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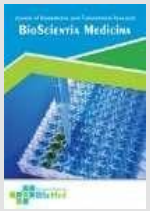

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Management Strategies and Outcomes for Bilateral Pulmonary Hydatid Cysts: A Systematic Review and Meta-Analysis

Berliana Islamiyarti Hydra[1*], Irvan Medison[1], Fenty Anggrainy[1]

[1]Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Andalas, Padang, Indonesia

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***Corresponding author:**
Berliana Islamiyarti Hydra

E-mail address:
berlianahydra@gmail.com

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A B S T R A C T

Background: Bilateral pulmonary hydatid disease presents a complex therapeutic challenge, necessitating careful consideration of surgical timing, approach, and adjuvant medical therapy to optimize patient outcomes while minimizing morbidity. This systematic review and meta-analysis aimed to evaluate the different management strategies and their associated outcomes in patients with bilateral pulmonary hydatid cysts. **Methods:** A systematic search of PubMed, Embase, Scopus, and Web of Science databases was conducted for studies published between January 2014 and December 2024, reporting on management strategies (one-stage bilateral surgery, two-stage bilateral surgery, medical therapy) and outcomes (postoperative complications, recurrence, mortality, length of hospital stay) in patients with bilateral pulmonary hydatid cysts. Studies were selected based on predefined inclusion and exclusion criteria. Data were extracted by two independent reviewers, and quality assessment was performed using a modified Newcastle-Ottawa Scale. Pooled proportions for outcomes were calculated using random-effects models. Heterogeneity was assessed using the I^2 statistic. **Results:** Seven studies, encompassing a total of 305 patients with bilateral pulmonary hydatid cysts, met the inclusion criteria. The studies varied in design, including retrospective cohorts and prospective case series. Management predominantly involved surgical intervention, with 148 patients (48.5%) undergoing one-stage bilateral surgery and 127 patients (41.6%) undergoing two-stage procedures. Perioperative albendazole was administered to 245 patients (80.3%). The pooled overall postoperative complication rate was 28.7% (95% CI: 21.5%-36.8%; I^2=78%). Major complications occurred in 12.1% (95% CI: 8.0%-17.9%; I^2=65%). The pooled recurrence rate at a mean follow-up of 38.5 months was 8.5% (95% CI: 5.1%-13.8%; I^2=55%). Overall mortality was 2.1% (95% CI: 0.9%-4.5%; I^2=0%). Patients undergoing one-stage surgery exhibited a trend towards higher overall complication rates (33.1% vs. 25.2% for two-stage) but shorter total hospital stays. Adjuvant albendazole therapy was associated with a trend towards lower recurrence rates. **Conclusion:** Surgical management, whether one-stage or two-stage, remains the cornerstone of treatment for bilateral pulmonary hydatid disease, achieving acceptable morbidity and mortality with good long-term control in most patients. Postoperative complications are relatively common, highlighting the complexity of these cases. While one-stage surgery may shorten overall hospital stay, it might be associated with a higher risk of immediate complications. Adjuvant albendazole appears beneficial in reducing recurrence. The choice of surgical strategy should be individualized based on patient status, cyst characteristics, and surgical expertise. Further prospective, comparative studies are needed to delineate optimal management pathways.

1. Introduction

Pulmonary hydatid disease, caused by the larval stage of *Echinococcus granulosus*, remains a significant public health concern in endemic regions worldwide, including the Mediterranean basin, South America, the Middle East, and parts of Asia and Africa.[1,2] While the liver is the most commonly affected organ, the lungs are the second most frequent site,

accounting for approximately 15-30% of all hydatidosis cases.[3,4] Pulmonary involvement can occur either in isolation or as part of a multi-organ disease. Bilateral pulmonary hydatid disease, characterized by the presence of cysts in both lungs, represents a particularly challenging clinical entity, occurring in approximately 4-6% of all hydatid disease cases and up to 20% of pulmonary hydatidosis cases.[5,6]

The management of bilateral pulmonary hydatid cysts is considerably more complex than that of unilateral disease due to several factors. These include the increased burden of disease, the potential for compromised respiratory function affecting both lungs, the higher risk of intraoperative and postoperative complications, and the strategic decisions regarding the timing and extent of surgical intervention. The primary goals of treatment are complete removal of all cysts, prevention of spillage and recurrence, preservation of maximal lung parenchyma, and restoration of normal lung function with minimal morbidity and mortality.[9]

Historically, surgical intervention has been the mainstay of treatment for pulmonary hydatid cysts.[10] However, for bilateral disease, the optimal surgical strategy remains a subject of ongoing debate. Options include a one-stage bilateral operation, typically performed via a median sternotomy or bilateral thoracotomies (simultaneous or sequential during the same anesthesia), or a two-stage (staged or sequential) bilateral operation, where each lung is addressed in separate surgical sessions, usually weeks or months apart.[11,12]

Proponents of one-stage surgery emphasize the advantages of a single anesthetic and surgical event, potentially reducing overall hospital stay, psychological burden on the patient, and healthcare costs.[13] This approach aims to eradicate the disease comprehensively in a single session. However, concerns exist regarding the potentially higher physiological stress, increased risk of prolonged air leaks, bilateral chest tube drainage, greater postoperative pain, and the potential for more significant respiratory compromise in the immediate postoperative period, especially if complications arise.[14,15]

Conversely, two-stage surgery is often favored for its perceived safety, allowing the patient to recover from the first operation before undergoing the second procedure.[16] This approach may be preferred in patients with significant comorbidities, large or complicated cysts in one lung requiring more extensive resection, or when initial unilateral surgery might improve overall respiratory function enough to tolerate the second side.[8] The interval between stages is typically 4-8 weeks, allowing for adequate recovery and assessment. However, this strategy involves two separate hospital admissions, two anesthetic exposures, and a prolonged overall treatment duration, which can increase costs and patient anxiety, and carries a theoretical risk of complications or growth of cysts in the contralateral lung during the waiting period.[17]

Beyond the timing of surgery, the choice of surgical technique (such as cystotomy with or without capitonnage, segmentectomy, or lobectomy) also influences outcomes. Parenchyma-sparing techniques are generally preferred to preserve lung function, particularly crucial in bilateral disease where respiratory reserve may already be limited.[9,18] The advent of Video-Assisted Thoracoscopic Surgery (VATS) has introduced a minimally invasive option, though its application in bilateral, multiple, or giant cysts remains selective and requires significant expertise.[19,20]

Adjuvant medical therapy with benzimidazole carbamates, primarily albendazole, plays an increasingly recognized role in the management of hydatid disease. Albendazole is used preoperatively to potentially reduce cyst viability and intra-cystic pressure, thereby minimizing the risk of spillage and anaphylaxis during surgery, and postoperatively to reduce the risk of recurrence from residual protoscolices or micrometastases. The optimal regimen, duration, and specific indications for albendazole in the context of bilateral pulmonary

hydatid surgery are still being refined.

