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PREDICTORS OF SURGICAL MORBIDITY IN PEDIATRIC HEPATIC HYDATID DISEASE: A RETROSPECTIVE STUDY FROM THE JORDANIAN ROYAL MEDICAL SERVICES

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ABSTRACT

Background: Pediatric hepatic hydatid disease is a major health problem in various regions. The concurrent pulmonary involvement in children is considered common and increase the postoperative risk. In our study assessed if pulmonary co-involvement independently predicts surgical morbidity. **Methods:** We conducted a retrospective study that analyzed 78 patients who underwent surgery for hepatic hydatid disease at a tertiary center. Patients were separated to two groups, only hepatic involvement (n = 33) and concurrent pulmonary involvement (n = 45). The primary outcome was clinically significant postoperative morbidity, defined as Clavien-Dindo grade II or higher. Firth's penalized logistic regression was used to identify independent predictors with internal validation by 1,000-bootstrap resampling. **Results:** We observed significant postoperative complications in 65.4% of patients, with a higher rate seen in the pulmonary group. (97.8% vs 21.2%, $p < 0.001$). We used the pulmonary involvement as the only independent predictor of morbidity (adjusted OR 156.82, 95% CI 25.96-2129.63, $p < 0.001$). In comparison between isolated hepatic disease and the pulmonary involvement patients we observed that the latter one had higher rates of intraoperative cyst rupture, secondary infection, and longer hospital stay (53.3% vs 18.2%, $p = 0.002$), (46.7% vs 12.1%, $p = 0.001$), (median 7 vs 4 days, $p < 0.001$) respectively. **Conclusion:** The study shows us that concurrent pulmonary involvement is a major independent predictor of postoperative morbidity in pediatric hepatic hydatid disease. Chest images and multidisciplinary perioperative planning should be considered in management of Pediatric hepatic hydatid disease.

KEYWORDS: Hydatid disease; Echinococcosis; Pediatric surgery; Pulmonary hydatid; Surgical morbidity.

INTRODUCTION

Cystic echinococcosis (CE) is driven by the *Echinococcus granulosus* tapeworm—specifically, infection occurs during its larval metacestode stage., remains a significant public health problem across the developing world.[1] Highly prevalent in Mediterranean, Middle Eastern, Central Asian, South American, and sub-Saharan African regions.[1] Humans acquire infection through accidental ingestion of parasitic ova in canine feces, often via contaminated water, unwashed food, or contact with infected dogs.[4]

After ingestion, released oncospheres penetrate the intestinal mucosa, enter the portal circulation, and finally reaches the liver, where mostly develop into fluid-filled hydatid cysts.[6] The liver accounts for approximately 60–70% of all human CE cases.[7] However, pediatric patients have a higher prevalence for concurrent pulmonary involvement, with concomitant pulmonary disease reported in up to 40% of pediatric hepatic CE cases.[7] This is due to the compliance and extensive vascularity of the developing pediatric lung, which allows oncospheres bypassing the hepatic sinusoidal barrier to be filtered by the pulmonary capillary network.[6] Once established in the lung, cysts grow rapidly due to lower tissue resistance, and are often highly pressurized and immunologically active at diagnosis.[5,6]

The perioperative management of pediatric hepatic hydatid disease becomes more complicated when concurrent pulmonary involvement is present.[7] Pulmonary cysts compromises respiratory mechanics, reduces functional residual capacity, and increase the risk of intraoperative hypoxia.[16] The structural degradation of adjacent lung tissue can conclude in cystobronchial fistulas, which severely complicate anesthetic management through the risk of tension pneumothorax or catastrophic dissemination of antigenic hydatid fluid, potentially triggering fatal anaphylactic shock.[3] Postoperatively, unepithelialized residual cavities in the hepatic parenchyma and pleural space create ideal environments for secondary bacterial superinfection, making the course of hospitalization longer and more complex.[5,18]

