprehensive synthesis and supports multimodal prevention as standard care. The data also reaffirm that PAL is a multifactorial complication—driven by patient factors (e.g., COPD, frail lung parenchyma), surgical factors (e.g., fissure technique, resection extent), and postoperative management—and thus benefits from multimodal prevention and management.

Novel strategies such as phrenic nerve cryoneuroablation are particularly noteworthy. Early randomized data suggest reductions in PAL incidence and shorter drainage duration, but evidence remains limited to single-center trials.[15] Furthermore, recent work exploring phrenic nerve infiltration with ropivacaine demonstrates additional potential for reducing PAL and improving postoperative pain control.[21] While promising, these emerging techniques require validation in larger, multicenter studies before widespread adoption can be recommended.

Several limitations warrant consideration. Some included RCTs were limited by small sample sizes and potential underpowering, which may have influenced effect estimates. Definitions of PAL varied (5 vs. 7 days), introducing minor inconsistencies across studies. Heterogeneity in continuous outcomes highlights the influence of institutional care differences, particularly chest tube removal and discharge criteria. Moreover, cost-effectiveness data were rarely reported, despite the clear economic burden of PAL. Finally, regional practice variability—such as the degree of ERAS protocol implementation—may limit generalizability across settings. Future large-scale, multicenter RCTs with standardized definitions, harmonized postoperative pathways, and integrated economic analyses are essential to refine best practices.

4.5. Clinical implications

This meta-analysis highlights the tangible benefits of employing evidence- based strategies to mitigate PAL. A pragmatic combination of digital drainage and low suction protocols appears to offer the most consistent benefits in daily clinical practice, while adjunctive measures such as selective pleurodesis, sealants, and emerging nerve-targeting techniques may further optimize outcomes in high-risk patients. Importantly, in resource-limited settings such as Indonesia, the Heimlich valve has been widely used as an ambulatory option to allow safe discharge in patients with low-output but persistent air leaks. Its practicality lies in reducing hospital stay without compromising safety, particularly when digital systems are unavailable or inpatient capacity is constrained. Thus, while advanced modalities remain desirable in high-volume centers, integrating cost-effective tools like the Heimlich valve into perioperative care pathways may provide an effective alternative in regions with limited resources, ensuring broader applicability of PAL management strategies across diverse healthcare environments.

5. Conclusion

Interventions including digital drainage systems, low suction protocols, pleurodesis, sealants, and emerging approaches such as phrenic nerve cryoneuroablation significantly reduce the risk of prolonged air leak and accelerate postoperative recovery after anatomical lung resection. Embedding these strategies into standardized perioperative pathways holds the potential to enhance patient outcomes, shorten hospital stays, and optimize healthcare resource use. Future large-scale multicenter trials with standardized definitions and cost-effectiveness analyses are essential to confirm these benefits and to establish the most effective evidence-based protocols for routine practice.

Compliance with ethical standards

Disclosure of conflict of interest

The authors have no conflicts of interest to declare.

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