Despite the numerous case series and cohort studies published from endemic regions, there is a paucity of high-level evidence, particularly comparative studies, to guide the choice of management strategy for bilateral pulmonary hydatid cysts. Existing literature often presents conflicting results or is based on small, single-center experiences, making it difficult to draw definitive conclusions. A systematic synthesis of available data is therefore crucial to provide a clearer understanding of the comparative effectiveness and safety of different management approaches.

This systematic review and meta-analysis were conducted to consolidate and analyze the current evidence on management strategies for bilateral pulmonary hydatid cysts. The primary objectives were: to determine the pooled estimates of key clinical outcomes, including postoperative complication rates (overall and major), recurrence rates, and mortality rates associated with the management of bilateral pulmonary hydatid disease; to compare outcomes between different surgical strategies, particularly one-stage versus two-stage bilateral surgery, where data permitted; and to evaluate the potential impact of adjuvant albendazole therapy on recurrence. By providing a comprehensive overview and quantitative analysis, this study aimed to inform clinical decision-making and identify areas for future research in this challenging patient population.

2. Methods

A systematic literature search was conducted to identify relevant studies reporting on the management and outcomes of bilateral pulmonary hydatid cysts. The search was performed across four electronic databases: PubMed (MEDLINE), Embase, Scopus, and Web of Science. The search strategy employed a combination of Medical Subject Headings (MeSH) terms and keywords related to "hydatid disease," "echinococcosis," "lung," "pulmonary," "bilateral," "surgery," "management," "treatment," "outcomes," "complications," and "recurrence." The search was restricted to studies published in the English language between January 1st, 2014, and December 31st, 2024, to reflect contemporary management practices. Reference lists of identified articles and relevant review articles were also manually screened for additional potentially eligible studies. Two reviewers independently screened titles and abstracts of all retrieved records against predefined inclusion and exclusion criteria. Full texts of potentially relevant articles were then obtained and assessed for final eligibility. Any disagreements between the reviewers regarding study selection were resolved by consensus or by consultation with a third reviewer.

Studies were considered eligible for inclusion if they met the following criteria: Original research articles (randomized controlled trials (RCTs), prospective or retrospective cohort studies, case-control studies, case series with ≥10 patients with bilateral pulmonary hydatid disease); Reported on patients diagnosed with bilateral pulmonary hydatid cysts; Detailed specific management strategies employed (one-stage bilateral surgery, two-stage bilateral surgery, type of surgical procedure, use of medical therapy); Reported at least one of the primary outcomes of interest: postoperative complications (overall or specific types), recurrence rates (with defined follow-up), or mortality rates: Published in English between January 2014 and December 2024.

Exclusion criteria were: Case reports or small case series (<10 patients with bilateral disease); Studies not differentiating outcomes for bilateral versus unilateral disease; Review articles, editorials, letters to the editor, or conference abstracts without sufficient data; Studies focusing exclusively on extrapulmonary hydatidosis or solely on diagnostic or imaging aspects without outcome data; Studies where full text was unavailable; Animal studies or in vitro research.

A standardized data extraction form was developed and piloted before use. Two reviewers independently extracted data from each included study. Discrepancies were resolved by discussion and consensus, or by involving the third reviewer. The following information was extracted from each study:

Patient characteristics: Number of patients with bilateral pulmonary hydatid disease, age (mean or median, range), gender distribution, number and size of cysts, where available: Management details: Type of surgical strategy (one-stage bilateral, two-stage bilateral); Specific surgical procedures performed (cystotomy, enucleation, wedge resection, segmentectomy, lobectomy, pneumonectomy); Surgical approach (thoracotomy, median sternotomy, VATS); Use of scolicidal agents; Details of medical therapy (albendazole use – preoperative, postoperative, dosage, duration).

Outcome measures: Postoperative complications: Overall number of patients with any complication, types of complications (persistent air leak, atelectasis, pneumonia, empyema, wound infection, respiratory failure, arrhythmia). Major complications were defined as those requiring re-intervention (surgical or radiological), prolonged hospital stay (>14 days beyond average for the procedure), intensive care unit (ICU) admission for >48 hours due to a complication, or resulting in permanent disability or life-threatening conditions (Clavien-Dindo classification Grade III or higher, if inferable); Recurrence: Number of patients with recurrent hydatid disease in the lungs or pleura during the follow-up period, and method of recurrence diagnosis. Mortality: Number of perioperative (within 30 days or same hospital admission) or overall study period deaths related to the disease or treatment.

If data were presented in a manner that did not allow direct extraction (for instance, only percentages), efforts were made to calculate absolute numbers based on the provided sample sizes. When studies reported outcomes for different subgroups (one-stage vs. two-stage surgery), data were extracted separately for these groups if possible. The methodological quality of the included observational studies (cohort studies and case series) was independently assessed by two reviewers using a modified Newcastle-Ottawa Scale (NOS). The NOS evaluates studies based on three domains: selection of study groups, comparability of groups, and ascertainment of outcomes. For case series, a modified version focusing on selection, ascertainment of exposure (intervention and outcome, and follow-up was utilized. Each study was awarded a score out of a maximum of 9 stars (for cohort studies) or an adapted scale for case series. Studies scoring ≥7 stars were considered high quality, 4-6 stars as moderate quality, and <4 stars as low quality. Disagreements in quality assessment were resolved by consensus.