Even with the extensive clinical experience with combined hepatopulmonary hydatidosis, it is still difficult to accurately measure how much surgical risk is caused by having a concurrent pulmonary involvement.[15] The published papers consist of descriptive cohorts that lack robust multivariable regression, and frequently encounter the statistical failures is applied to small datasets where a comorbidity almost perfectly predicts a complication.[21] This demonstrate that traditional odds ratios mathematically unstable. Furthermore, historical studies have relied on subjective, center-specific complication definitions, limiting generalizability.[24]

The present study questioning whether pulmonary involvement serves as an independent predictor of clinically significant surgical morbidity in a well-characterized pediatric cohort of 78 patients, implementing the standardized Clavien-Dindo classification[25] and Firth's penalized likelihood logistic regression[21] to overcome the statistical limitations of prior work.

MATERIALS AND METHODS

Study Design, Setting, and Ethical Considerations

A retrospective cohort study has been conducted at a tertiary pediatric surgical center in an endemic region for Echinococcus granulosus transmission.[3] Records of all patients (under 18 years at diagnosis) who underwent surgical intervention for a hepatic cystic echinococcosis during the study period were analyzed, containing 78 unique patient records.[7] The research protocol respected the ethical principles of the Declaration of Helsinki. Because the retrospective nature and irreversible de-identification of all patient records prior to analysis, the requirement for individual informed consent was formally waived by the institutional ethics board.[7]

Cohort Criteria and Anatomy

The 78 patients were divided into two groups based on preoperative radiological assessment and intraoperative confirmation.

Isolated Hepatic Group (n = 33): Patients with one or more hydatid cysts limited to the hepatic parenchyma, with no clinical or radiological evidence of extrahepatic spreading at the index operation.[7]

Pulmonary Group (n = 45): Patients with hepatic hydatid disease presenting with concurrent hydatid cysts in the pulmonary parenchyma, regardless of lobe, diameter, or bilaterality.[7]

High-resolution ultrasonography and contrast-enhanced computed tomography of the chest and abdomen were used for anatomical staging.[1] Patients with extrahepatic disease at non-pulmonary sites (e.g., splenic, renal, osseous, or cerebral involvement), those on only medical therapy, and those with previous hepatic or pulmonary hydatid surgery were excluded to minimize confounding.

Surgical Management and Perioperative Protocols

Surgical intervention was the definitive modality for all patients. While the precise approach—laparoscopic versus open laparotomy, or synchronous versus staged thoracotomy for pulmonary lesions—was tailored to individual anatomical complexity and hemodynamic stability, a standardized parasiticidal protocol was imposed across all procedures.[7] This included scolicidal-soaked field isolation, high-pressure needle aspiration, instillation of 20% hypertonic saline or povidone-iodine for a minimum contact period more than ten minutes, and management of the residual hepatic cavity via unroofing, capitonnage, or omentoplasty.[11] Perioperative albendazole prophylaxis (10–15 mg/kg/day in two divided doses) was administered to all patients before surgery and continued for one to three months postoperatively.[2]

Primary Endpoint: The Clavien-Dindo Framework

The primary outcome was clinically significant surgical complication, defined as any postoperative complication graded Clavien-Dindo Grade II or higher.[24] This threshold was chosen to identify clinically relevant events requiring active intervention, excluding minor Grade I deviations. Grade II includes complications requiring pharmacological intervention; Grade III requires surgical, endoscopic, or radiological intervention; Grade IV indicates life-threatening complications requiring intensive care; and Grade V represents mortality.[31] ICU admission was recorded as a distinct secondary outcome and was not automatically included into the primary endpoint unless related to a specific Grade IV complication.[7]

