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Propensity score analysis of the surgical approach in the management of liver hydatid disease: open vs. laparoscopic surgery. High-volume single center experience from endemic region

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Abstract

Background

Laparoscopic surgery for hepatic hydatid disease (HHD) is associated with faster recovery, but published comparisons are vulnerable to selection bias. This study evaluated operative management and outcomes after open versus laparoscopic surgery using propensity score methods.

Methods

Single center series of 1527 patients who underwent surgery for HHD between 1963 and 2025 were evaluated. Propensity score analysis was performed for the period after the introduction of laparoscopy (2003), including 598 patients: 543 underwent open and 55 laparoscopic surgery. Overlap weighting (OW) was applied, with continuous outcomes expressed as mean differences (MD) and binary outcomes as risk differences (RD).

Results

OW substantially reduced between-group differences in baseline covariates, with a maximum absolute standardized mean difference of approximately 2.9×10^{-5}. Patients in the laparoscopic group more often had smaller cysts, unilocular morphology, left-sided or peripheral localization, and Gharbi I class cyst, while open surgery was more often used in patients with larger, multilocular, right-sided, bilobar, or centrally located cysts. Compared with open surgery, laparoscopy was associated with shorter hospital stay (MD − 3.49 days, 95% CI − 5.05 to − 1.92, $p < 0.001$). OW-weighted RD estimates for reoperation, recurrence, any complication, and biliary leakage were not statistically significant. In sensitivity analyses using propensity score matching, the reduction in hospital stay remained consistent (MD − 3.33 to − 3.25 days across 1:1 to 1:4 matches, all $p < 0.005$).

Conclusion

Laparoscopic approach is associated with shorter hospital stay compared to open surgery in patients operated for HHD. Other outcome comparisons remain inconclusive.

INTRODUCTION

Hepatic hydatid disease (HHD) is a worldwide zoonosis carrying considerable public health impact. Due to a global travel it is increasingly observed in non-endemic countries in variable clinical presentations. As stated in the latest epidemiological report it is characterized by a growing incidence in both genders.[1] According to WHO Informal Working Group on Echinococcosis (WHO-IWGE) the treatment is guided by

the stage-oriented approach and is needed for patients with an active disease only.[2,3] Consistent with the American College of Gastroenterology Guidelines, surgery, either laparoscopic or open, is recommended treatment option in patients with complicated hydatid cysts with multiple vesicles, daughter cysts, fistulas, rupture, hemorrhage, or secondary infection.[4]

Based on single-center cohort studies from endemic regions laparoscopic management of liver hydatid disease is considered safe, effective, and superior to open surgery in carefully selected patients in respect to shorter hospital stay and recovery indicators.[5–10] A recent systematic review and meta-analysis confirmed that laparoscopic approach is superior to open surgery in terms of length of hospital stay, recovery time of gastrointestinal function, total complications, and incision infection risk.[11,12] However, the validity of this conclusion is hampered by the small sample size of reported studies and selection bias evidenced by performing laparoscopic approach in patients with hydatid cyst located superficially in the anterior liver segments and considering open surgery in patients with complex, large, centrally located cysts, or cysts located deep in the liver parenchyma.

In the absence of randomized controlled trials, propensity-score analysis may provide a more balanced comparison of surgical approaches in HHD. However, outcome interpretation should account for clinical selection and the small number of laparoscopic cases. For surgeons working in endemic regions, the relevant question is not only whether laparoscopy can shorten postoperative recovery, but also how often it is applicable in routine practice and how to select patients for this surgical approach. The aim of this study was to clarify the role of laparoscopic surgery for HHD within a large endemic surgical cohort by evaluating selection patterns for laparoscopy and comparing adjusted postoperative outcomes between laparoscopic and open surgery within the minimally invasive era.

METHODS

Patients

From 1963 until 2025, 1527 patients underwent surgical treatment for hepatic hydatid disease at the HPB Unit, Clinic for Digestive Surgery, University Clinical Center of Serbia. For the present study, all patients were classified into laparoscopic and open surgery groups based on operative approach. The marked imbalance between groups reflects institutional practice over time, as open surgery represented the standard approach for several decades, whereas laparoscopic treatment of hepatic hydatid disease was introduced at the study center in 2003 and was thereafter applied selectively in appropriately indicated patients. Given the substantial discrepancy in group size and the non-randomized nature of treatment allocation, propensity score-based adjustment was used to improve comparability between groups.