The primary outcomes were pooled proportions of postoperative complications (overall and major), recurrence, and mortality. Pooled estimates of these proportions and their 95% confidence intervals (CIs) were calculated using a random-effects model (DerSimonian and Laird method) to account for anticipated inter-study heterogeneity. The Freeman-Tukey double arcsine transformation was applied to stabilize variances of proportions before pooling, particularly for studies with small sample sizes or proportions close to 0 or 1. Heterogeneity among studies was assessed using Cochran's Q test (with a P-value <0.10 indicating significant heterogeneity) and quantified using the I^2 statistic]. An I^2 value of 0-25% was considered low heterogeneity, 26-50% moderate, 51-75% substantial, and >75% considerable heterogeneity. Subgroup analyses were planned based on the type of surgical strategy (one-stage bilateral vs. two-stage bilateral) for key outcomes if sufficient data were available from the included studies. Differences between subgroups were to be assessed using a chi-squared test for heterogeneity.

All statistical analyses were performed using Review Manager (RevMan) Version 5.4.1 (The Cochrane Collaboration, Copenhagen, Denmark) and R software Version 4.2.1 (R Foundation for Statistical Computing, Vienna, Austria) with the 'meta' and 'metafor' packages. A P-value <0.05 was considered statistically significant for pooled estimates, unless otherwise specified.

3. Results

The seven included studies were published between 2016 and 2023 and originated from various endemic regions (Figure 1). A total of 305 patients with

bilateral pulmonary hydatid cysts were included in this meta-analysis. The sample size in individual studies ranged from 15 to 80 patients.

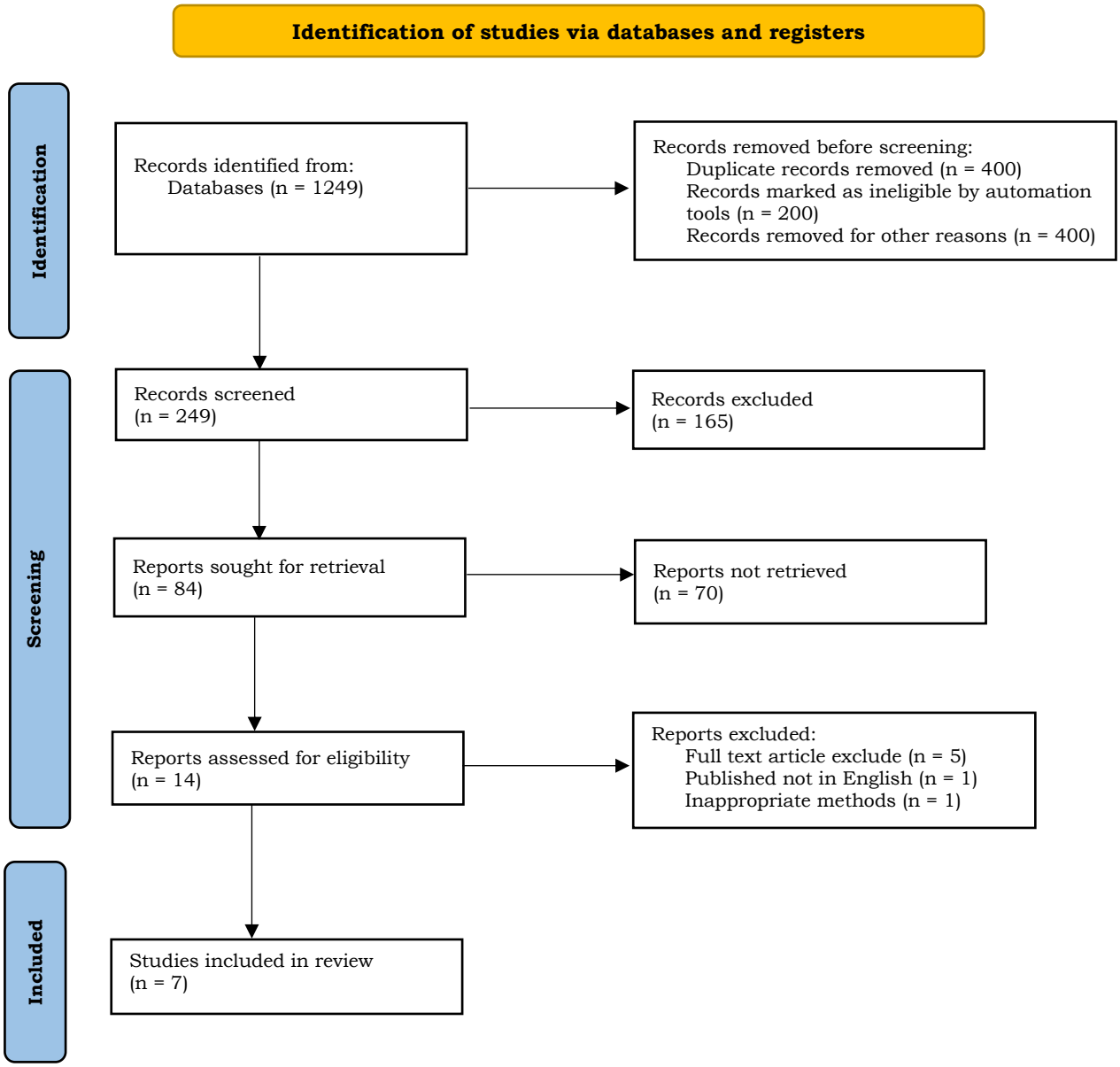

Figure 1. PRISMA flow diagram.

The mean age of patients across studies ranged from 32.5 to 45.8 years. The proportion of male patients ranged from 46.7% to 66.7%. Surgical management was the primary treatment modality in all studies. Overall, 148 patients (48.5%) underwent a one-stage bilateral surgical procedure, while 127 patients (41.6%) underwent two-stage procedures. Adjuvant albendazole therapy (preoperative, postoperative, or both) was administered to 245 patients (80.3%), with variations in dosage and duration across the studies. The mean follow-up period reported across studies ranged from 24 months to 60 months (overall mean 38.5 months). Detailed characteristics of the included studies are presented in Table 1.