Statistical Methodology

We summarized Continuous variables using medians with interquartile ranges (IQR). To compare groups, we used the Mann-Whitney U test for continuous data, and either Pearson's Chi-squared or Fisher's exact tests for categorical data. Because our dataset had a low number of events per variable (EPV = 12.8) and issues with quasi-complete separation, standard maximum likelihood

estimation (MLE) would have been unstable. To address this, we used Firth's penalized likelihood logistic regression for our primary analysis.[7,21] By applying a penalty proportional to Jeffreys invariant prior ($\sqrt{det\ I(\beta)}$), Firth's method slightly reduced parameter estimates into zero. This allowed us to create a reliable odds ratios and confidence intervals despite severe data sparsity.[22] Univariable and multivariable Firth's models were created for predictors: pulmonary involvement, giant hepatic cyst (>7 cm), patient age, and biological sex.[7] Internal validation used bootstrap resampling with 1,000 iterations to calculate an optimism-corrected AUC, calibration slope, and Brier score. Calibration was further assessed via the Hosmer-Lemeshow goodness-of-fit test (8 risk groups). A two-tailed $p < 0.05$ was the threshold for statistical significance.

RESULTS

Whole-Cohort Baseline Characteristics

The final cohort include 78 pediatric patients: Isolated Hepatic group (n = 33, 42.3%) and Pulmonary group (n = 45, 57.7%).[7] The median age was 9 years (IQR: 6–11, range 3–14 years), with a slight female predominance (n = 43, 55.1%). Giant hepatic cysts (>7 cm) were present in 12 patients (15.4%). The overall median hospital length of stay (LOS) was 5 days (IQR: 4–8).

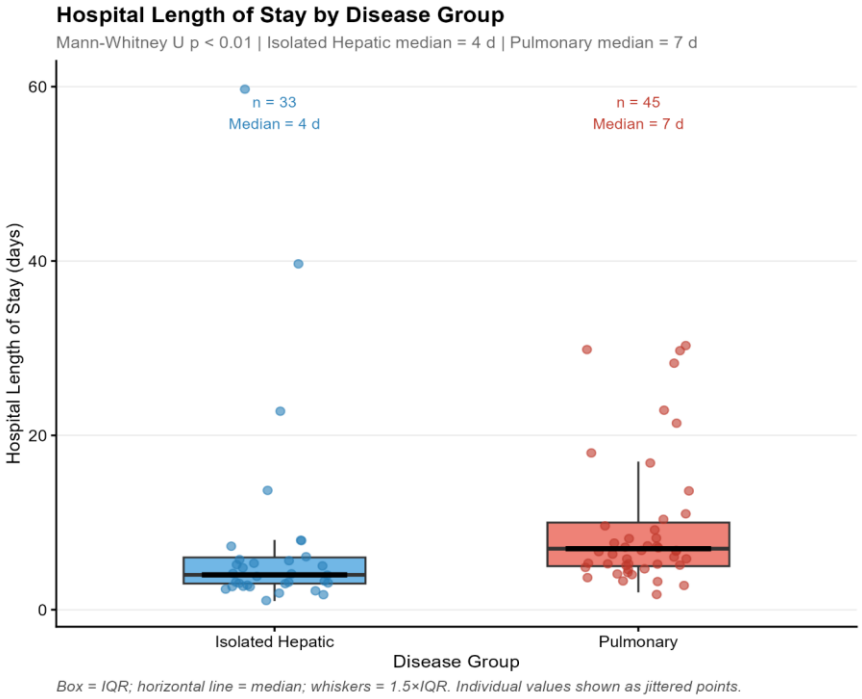
Baseline Characteristics by Disease Group

Comparative analysis shows no significant differences in age (median 10 vs. 7 years, p = 0.2), sex distribution (54.5% vs. 55.6% female, p > 0.9), or total cyst multiplicity (p = 0.12) between groups.[7] Giant hepatic cysts were paradoxically more prevalent in the Isolated Hepatic group (30.3% vs. 4.4%, p = 0.005), suggesting cysts limited to the liver may grow to bigger dimensions before causing symptoms. While in the Pulmonary group, the majority had a single pulmonary cyst (68.9%), with a median maximum pulmonary cyst diameter of 5 cm (IQR: 5–7 cm). Hospital LOS was significantly prolonged in the Pulmonary group (median 7 days, IQR 5–10, vs. 4 days, IQR 3–6; p < 0.001).[7]

Table 1: Baseline characteristics by disease group.