Data were extracted from a prospectively maintained institutional database and subsequently evaluated retrospectively. Patients with incomplete medical records that limited precise assessment of the operative approach or evaluation of study variables were removed from the relevant analyses. Among

1527 patients in the overall cohort, 1238 had complete data for all prespecified preoperative covariates. Because laparoscopic surgery for HHD was introduced in 2003, all propensity score analyses were restricted to the minimally invasive era, defined as the period from 2003 till the end of 2025. This restriction was applied to avoid direct comparison between historical open surgery and contemporary laparoscopic practice. The propensity score analytic cohort included 598 patients, comprising 543 open and 55 laparoscopic procedures (Fig. 1 Study flow chart). Follow-up data and recurrence status were updated through the end of 2025 when available in the prospectively managed institutional records. The study protocol was approved by the institutional review board. Written informed consent was obtained from all patients before treatment, in accordance with institutional practice. The study was reported in accordance with the STROBE recommendations for observational cohort studies.

Preoperative assessment

All patients underwent standard preoperative evaluation, including clinical examination, laboratory tests, and radiological assessment. Imaging work-up included abdominal ultrasonography and cross-sectional imaging with computed tomography or magnetic resonance imaging, depending on the treatment period and clinical indication.

The diagnosis of hepatic hydatid disease was confirmed according to the WHO Informal Working Group on Echinococcosis (WHO-IWGE) incorporating clinical manifestations, imaging findings, and serological assessment when applicable.[2] In the standard practice, diagnosis predominantly relied on distinctive imaging morphology within the relevant clinical context, while serology served as a supplementary rather than independent diagnostic tool. Ultrasonography was used as the principal imaging modality for initial detection and morphological assessment of cystic lesions, whereas abdominal MDCT and/or MR were used for the further evaluation of cyst size, number, segmental distribution, internal architecture, and relationship to major vascular and biliary structures, as well as for the assessment of operability.

Due to the study's duration over several decades, neither the WHO-IWGE stage nor the Gharbi classification could be consistently applied to all patients retrospectively; therefore, these classifications were excluded as covariates in the adjusted analyses.

Demographic, clinical, and cyst-related variables were recorded from the institutional database. These included age, sex, place of residence, symptomatic or asymptomatic disease, lobar location of cyst, number of involved liver segments, central versus peripheral location of the cyst, locularity, and the presence of complicated disease. Largest cyst diameter was defined as the maximum preoperative cyst diameter measured on ultrasonography, CT or MR imaging. Central cyst localization was defined as cyst involvement of segments S4a, S4b, S5 or S8, whereas peripheral localization referred to cysts located in segments S2, S3, S6 or S7. Symptomatic disease was characterized by the presence of one or more preoperative symptoms associated with hepatic hydatid disease including abdominal pain, fever, dyspepsia, palpable abdominal mass, jaundice, weight loss, dyspnea, pleural effusion, cutaneous rash, cholangitis, or bilioptysis,

A complicated hepatic hydatid cyst was defined as the presence of at least one preoperative feature indicating advanced or clinically complex disease, including radiologically suspected cystobiliary communication, free rupture into the peritoneal cavity, abscess formation due to secondary bacterial infection, or systemic manifestations such as anaphylaxis or cholangitis. Locularity, the internal architecture appearance of the cyst on preoperative imaging, as categorized as unilocular or multilocular.

According to the institutional protocol applicable at the time of the treatment, perioperative albendazole was administered whenever clinically feasible, two weeks prior to surgery at a total daily dose of 10 mg/kg divided into two doses, and continued for two postoperative treatment cycles.

Operative approach and surgical procedures

Two operative approaches were used in the treatment of hepatic hydatid disease: open and laparoscopic. Open surgery represented the standard approach for most of the study period, whereas laparoscopic surgery was introduced later and subsequently applied selectively in appropriately indicated patients. The first laparoscopic procedure for HHD was performed in 2003.