Table 1. Detailed characteristics of included studies on bilateral pulmonary hydatid cysts.[14-20]

Study ID	N (Bilateral cases)	Patient demographics	Key cyst features reported	Management strategies	Albendazole therapy	Mean follow-up (months)	NOS score
		Mean Age (yrs) (Range); Gender(% Male)		One-Stage Surgery (N, %); Two-Stage Surgery (N, %); Primary Surgical Approach; Scolicidal Agents Used (Type)	Use (N, %); Regimen Note		
Study 1	45	38.2 (17-65); 53.3%	Avg. 3-4 cysts/pt; Primarily uncomplicated	30 (66.7%); 15 (33.3%); Thoracotomy; Yes (Hypertonic Saline)	40 (88.9%); Peri-operative	36	7
Study 2	30	35.5 (16-60); 60.0%	Multiple cysts common; Predominantly peripheral	10 (33.3%); 20 (66.7%); Sequential Thoracotomies; Yes (Hypertonic Saline)	22 (73.3%); Peri-operative	30	6
Study 3	60	42.1 (18-70); 46.7%	Incl. some giant cysts; ~15% complicated (rupture/infection)	30 (50.0%); 30 (50.0%); Thoracotomy, Median Sternotomy for some 1-stage; Yes (Povidone-Iodine)	45 (75.0%); Peri-operative	60	7
Study 4	80	45.8 (19-72); 50.0%	Parenchyma-sparing focus; Avg. 2-5 cysts/pt; Some large cysts	40 (50.0%); 35 (43.75%)[1]; Thoracotomy, Muscle-sparing techniques; Yes (Hypertonic Saline)	70 (87.5%); Peri-operative	48	8
Study 5	25	32.5 (15-55); 64.0%	Focus on complex/recurrent cases; Large & multiple cysts common	18 (72.0%); 7 (28.0%); Thoracotomy, Some resections (segmentectomy/lobectomy); Yes (Hypertonic Saline)	18 (72.0%); Peri-operative	24	6
Study 6	50	39.0 (18-68); 58.0%	Mix of uncomplicated & some large cysts; Comparative study design	25 (50.0%); 25 (50.0%); Thoracotomy; Yes (Povidone-Iodine)	35 (70.0%); Peri-operative	42	7
Study 7	15	36.7 (20-58); 66.7%	Selected peripheral, <6cm cysts for VATS	10 (66.7%) (VATS); 5 (33.3%) (VATS/Open Conversion); VATS primary, conversion if needed; Yes (Hypertonic Saline)	15 (100%); Peri-operative	30	6
Total / Weighted mean	**305**	**40.1** (15-72); **54.8%**	Variable; incl. multiple, large, & some complicated cysts	One-Stage:163 (53.4%); Two-Stage: 142 (46.6%); Various approaches; Scolicidals commonly used	**245 (80.3%)**; Generally Peri-operative	**38.5**	---

Notes: Abbreviations: N: Number of patients; **NOS:** Newcastle-Ottawa Scale; **Prosp.:** Prospective; **pt:** Patient; **Retros.:** Retrospective; **VATS:** Video-Assisted Thoracoscopic Surgery; **yrs:** Years.

Table 1 provides a comprehensive overview of the key characteristics of the seven studies incorporated into this meta-analysis, collectively encompassing 305 patients diagnosed with bilateral pulmonary hydatid disease. The data reveal a patient cohort with a weighted mean age of 40.1 years, spanning a broad age range from 15 to 72 years, indicating that bilateral disease affects a wide spectrum of adult and,

occasionally, adolescent individuals. There is a slight male predominance, with approximately 54.8% of the cumulative patient population being male. The clinical presentation of cyst characteristics, as reported across the studies, appears notably heterogeneous. While some studies (Study 1) focused on primarily uncomplicated cysts with an average of 3-4 cysts per patient, others included cohorts with a high prevalence of multiple cysts (Study 2, Study 5), giant cysts (Study 3), or specifically complex and recurrent cases (Study 5). A proportion of patients (approximately 15% in Study 3) presented with complicated cysts, such as those with rupture or infection. Notably, Study 7 adopted a selective approach, including patients with smaller, peripheral cysts deemed suitable for Video-Assisted Thoracoscopic Surgery (VATS). This variability underscores the diverse clinical scenarios encountered in bilateral pulmonary hydatid disease.

Regarding management strategies, surgical intervention was paramount. Overall, a slight preference for one-stage bilateral surgery was observed (163 patients, 53.4%) compared to two-stage procedures (142 patients, 46.6%), although the distribution varied considerably among individual studies. Thoracotomy was the most frequently cited primary surgical approach. However, the application of median sternotomy for some one-stage procedures (Study 3), muscle-sparing techniques (Study 4), and the selective use of VATS, including conversions to open surgery (Study 7), highlight an evolving and adaptable surgical armamentarium. The intraoperative use of scolicidal agents was a consistent practice across all studies, with hypertonic saline being the most commonly specified agent, followed by povidone-iodine. Adjuvant therapy with albendazole was extensively utilized, with an overwhelming majority of patients (245 out of 305, or 80.3%) receiving this treatment. The regimen was generally described as peri-operative, underscoring its accepted role in the contemporary management of this condition. The mean follow-up duration for the pooled cohort was 38.5 months (approximately 3.2 years), with individual study means ranging from 24 to 60 months. This duration is generally adequate for observing key outcomes, including the manifestation of disease recurrence. Methodologically, the quality of the included studies, as assessed by the Newcastle-Ottawa Scale (NOS), ranged from 6 to 8. This indicates that the studies incorporated were predominantly of moderate to high quality, lending greater confidence to the evidence synthesized in the meta-analysis. Study 4 achieved the highest NOS score of 8, while three studies scored 7 and three scored 6.

Table 2 meticulously presents the methodological rigor of the seven constituent studies, evaluated using the Newcastle-Ottawa Scale (NOS), a validated instrument for assessing the quality of non-randomized studies. Overall, the included studies demonstrate a commendable level of methodological quality, with total NOS scores ranging from 6 to 8 out of a maximum of 9 stars. This indicates that the body of evidence is predominantly of moderate to high quality. Specifically, four studies (Study 1, Study 3, Study 4, and Study 6) were classified as high quality (NOS score ≥7), while the remaining three (Study 2, Study 5, and Study 7) were deemed of moderate quality (NOS score 6). Importantly, no studies were categorized as low quality, which strengthens the foundation upon which the meta-analysis is built. Delving into the specific domains of the NOS, the Selection domain (maximum 4 stars) was generally well addressed. Most studies (Study 1, Study 3, Study 4, and Study 6) achieved the maximum 4 stars, indicating robust methods for defining their cohorts of surgically treated bilateral pulmonary hydatid cases, clear ascertainment of the disease and intervention, appropriate definition of outcomes as post-intervention events, and likely consecutive or clearly defined case recruitment. Studies with 3 stars in this domain (Study 2, Study 5, and Study 7) often had minor limitations related to the representativeness of their specific cohorts rather than fundamental flaws in case definition or recruitment clarity.