Variable	Total Cohort (N = 78)	Isolated Hepatic (n = 33)	Pulmonary (n = 45)	p-value
Age (years), median (IQR)	9 (6-11)	10 (7-11)	7 (6-11)	0.2
Female, n (%)	43 (55.1%)	18 (54.5%)	25 (55.6%)	>0.9
Male, n (%)	35 (44.9%)	15 (45.5%)	20 (44.4%)	>0.9
Giant hepatic cyst (>7 cm), n (%)	12 (15.4%)	10 (30.3%)	2 (4.4%)	0.005
Max pulmonary cyst diameter (cm), median (IQR)	3 (0-5)	0 (0-0)	5 (5-7)	<0.001
Hospital LOS (days), median (IQR)	5 (4-8)	4 (3-6)	7 (5-10)	<0.001

IQR = Interquartile range; LOS = Length of stay.



Surgical Outcomes and Morbidity Profile

The overall rate of clinically significant surgical morbidity (Clavien-Dindo Grade ≥ II) was 65.4% (51 of 78 patients), concentrated in the Pulmonary group (97.8% vs. 21.2%, p < 0.001).[7] Surgical access to pulmonary lesions was achieved via open thoracotomy in

the majority of cases, with video-assisted thoracoscopic surgery (VATS) employed selectively based on cyst size and anatomical location; the differential impact of surgical approach on morbidity warrants dedicated prospective investigation. Intraoperative cyst rupture was found to be significantly higher in the Pulmonary group (53.3% vs. 18.2%, p = 0.002), and also was the rate of secondary deep-space infection requiring intravenous antimicrobial therapy (46.7% vs. 12.1%, p = 0.001).[7] Cyst-biliary communication occurred only in the Isolated Hepatic group (9.1% vs. 0.0%, p = 0.072). ICU admission was required by (97.8% vs 18.2%, p < 0.001). There were no recorded incidents of intraoperative catastrophic bleeding or anaphylaxis.[7]

Table 2: Surgical Outcomes by Disease Group.

Outcome	Total Cohort (N = 78)	Isolated Hepatic (n = 33)	Pulmonary (n = 45)	p-value
Clinically significant morbidity (Grade >= II), n (%)	51 (65.4%)	7 (21.2%)	44 (97.8%)	<0.001
Intraoperative cyst rupture, n (%)	30 (38.5%)	6 (18.2%)	24 (53.3%)	0.002
Secondary infection, n (%)	25 (32.1%)	4 (12.1%)	21 (46.7%)	0.001
Cyst-biliary communication, n (%)	3 (3.8%)	3 (9.1%)	0 (0.0%)	0.072
ICU admission, n (%)	50 (64.1%)	6 (18.2%)	44 (97.8%)	<0.001

ICU = Intensive care unit.