The choice of operative approach was based on preoperative imaging, cyst characteristics, anatomical considerations, and the surgeon's judgment. Operative techniques included partial pericystectomy, total cystopericystectomy, minor hepatic resections, major hepatic resections and marsupialization. Partial pericystectomy was defined as resection of the protruding dome of cyst with evacuation of its contents, leaving part of the pericyst in place[13]. Total cystopericystectomy was defined as the complex excision of the cyst together with the entire pericystic layer[13]. Minor hepatic resection referred to resection of up to two Couinaud segments, whereas major hepatic resection involved three or more segments, in accordance with the Brisbane 2000 terminology of liver anatomy and resections[14]. Marsupialization, historically reserved for selected complicated cysts, was defined as external drainage by suturing the edges of the open cyst to the abdominal wall.

Postoperative outcomes

The primary outcome of the study was postoperative length of hospital stay. Secondary outcomes included recurrence, reoperation, overall postoperative morbidity, biliary leakage, and intra-abdominal abscess. Postoperative outcomes were assessed from the institutional database and source documentation.

Overall postoperative morbidity was defined as the occurrence of at least one recorded postoperative complication during index hospitalization. Individual complications were analyzed separately when available, including fever, cardiac complications, respiratory complications, wound-related complications, biliary leakage, intra-abdominal abscess, and postoperative jaundice. Biliary leakage was defined according to the recommendations of the International Study Group of Liver Surgery (ISGLS)[15]. Other postoperative complications were recorded on the basis of standard clinical, biochemical, radiological,

and operative criteria. Length of hospital stay was recorded in days. Reoperation was defined as any repeat operative intervention related to postoperative complications or disease recurrence. Recurrence was defined as radiologically documented reappearance of HHD during postoperative follow up. Because follow up practice changed over the long study period, recurrence was recorded when postoperative imaging and the clinical record both supported the diagnosis.

Statistical analysis

Both descriptive and analytical statistics were used. Categorical variables were expressed as counts and percentages and compared using χ^2 test or Fisher's exact test, as appropriate, whereas continuous variables were summarized as mean (standard deviation) or median (interquartile range) and compared using Student's t test or the Mann–Whitney U test, depending on distribution. Baseline characteristics were first compared between the laparoscopic and open groups in the unadjusted cohort.

Because treatment allocation was not randomized and the laparoscopic group was substantially smaller than the open group, propensity score methodology was used to reduce confounding by indication. Propensity score analyses were performed only within the minimally invasive-era cohort, because open surgery was the only available operative approach before 2003. The primary adjusted analysis was based on overlap weighting, which was chosen because it preserves the full eligible cohort while emphasizing patients with overlapping probabilities of undergoing either laparoscopic or open surgery, thereby improving comparability between groups despite marked asymmetry in group size.[16,17]

Propensity scores, reflecting the probability of undergoing laparoscopic rather than open surgery, were estimated using multivariable logistic regression. The model included only preoperative variables considered clinically relevant for treatment selection: sex, age, urban versus rural residence, symptomatic disease, complicated hepatic echinococcosis, largest cyst diameter, lobar location, number of involved liver segments, central versus peripheral location, and locularity. Variables that were not consistently available throughout the study period, including WHO-IWGE and Gharbi classifications, were excluded from the propensity score model.

Covariate balance before and after weighting was assessed using standardized mean differences, and the effective sample size was examined in the weighted cohort. Continuous outcomes were analyzed using weighted linear regression with robust standard errors and are reported as adjusted mean differences with 95 percent confidence intervals. Binary outcomes were analyzed using weighted generalized linear models with robust standard errors and are reported as adjusted risk differences with 95 per cent confidence intervals. Odds ratios were additionally explored when feasible, although risk differences were considered the principal effect measure for binary outcomes because several postoperative events were rare.

As a sensitivity analysis, propensity score matching was performed using nearest-neighbor matching on the logit of the propensity score with a caliper width of 0.2 standard deviations. This analysis was used to test the robustness of the primary findings within a more conventional matched framework and to

assess whether the direction and magnitude of treatment effects remained consistent after direct comparison of patients with similar preoperative profiles. Several matching ratios were evaluated. Post-matching balance was assessed using standardized mean differences. In matched analyses, continuous outcomes were evaluated using regression methods appropriate for matched samples, whereas binary outcomes were analyzed using models with cluster-robust standard errors at the matched-set level.