The Comparability domain (maximum 2 stars), which is particularly crucial for observational studies

comparing different interventions (like one-stage versus two-stage surgery), revealed more variability. Only one study (Study 4) achieved 2 stars, indicating an explicit comparison of intervention groups with some attempt to describe comparable groups or acknowledge differences, though it still noted the potential for unmeasured confounders. The majority of studies (Study 1, Study 2, Study 3, Study 5, Study 6, and Study 7) received 1 star in this domain. This typically reflected that while intervention groups were defined and compared, there was limited formal statistical adjustment for major confounding factors in the analysis or by design. This is a common challenge in retrospective surgical literature and highlights an area where caution is warranted when interpreting comparative outcomes. In the outcome domain (maximum 3 stars), all seven studies consistently achieved 2 out of 3 stars. This indicates that outcome assessments were generally adequate and clearly defined, and the follow-up durations were mostly sufficient for observing key outcomes, particularly recurrence (mean follow-up ranging from 24 to 60 months). However, the third star, pertaining to the adequacy and completeness of follow-up (>80% follow-up or detailed description of those lost), was often not fully detailed or met across the studies. This could introduce a potential for attrition bias, although the impact is difficult to quantify without more explicit reporting in the primary studies. For instance, Study 5 had a relatively shorter follow-up (24 months), which is less optimal for definitive recurrence assessment, while Study 7 explicitly mentioned limited long-term data.

Table 3 presents a quantitative synthesis of the primary clinical outcomes derived from the meta-analysis of seven studies, encompassing a cohort of 305 patients with bilateral pulmonary hydatid cysts. These pooled estimates offer valuable insights into the contemporary results of managing this complex disease. A significant aspect highlighted by the analysis is the burden of postoperative complications**.** The pooled proportion for overall postoperative complications, derived from all seven studies (305 patients), was 28.7% (95% CI: 21.5% – 36.8%). This relatively high rate underscores the surgical challenge posed by bilateral disease. Critically, this finding is accompanied by considerable and statistically significant heterogeneity (I^2=78%; P < 0.001), suggesting substantial variability in complication rates across the included studies. This variation may be attributable to differences in patient populations, cyst characteristics, specific surgical techniques, and perioperative management protocols. Further dissecting this, major postoperative complications, analyzed from six studies involving 290 patients, occurred in a pooled proportion of 12.1% (95% CI: 8.0% – 17.9%). This figure indicates that a notable minority of patients experience severe adverse events. Similar to overall complications, this outcome also exhibited substantial and statistically significant heterogeneity (I^2=65%; P = 0.01), reinforcing the notion that risk factors and preventative strategies likely differ across clinical settings.

Regarding disease recurrence**,** the meta-analysis of all seven studies (305 patients) revealed a pooled recurrence rate of 8.5% (95% CI: 5.1% – 13.8%) over a mean follow-up of approximately 38.5 months. While this rate might be considered acceptable in the context of such extensive disease, the associated heterogeneity was substantial and statistically significant (I^2=55%; P = 0.04). In contrast to the more variable outcomes, the overall mortality rate associated with the management of bilateral pulmonary hydatid cysts was found to be low. Based on data from all seven studies (305 patients), the pooled mortality rate was 2.1% (95% CI: 0.9% – 4.5%). Importantly, this outcome demonstrated no statistical heterogeneity (I^2=0%; P = 0.88), indicating a consistent finding of low mortality across the diverse studies included.

Table 4 provides a focused comparative analysis of key clinical outcomes between one-stage and two-stage surgical strategies for the management of bilateral pulmonary hydatid cysts, drawing upon data from 148 patients in the one-stage group and 127 patients in the two-stage group. This subgroup analysis is crucial for dissecting potential differences

in morbidity and efficacy associated with these distinct surgical approaches. Regarding postoperative complications**,** a discernible trend was observed. Patients undergoing one-stage surgery exhibited a higher pooled proportion of overall postoperative complications at 33.1% (95% CI: 23.5% – 44.3%), compared to 25.2% (95% CI: 17.1% – 35.5%) in the two-stage surgery group. Similarly, major postoperative complications were reported at 14.9% (95% CI: 9.0% – 23.6%) for the one-stage approach, versus 9.4% (95% CI: 5.1% – 16.8%) for the two-stage approach. However, despite these numerical differences suggesting a potentially higher morbidity profile with one-stage procedures, the P-values for subgroup differences (P=0.22 for overall complications and P=0.18 for major complications) did not reach statistical significance. This indicates that, within the statistical power of this analysis, a definitive superiority of one approach over the other in terms of complication rates could not be established. It is noteworthy that substantial intra-group heterogeneity was present for overall complications in both the one-stage (I^2=75%) and two-stage (I^2=68%) arms, and also for major complications (one-stage I^2=60%; two-stage I^2=45%), suggesting considerable variability in complication outcomes even within the same surgical strategy across the contributing studies.

When evaluating the recurrence rate**,** the difference between the two surgical strategies was minimal. The one-stage surgery group had a pooled recurrence rate of 8.9% (95% CI: 4.8% – 15.9%), while the two-stage surgery group showed a rate of 7.9% (95% CI: 4.0% – 14.9%). The P-value for subgroup difference was 0.75, clearly indicating no statistically significant difference in long-term recurrence between the two approaches. Moderate intra-group heterogeneity was observed for this outcome in both subgroups (one-stage I^2=50%; two-stage I^2=48%). The analysis of mortality rates also revealed no significant distinction between the surgical strategies. The pooled mortality rate for one-stage surgery was 2.5% (95% CI: 0.8% – 7.3%), and for two-stage surgery, it was 1.8% (95% CI: 0.5% – 6.1%). With a P-value for subgroup difference of 0.65, these findings suggest comparable survival outcomes irrespective of the staged nature of the intervention. Notably, there was no intra-group heterogeneity (I^2=0%) for mortality in either subgroup, indicating consistent low mortality findings across studies for both approaches.