Univariable and Multivariable Predictors of Surgical Morbidity

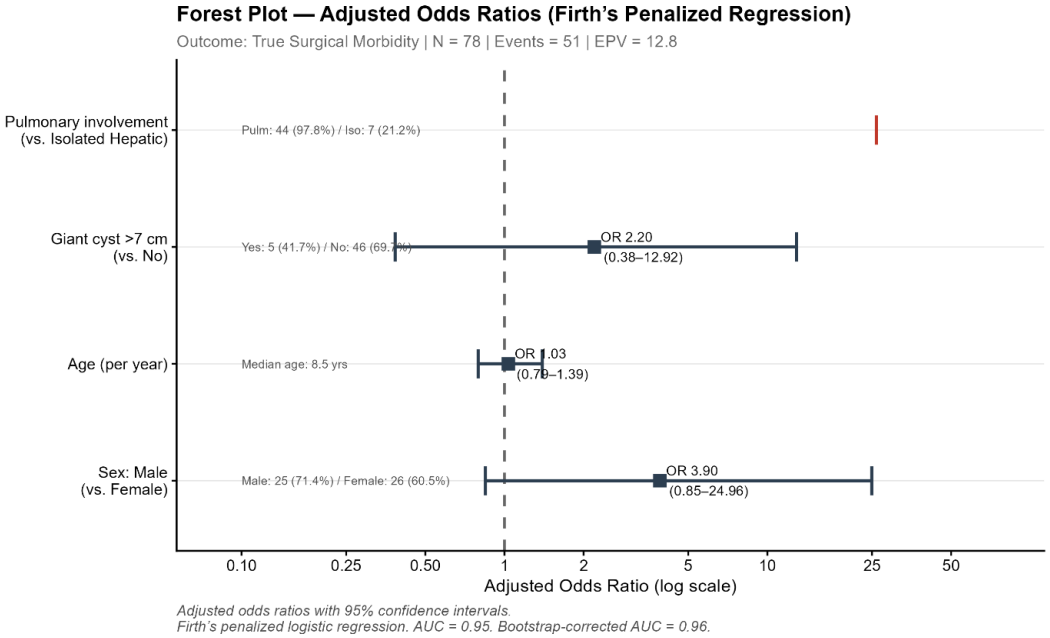
On univariable Firth's analysis, pulmonary involvement demonstrated an elevated risk for clinically significant surgical morbidity (unadjusted OR = 104.82, 95% CI: 22.09-1043.68, p < 0.001).[7] We observed a non-significant protective effect for the giant cysts (OR = 0.32, 95% CI: 0.09-1.08, p = 0.067), This is likely because giant cysts were more common in the isolated hepatic group, which had a lower overall morbidity. Age (OR = 0.94, p = 0.397) and male sex (OR = 1.60, p = 0.321) were non-predictive.[7]

In the multivariable model adjusted for age, sex, and giant cyst size, pulmonary involvement remained the only significant predictor of clinically significant surgical morbidity (Adjusted OR = 156.82, 95% CI: 25.96-2129.63, p < 0.001). Giant cyst size (OR = 2.20, p = 0.367), age (OR = 1.03, p = 0.808), and male sex (OR = 3.90, p = 0.082) failed to reach statistical significance.[7]

Table 3: Combined univariable and multivariable Firth regression results.