Given the small number of laparoscopic cases, an additional power analysis was performed for the main binary outcomes. The analysis used the minimally invasive-era cohort of 543 open and 55 laparoscopic cases, with two-sided alpha level of 0.05 and 80% power. Based on this analysis, uncommon events such as recurrence, reoperation, and biliary leakage had limited impact on the interpretation of the final results. Therefore, non-significant findings were not interpreted as evidence of equivalence.

All tests were two-sided, and $p < 0.05$ was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 27.0 (IBM Corp., Armonk, NY, USA) and R software.

RESULTS

Demographic and clinical profiles of patients operated by open or laparoscopic approach

In the context of a high-volume tertiary referral center with an institutional HHD registry extending back to 1963, the overall proportion of laparoscopic procedures was necessarily influenced by the long pre-laparoscopic period. Laparoscopy accounted for 55 of 1527 procedures in the full cohort (3.6%), but after its introduction in 2003, it represented 55 of 598 cases in the minimally invasive-era analytic cohort (9.2%), corresponding to approximately one in ten patients. This difference reflects the later introduction and gradual selective uptake of minimally invasive surgery, and provides important context for interpreting baseline differences between the open and laparoscopic groups.

Female gender was dominant in both open and laparoscopic group without significant difference between the groups ($p = 0.228$). There was no difference between the study groups concerning the patient age either ($p = 0.894$). Symptomatic disease with abdominal pain, malaise and palpable mass was more common in the open than in the laparoscopic group ($p < 0.001$). No difference was found between the two groups in respect to other clinical features, such as jaundice and cholangitis ($p = 1.000$). A history of rural habitats and contact with domestic animals were the prevailing features of the entire cohort and occurred more commonly in the laparoscopic group ($p = 0.012$ and $p = 0.009$, respectively). The baseline cyst profile suggests that laparoscopy was used in a selected subset of patients rather than as a uniform alternative to open surgery. Cysts treated laparoscopically were more often unilocular, while multilocular disease was more frequent in the open group (80% vs 62% and 20% vs 38% respectively; $p = 0.029$). A similar pattern was seen in anatomical distribution: laparoscopic surgery was more often used for left-sided and peripheral cysts, whereas right-sided, bilobar, and centrally located cysts were more commonly managed by open approach ($p < 0.001$ for lobar distribution; $p = 0.029$ for central versus peripheral localization). Among patients with available Gharbi

classification, class I cysts were more frequent in the laparoscopic group (65.5% vs 33.8%; p = 0.004). In general, these differences suggest that the laparoscopic approach was selected as the preferred method for cysts with more favorable morphology and location, while open surgery continued to be the predominant method for complex anatomical presentations. The demographic and clinical profiles of the cohort as well as Gharbi classification are summarized in Table 1.

Table 1
Baseline clinicopathological and demographic profile of patients based on surgical approach (unadjusted)

Variable	Open approach (n = 1472)	Laparoscopic approach (n = 55)	SMD	p-value
Age, years (mean ± SD)	45.53 (15.36)	44.89 (14.76)	0.043	0.894
Sex				0.228
Male	567 (38.5%)	27 (49.1%)	0.204	
Female	905 (61.5%)	28 (50.9%)		
History of rural habitat (Yes)	912 (62.0%)	46 (83.6%)	0.479	0.012
Contact with domestic animals (Yes)	1049 (71.3%)	50 (90.1%)	0.536	0.009
Symptomatic disease (Yes)	1273 (86.5%)	30 (54.5%)	0.756	< 0.001
Abdominal pain	1164 (79.1%)	25 (45.4%)	0.734	< 0.001
Dyspepsia	550 (37.4%)	16 (29.1%)	0.188	0.287
Vomiting	313 (21.3%)	6 (10.9%)	0.270	0.155
Malaise	267 (18.1%)	2 (3.6%)	0.513	0.020
Weight loss	157 (10.7%)	2 (3.6%)	0.317	0.168
Palpable mass	503 (34.2%)	0 (0.0%)	1.019	< 0.001
Jaundice	68 (4.6%)	2 (3.6%)	0.093	1.000
Cholangitis	17 (1.2%)	0 (0.0%)	0.153	1.000
Pleural effusion	39 (2.6%)	0 (0.0%)	0.230	1.000
Ascites	10 (0.7%)	0 (0.0%)	0.123	1.000
Splenomegaly	9 (0.6%)	0 (0.0%)	0.111	1.000
Extrahepatic localization of hydatid cyst	72 (4.9%)	3 (5.4%)	0.037	0.689
Free cyst rupture	71 (4.8%)	0 (0.0%)	0.318	0.407
Abscess-forming cyst	168 (11.4%)	3 (5.4%)	0.207	0.433
Cyst locularity				0.029
Unilocular	912 (62.0%)	44 (80.0%)	0.406	