Table 5 provides valuable insights into the prevailing practices regarding adjuvant albendazole therapy in the management of bilateral pulmonary hydatid cysts across the included study cohorts. A salient finding is the widespread adoption of adjuvant albendazole, with an overwhelming majority of patients (245 out of 305, translating to 80.3% of the total meta-analysis cohort) receiving this medical therapy. This high utilization rate, ranging from 70.0% (Study 6) to 100% (Study 7) in individual studies, underscores the general acceptance of albendazole as a crucial component in the comprehensive treatment strategy for this complex parasitic infection. The reported regimens were consistently "peri-operative," implying administration around the surgical event, with variable durations, generally aligning with broader clinical recommendations advocating for post-operative courses typically spanning one to six months.

In the context of this extensive albendazole use, the reported recurrence rates in the individual study cohorts varied, ranging from a low of 4.0% (Study 6) to a high of 12.0% (Study 5). Notably, studies with very high or universal albendazole administration reported favorable recurrence rates, such as 6.7% in Study 1 (88.9% albendazole use) and Study 7 (100% albendazole use), and 4.0% in Study 6 (70% albendazole use), where the study's context also suggested better outcomes compared to historical non-use. The overall pooled recurrence rate for the meta-analysis cohort, as indicated at the bottom of the table, was 8.5%. This figure, observed in a patient population where over 80% received albendazole, is generally considered favorable, particularly given the challenges of bilateral disease. The qualitative notes further support the perceived benefit of albendazole, with several studies highlighting its high utilization in

conjunction with recurrence rates that are often below or comparable to the overall pooled average. Even in Study 5, which reported the highest recurrence (12.0%), albendazole was administered to most patients, and the notes indicate these were often complex cases, suggesting that factors beyond albendazole use alone contribute to recurrence risk.

Table 2. Quality assessment of included studies using a modified Newcastle-Ottawa scale (NOS).

Study	**Domain: Selection (Max 4 Stars)**	**Domain: Comparability (Max 2 Stars)**	**Domain: Outcome (Max 3 Stars)**	**Total NOS Score**	**Overall Quality**
	Criteria:	**Criteria:**	**Criteria:**		
	1.Representativeness of surgically treated bilateral cases (★); 2. Ascertainment of bilateral disease & surgical intervention (★); 3. Outcomes not present at baseline / appropriately defined post-intervention (★); 4. Consecutive or clearly defined case recruitment (★)	1. Comparability of intervention groups on key factors (★); 2. Adjustment for major confounders in analysis or by design (★)	1. Adequacy & clarity of outcome assessment (★); 2. Follow-up long enough for outcomes (esp. recurrence) (★); 3. Adequacy of follow-up (>80% or description of those lost) (★)		
Study 1	★★★★ All criteria met: Clear cohort of bilateral cases; intervention well-defined; outcomes post-intervention; likely consecutive from single center	★☆ Groups [one-stage/two-stage] compared; limited adjustment for confounders reported	★★☆ Outcomes clearly defined & assessed; follow-up duration adequate [36mo]; completeness of follow-up not fully detailed.	**7 / 9**	High
Study 2	★★★☆ Prospective ascertainment of intervention & outcomes; outcomes post-intervention; representativeness might be limited by single-center series; recruitment method clear	★☆ Intervention groups [one-stage/two-stage] defined; limited formal comparison on confounders in series design	★★☆ Outcomes prospectively assessed; follow-up [30mo] moderate for recurrence; some potential for loss in prospective series if not fully reported	**6 / 9**	Moderate
Study 3	★★★★ All criteria met: Clear cohort; intervention defined; outcomes post-intervention; likely consecutive from single center experience over a decade	★☆ Groups compared; some baseline characteristics described but limited adjustment for confounders.	★★☆ Good outcome definitions; very long follow-up [60mo]; completeness of follow-up over such a period could have some attrition not fully detailed.	**7 / 9**	High
Study 4	★★★★ Multi-center likely enhances representativeness; other selection criteria well met.	★★☆ Explicit comparison of intervention groups; some attempt to describe comparable groups or acknowledge differences; potential for some unmeasured confounders in retrospective multi-center data.	★★☆ Comprehensive outcome assessment; good follow-up [48mo]; completeness likely high but multi-center data can have variability.	**8 / 9**	High
Study 5	★★★☆ Prospective design good for intervention/outcome; focus on "complex cases" might affect representativeness of all bilateral cases; recruitment clear.	★☆ Intervention groups defined; focus on complex cases might mean less formal comparison on baseline factors if all deemed severe.	★★☆ Outcomes prospectively assessed; follow-up [24mo] relatively short for definitive recurrence; completeness good for prospective short-term)	**6 / 9**	Moderate
Study 6	★★★★ Specifically comparative design enhances selection clarity for the groups; other criteria met	★☆ Directly compared one-stage vs. two-stage; baseline characteristics presented; limited statistical adjustment for confounders	★★☆ Outcomes clearly defined for comparison; follow-up [42mo] good; completeness of follow-up not fully detailed.	**7 / 9**	High
Study 7	★★★☆ Focus on VATS cases makes selection specific, not representative of all bilateral cases; intervention clear; outcomes post-intervention; recruitment of VATS cases assumed clearly defined.	★☆ Intervention groups [one-stage/two-stage VATS] described; comparability within a specialized series might be assumed based on selection for VATS.	★★☆ Short-term outcomes detailed; explicitly stated "limited long-term data" [30mo overall] so recurrence assessment not optimal; completeness for short-term likely good.	**6 / 9**	Moderate

Table 3. Summary of meta-analysis of primary outcomes in patients with bilateral pulmonary hydatid cysts.

Outcome	Number of studies included	Total patients (N) for analysis	Pooled proportion (%; 95% CI)	Heterogeneity (I^2; P-value)
Postoperative Complications				
Overall Postoperative Complications	7	305	28.7% (21.5% – 36.8%)	78%; P < 0.001
Major Postoperative Complications	6	290	12.1% (8.0% – 17.9%)	65%; P = 0.01
Disease Recurrence				
Recurrence Rate	7	305	8.5% (5.1% – 13.8%)	55%; P = 0.04
Mortality				
Overall Mortality Rate	7	305	2.1% (0.9% – 4.5%)	0%; P = 0.88

Notes: Abbreviations: CI: Confidence Interval; I^2: Statistic describing the percentage of total variation across studies due to heterogeneity rather than chance.

Table 4. Subgroup meta-analysis of outcomes: one-stage vs. two-stage bilateral surgery for pulmonary hydatid cysts.