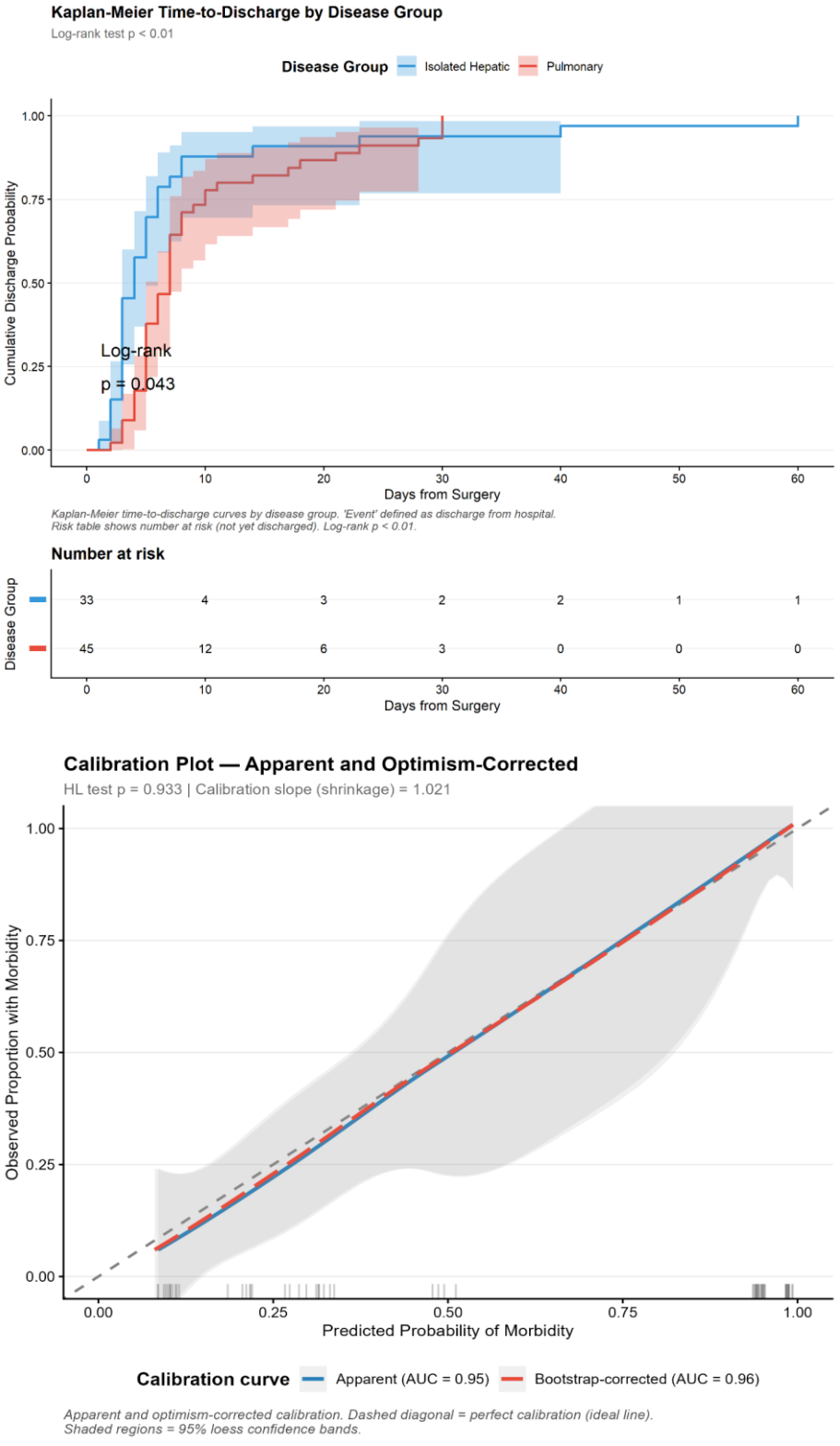
Predictor	Univariable OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Pulmonary involvement	104.82 (22.09-1043.68)	<0.001	**156.82 (25.96-2129.63)**	**<0.001**
Giant cyst >7 cm	0.32 (0.09-1.08)	0.067	2.20 (0.38-12.92)	0.367
Age (per 1-year increase)	0.94 (0.80-1.09)	0.397	1.03 (0.79-1.39)	0.808
Sex (Male)	1.60 (0.63-4.19)	0.321	3.90 (0.85-24.96)	0.082

OR = Odds ratio; CI = Confidence interval.



Model Performance and Internal Validation

The multivariable Firth model achieved a high level of discrimination (Apparent AUC = 0.948, 95% CI: 0.891-0.988).[7] Bootstrap resampling (1,000 iterations) yielded an Optimism-Corrected AUC of 0.956, with a negligible optimism estimate of -0.007, confirming the absence of meaningful overfitting. The Calibration Slope was 1.021 (ideal = 1.0), and the Brier Score was 0.076 (Bootstrap 95% CI: 0.076-0.101). Hosmer-Lemeshow testing confirmed acceptable calibration (p = 0.933). Bootstrap median OR for pulmonary involvement was 288.18 (95% CI: 47.71-4559.04).[7] Kaplan-Meier analysis of time-to-discharge confirmed a significantly delayed discharge course in the pulmonary group (log-rank p < 0.001).