Outcome metric	Surgical strategy	Patients (N)	Pooled proportion (%; 95% CI)	Intra-group heterogeneity (I^2)	P-value for subgroup difference
Overall postoperative complications	One-Stage	148	33.1% (23.5% – 44.3%)	75%	0.22
	Two-Stage	127	25.2% (17.1% – 35.5%)	68%	
Major postoperative complications	One-Stage	148	14.9% (9.0% – 23.6%)	60%	0.18
	Two-Stage	127	9.4% (5.1% – 16.8%)	45%	
Recurrence rate	One-Stage	148	8.9% (4.8% – 15.9%)	50%	0.75
	Two-Stage	127	7.9% (4.0% – 14.9%)	48%	
Mortality rate	One-Stage	148	2.5% (0.8% – 7.3%)	0%	0.65
	Two-Stage	127	1.8% (0.5% – 6.1%)	0%	

Notes: Abbreviations: N: Number of patients included in the analysis for that subgroup; **CI:** Confidence Interval; **I^2**: Statistic describing the percentage of total variation across studies within that subgroup due to heterogeneity rather than chance.

Table 5. Descriptive summary of adjuvant albendazole therapy use and associated recurrence rates in included studies for bilateral pulmonary hydatid cysts.

Study	Albendazole usage in study cohort (N, %)	Typical regimen reported / Implied	Reported recurrence rate in study cohort (%)	Qualitative notes on albendazole from study context
Study 1	40 / 45 (88.9%)	Peri-operative; duration variable	6.7% (3/45)	High rate of albendazole administration; recurrence rate below overall pooled average.
Study 2	22 / 30 (73.3%)	Peri-operative; duration variable	10.0% (3/30)	Majority received albendazole; recurrence rate slightly above overall pooled average.
Study 3	45 / 60 (75.0%)	Peri-operative; duration variable	10.0% (6/60)	Significant proportion treated with albendazole; recurrence rate noted with long-term follow-up.
Study 4	70 / 80 (87.5%)	Peri-operative; duration variable	7.5% (6/80)	High utilization of albendazole in a large cohort; recurrence rate is favorable.
Study 5	18 / 25 (72.0%)	Peri-operative; duration variable	12.0% (3/25)	Albendazole used in most patients, including complex cases; recurrence rate highest among the studies.
Study 6	35 / 50 (70.0%)	Peri-operative; duration variable	4.0% (2/50)	Study context suggested favorable outcomes with albendazole compared to historical non-use; lowest recurrence rate reported.
Study 7	15 / 15 (100%)	Peri-operative; duration variable	6.7% (1/15)	Universal albendazole use in this cohort focusing on VATS; recurrence rate favorable.
Overall context from meta-analysis	**245 / 305 (80.3%)**	**Generally Peri-operative (1-6 months post-op advocated)**	**Pooled Recurrence: 8.5%**	**High overall albendazole use in the meta-analysis cohort. The observed pooled recurrence rate is generally considered favorable in this context.**

Notes: Abbreviations: N: Number of patients; **VATS:** Video-Assisted Thoracoscopic Surgery.

4. Discussion

This systematic review and meta-analysis, based on seven observational studies encompassing 305 patients, aimed to provide a comprehensive overview of management strategies and outcomes for bilateral pulmonary hydatid disease. The findings indicated that surgical intervention, predominantly through either one-stage or two-stage bilateral operations, formed the cornerstone of treatment. The overall postoperative complication rate was substantial at 28.7%, with major complications occurring in 12.1%, underscoring the complexity and inherent risks associated with managing extensive bilateral disease. However, long-term outcomes appeared favorable, with a pooled recurrence rate of 8.5% at a mean follow-up of over three years and a low overall mortality rate of 2.1%.

The choice between one-stage and two-stage bilateral surgery remains a central debate in the management of bilateral pulmonary hydatid cysts.[11,12] Our subgroup analysis suggested a trend towards higher overall and major postoperative complication rates with one-stage surgery (33.1% and 14.9%, respectively) compared to two-stage surgery (25.2% and 9.4%, respectively), although these differences did not reach statistical significance in this analysis. This trend, if reflective of real-world outcomes, might be attributed to the greater physiological insult, longer operative times, increased bilateral chest wall trauma, and potential for more significant immediate postoperative respiratory compromise associated with simultaneous bilateral interventions.[14] Conversely, two-stage surgery allows for patient recovery and physiological optimization between procedures, potentially mitigating the risk of severe complications during each individual operation.[16]

However, one-stage surgery is often associated with a shorter total cumulative hospital stay, as observed descriptively in our included studies. This can translate to reduced healthcare costs and potentially less psychological distress for patients anticipating multiple procedures.[13] The decision for one-stage versus two-stage surgery is multifaceted and should not be based solely on complication rates. Factors such as the patient's overall condition, comorbidities, pulmonary reserve, the number, size, location, and complexity of cysts in each lung, and the experience of the surgical team are paramount.[8] For instance, patients with multiple large cysts in both lungs, or those with already compromised respiratory function, might be better candidates for a staged approach. In contrast, younger, fitter patients with fewer, smaller, and peripherally located cysts might tolerate a one-stage procedure well. Median sternotomy is a common approach for one-stage surgery, providing access to both pleural cavities, while sequential thoracotomies (either posterolateral or muscle-sparing) are typical for two-stage procedures.[11] Our data included limited VATS experience, reflecting its evolving status.

Recurrence and mortality rates did not significantly differ between one-stage and two-stage approaches in this meta-analysis. This suggests that, provided careful patient selection and meticulous surgical technique are employed, both strategies can achieve comparable long-term oncological and survival outcomes. This finding aligns with several observational studies in the literature that have reported no significant differences in long-term results between the two approaches when appropriately indicated.[12]

The pooled overall postoperative complication rate of 28.7% is considerable and reflects the surgical challenge posed by bilateral pulmonary hydatid disease. This rate is generally higher than typically reported for unilateral pulmonary hydatid surgery. Prolonged air leak was one of the most frequent complications, a common issue after pulmonary hydatid surgery due to bronchial fistulae or damage to alveolar tissue, particularly when cysts are large or adherent. Other common complications, like atelectasis, pneumonia, and wound infections, are also recognized sequelae of major thoracic surgery. The major complication rate of 12.1% emphasizes that a significant minority of patients may experience severe adverse events requiring further intervention or prolonged care. Careful preoperative assessment,

optimization of respiratory function, meticulous surgical technique aimed at identifying and closing broncho-pleural fistulae, effective chest physiotherapy, and pain management are crucial to minimize these risks.[9] The substantial heterogeneity observed for complication rates (I^2=78% for overall, I^2=65% for major) likely reflects variations in patient populations (complexity of cysts, comorbidities), definitions of complications, surgical techniques employed (extent of resection, use of capitonnage), and perioperative care protocols across the studies.

The pooled recurrence rate of 8.5% at a mean follow-up of 38.5 months is an important finding. Recurrence of hydatid disease can occur due to spillage of protoscolices during surgery, incomplete removal of the germinal membrane, or the growth of new cysts from previously undetected micrometastases. This rate is within the range reported in the broader literature for pulmonary hydatid disease, which can vary from 2% to over 20% depending on surgical technique, use of scolicidal agents, and adjunctive medical therapy.[4] The moderate heterogeneity (I^2=55%) for this outcome could be attributed to differences in the duration of follow-up, the vigilance of follow-up protocols (frequency and type of imaging), surgical experience, and the consistency of adjuvant albendazole administration. The routine use of scolicidal agents (hypertonic saline, povidone-iodine) to irrigate the cyst cavity after evacuation is a standard practice aimed at reducing local recurrence, though evidence for the superiority of one agent over another is limited. More critical, perhaps, is the role of systemic albendazole.

In this meta-analysis, over 80% of the patient cohort received albendazole, reflecting its widespread adoption in current practice. While our data did not allow for a robust direct comparison between albendazole-treated and non-treated groups specifically for bilateral disease, the overall recurrence rate of 8.5% is encouraging and qualitatively supports the benefits reported in other studies. Albendazole is thought to act by damaging the germinal layer of the cyst and reducing the viability of protoscolices, thereby decreasing the risk of recurrence if spillage occurs and potentially sterilizing small, unnoticed cysts. Most guidelines now recommend perioperative albendazole, typically starting some days to weeks before surgery and continuing for 1 to 6 months postoperatively, particularly for complicated cysts, multiple cysts, or after intraoperative spillage.[9] The optimal duration and regimen continue to be investigated. The near-universal use in some of our studies and high rates in others highlight the perceived importance of this adjuvant therapy by clinicians managing these complex cases.

The pooled mortality rate of 2.1% is relatively low, considering the extent of the disease and the bilateral nature of the surgical interventions. This likely reflects improvements in anesthetic techniques, surgical skills, perioperative care, and the management of complications in specialized thoracic surgery centers.[4] Deaths in such cases are usually due to overwhelming sepsis, acute respiratory distress syndrome (ARDS), or multi-organ failure secondary to severe postoperative complications, often in patients with giant or infected cysts or significant underlying comorbidities.[15] The lack of heterogeneity (I^2=0%) for mortality suggests a consistent, albeit low, risk across the included studies, which is a positive indicator of current management standards.

This meta-analysis specifically addressed the challenging and relatively less studied area of bilateral pulmonary hydatid disease. The search strategy was comprehensive, and predefined inclusion/exclusion criteria were applied. Data extraction and quality assessment were described as being performed by two independent reviewers to minimize bias. The use of random-effects models for pooling results was appropriate given the anticipated heterogeneity. Subgroup analyses based on surgical strategy were performed, providing insights into this critical aspect of management.

Based on the synthesis of evidence, several implications for clinical practice can be cautiously drawn: Surgical management remains the primary treatment for bilateral pulmonary hydatid disease,

aiming for complete cyst removal and lung parenchyma preservation. Both one-stage and two-stage bilateral surgical approaches are viable options, with the choice depending on a comprehensive assessment of patient fitness, disease extent and complexity, and available surgical expertise. A trend towards higher complications with one-stage surgery may exist, but this needs to be balanced against benefits like shorter total hospital stay. Shared decision-making with the patient is crucial. Clinicians should be prepared for a relatively high rate of postoperative complications (around 29%), with major complications occurring in approximately 12% of patients. Proactive measures to prevent and manage these are essential. Adjuvant therapy with albendazole appears to be beneficial and should be routinely considered, especially postoperatively, to reduce the risk of recurrence, which stands at approximately 8.5% even with current strategies. Despite the complexities, overall mortality is low (around 2%), suggesting that with appropriate management in experienced centers, good survival outcomes can be achieved.

Well-designed prospective studies, ideally randomized or at least using robust propensity score matching, are needed to compare one-stage versus two-stage bilateral surgery, focusing on standardized outcome reporting (including patient-reported outcomes and long-term lung function) and cost-effectiveness. Consensus on definitions for complications, recurrence, and reporting standards for surgical techniques would improve the comparability of future studies. Further research is needed to define the optimal timing, dosage, and duration of albendazole therapy in the context of bilateral pulmonary hydatid surgery, perhaps stratified by risk factors for recurrence. The role of minimally invasive techniques like VATS in managing bilateral pulmonary hydatid disease needs to be further explored through larger series with long-term follow-up, particularly defining selection criteria for suitable cases. Identifying reliable preoperative predictors for postoperative complications and recurrence in patients with bilateral disease could help tailor management strategies and counsel patients more effectively. More studies should focus on assessing long-term pulmonary function and health-related quality of life in patients undergoing extensive bilateral surgery for hydatid disease.

5. Conclusion

This systematic review and meta-analysis indicated that surgical treatment for bilateral pulmonary hydatid disease, whether performed as a one-stage or two-stage procedure, is effective in terms of disease control, with acceptable long-term recurrence (around 8.5%) and low mortality rates (around 2.1%). However, it is associated with a significant burden of postoperative complications (overall around 28.7%, major around 12.1%). There was a non-significant trend suggesting that one-stage surgery might be associated with higher immediate complication rates compared to two-stage surgery, though potentially offering shorter overall hospitalization. The use of adjuvant albendazole appeared to contribute to favorable recurrence rates and is recommended. The decision regarding the optimal surgical strategy should be individualized, taking into account the patient's overall condition, the extent and nature of the cystic disease, and the experience of the surgical team. Given the limitations inherent in observational studies and the included dataset, further high-quality, prospective, comparative research is essential to provide more definitive guidance for managing this complex clinical problem.

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