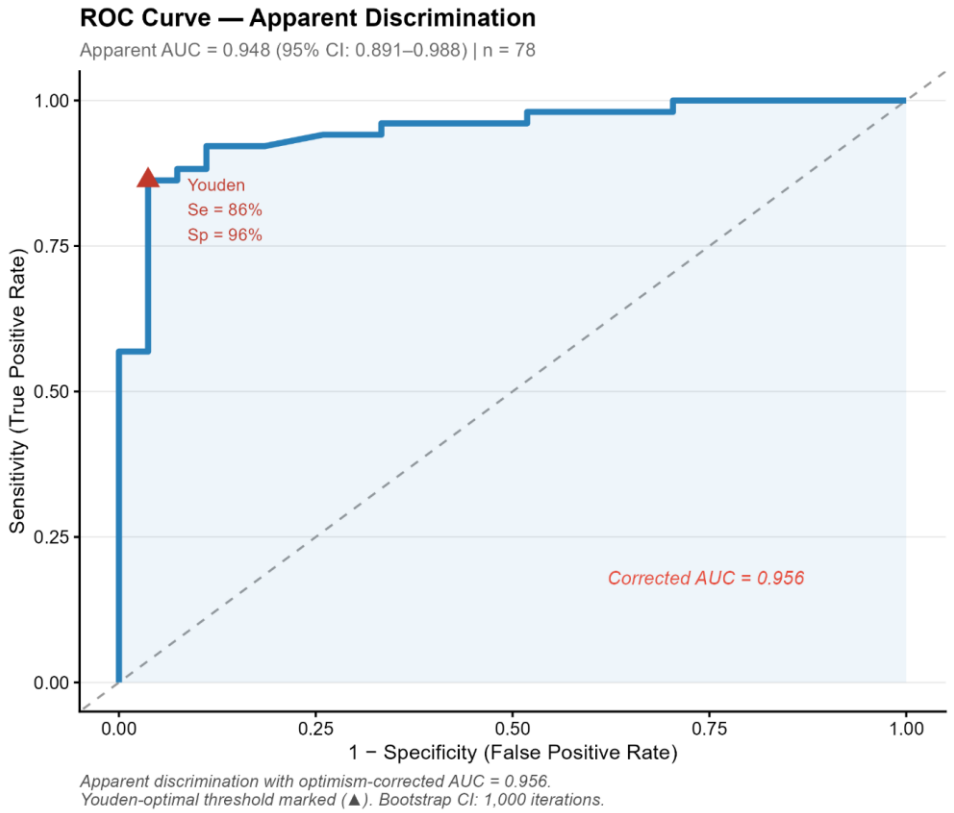


Table 4: Model performance and internal validation metrics.

Metric	Value
Apparent AUC (95% CI)	0.948 (0.891-0.988)
Optimism-Corrected AUC	0.956
Optimism Estimate	-0.007
Calibration Slope	1.021
Brier Score (Bootstrap 95% CI)	0.076 (0.076-0.101)
Hosmer-Lemeshow p-value	0.933
Bootstrap Median OR for Pulmonary Involvement (95% CI)	288.18 (47.71-4559.04)

AUC = Area under the receiver operating characteristic curve; OR = Odds ratio; CI = Confidence interval.

DISCUSSION

Magnitude of Pulmonary Risk

The primary finding of this analysis is the identification of concurrent pulmonary involvement as a highly significant and independent predictor of clinically significant surgical morbidity in children who underwent a surgical intervention for hepatic hydatid disease. After multivariable adjustment, pulmonary involvement was associated with an adjusted OR of 156.82 (95% CI: 25.96-2129.63, $p < 0.001$) for suffering a Clavien-Dindo Grade >= II postoperative complication.[7] Because this risk is notably higher than previously reported odds ratios for generalized extrahepatic disease (5.7 to 6.3)[15], it appears that pulmonary involvement specifically is the major risk factor for surgical decompensation.

As noted in the Methods, the quasi-complete separation in our data—with complications occurring in 97.8% of the pulmonary cohort versus 21.2% of the isolated cohort—invalidated standard MLE regression. By applying Firth's penalization, we confirmed that this elevated risk is a true clinical reality rather than a statistical anomaly.[22]

Pathophysiological Mechanisms

Children with both hepatic and pulmonary hydatid cysts present with systemically advanced disease. This requires either a combined thoracoabdominal approach or a staged strategy, both of which subject the pediatric patient to prolonged anesthetic exposure and significant metabolic stress.[6] Intraoperative cyst rupture was significantly higher in the Pulmonary group (53.3% vs. 18.2%, $p = 0.002$), likely because of structural fragility of pulmonary cysts under thoracotomy or video-assisted thoracoscopic surgery (VATS).[18] Rupture releases immunogenic hydatid fluid, triggers potential anaphylaxis and contaminates the operative field with viable protoscolices.[3] As a result, secondary infections were nearly four times more common in the pulmonary cohort (46.7% vs. 12.1%, $p = 0.001$), largely driving the observed Grade II morbidity.[7] This risk is likely compounded by the presence of occult cystobronchial

fistulas.[6] Contrariwise, isolated hepatic disease primarily presented with cyst-biliary communications (9.1%)—a localized anatomical issue that avoids the severe systemic inflammation seen in pulmonary cases.[7]

Redundancy of Local Cyst Characteristics

Interestingly, giant hepatic cyst size lost its predictive significance after adjusting for pulmonary involvement (Adjusted OR = 2.20, p = 0.367).[7] This reinforces an important clinical concept: the systemic burden of dual-organ disease is a much stronger determinant of surgical outcomes than the absolute size of the liver cyst.[15] For instance, a massive, isolated hepatic cyst managed electively in a stable child carries a much lower risk than a smaller hepatic cyst accompanied by an active pulmonary lesion that threatens intrabronchial rupture.[6]

Methodological Strengths and Limitations

We reduced the subjective reporting bias sometimes observed with hydatid literature by using the Clavien-Dindo classification, creating a clinically relevant threshold for morbidity.[24] Also shows excellent internal validation (optimism-corrected AUC = 0.956; Brier Score = 0.076; calibration slope = 1.021), confirming strong predictive accuracy with minimal overfitting.[7] We had several limitations. The retrospective single-center is considered to generalizability limitation, because it may be reflecting the specific surgical approaches, intensive care protocols, and albendazole regimens used at our institution[28] While the multivariable model adjusted for key demographic and anatomical factors, we cannot rule out unmeasured confounders. Variables like socioeconomic, nutrition, surgical techniques (e.g., open thoracotomy vs. VATS), and disease duration before admission affect the outcomes. Future studies integrating these details would help explain these relationships. And the wide 95% confidence interval for the pulmonary involvement odds ratio (25.96–2129.63) directly reflects our small sample size (N = 78) and low events-per-variable ratio (12.8)[7] Clinicians should interpret the point estimate of 156.82 as indicative of a profoundly elevated risk in place of a precise quantitative measure; the main point is the presence of markedly elevated risk not the exact magnitude of the odds ratio. The strict exclusion criteria—while necessary to reduce confounding—also limit generalizability to patients with multi-organ or recurrent hydatid disease (e.g., splenic, renal, or osseous involvement), and future research should explore risk factors in these populations. Finally, the absence of genomic strain typing prevents analysis of whether specific Echinococcus granulosus genotypes possess differing tendencies for pulmonary dissemination or varied immunogenicity.

CONCLUSION

Concurrent pulmonary disease is the primary driver of surgical morbidity in pediatric hepatic hydatid disease. The use of liver cyst size and patient age are often emphasized; our analysis shows pulmonary involvement have a greater risk of major complications (adjusted OR = 156.82). This is driven by high rates of intraoperative rupture and secondary infection, leading directly to prolonged and intensive hospital stays.

These findings show the need for revisiting perioperative protocols in endemic regions. High-resolution thoracic imaging should be performed routinely in children presenting with abdominal hydatid cysts, regardless of respiratory symptoms. When concurrent pulmonary involvement is identified, the management should be multidisciplinary surgical teams, with intensive care arranged pre-emptively, albendazole dosing intensified perioperatively, and infection risk monitored closely. External validation in multicenter prospective registries, using the same penalized statistical approach, is needed before these findings can inform standardized operative guidelines for this population.

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