Variable	Open approach (n = 1472)	Laparoscopic approach (n = 55)	SMD	p-value
Multilocular	560 (38.0%)	11 (20.0%)		
Largest cyst diameter, cm (mean ± SD)	9.08 (3.75)	7.29 (3.23)	0.513	0.004
Hepatic lobe involved				< 0.001
Left	286 (19.4%)	26 (47.3%)	0.613	
Right	930 (63.2%)	24 (43.6%)		
Bilobar	256 (17.4%)	5 (9.1%)		
Cyst localization*				0.029
Central	530 (36.0%)	13 (23.6%)	0.291	
Peripheral	942 (64.0%)	42 (76.4%)		
Number of liver hydatid cysts (mean ± SD)	1.43 (1.06)	1.17 (0.45)	0.320	0.086
Gharbi classification (n = 1379)**				0.004
Gharbi class I	448 (33.8%)	36 (65.5%)	0.673	
Gharbi class II	183 (13.8%)	3 (5.5%)		
Gharbi class III	394 (29.8%)	8 (14.5%)		
Gharbi class IV	155 (11.7%)	6 (10.9%)		
Gharbi class V	144 (10.9%)	2 (3.6%)		

Values are presented as absolute numbers with percentages unless otherwise stated; continuous variables are presented as mean ± standard deviation; Percentages were calculated using available data for each variable.

*Cyst localization-central localization for cysts in segments IVa/IVb, V, and VIII; peripheral localization: cyst in segments II, III, VI, VII;

**Gharbi classification was established in 1981; thereafter, only subsequent patients were classified accordingly. Percentages for Gharbi classification were calculated among patients with available Gharbi data;

SMD = standardized mean difference.

Laboratory profiles of patients operated by open or laparoscopic approach

Leukocytosis was significantly more prevalent in the open group than in the laparoscopic group ($p < 0.001$). Postoperative day 3 values of bilirubin, AST, ALP and GGT were higher in open than in the laparoscopic group (Supplementary Table 1).

Table S1
Perioperative factors and early postoperative laboratory values (unadjusted)

Characteristic	Open (n = 1472)	Laparoscopic (n = 55)	SMD	p-value
Complicated hydatid cyst*	341 (23.1%)	11 (20.0%)	0.075	0.667
Leukocytosis**	413 (28.0%)	2 (3.6%)	0.742	< 0.001
Peritoneal dissemination	40 (2.7%)	0 (0.0%)	0.239	1.000
Lung involvement	9 (0.6%)	0 (0.0%)	0.111	1.000
Retroperitoneal involvement	7 (0.5%)	0 (0.0%)	0.098	1.000
Cystobiliary communication	305 (20.7%)	6 (10.9%)	0.255	0.178
Diaphragmatic involvement	7 (0.5%)	3 (5.5%)	0.306	0.017
Intraoperative cholangiography	334 (22.7%)	5 (9.1%)	0.395	0.048
Hypertrophy of the contralateral lobe	166 (11.3%)	2 (3.6%)	0.334	0.169
Number of abdominal drains			0.967	< 0.001
0 drains	12 (0.8%)	0 (0.0%)		
1 drain	332 (22.5%)	36 (65.5%)		
2 drains	686 (46.6%)	14 (25.5%)		
3 drains	342 (23.2%)	5 (9.1%)		
4 drains	80 (5.4%)	0 (0.0%)		
5 drains	14 (1.0%)	0 (0.0%)		
6 drains	5 (0.3%)	0 (0.0%)		
7 drains	1 (0.1%)	0 (0.0%)		
ALP on POD3 (mean ± SD)	132.37 (34.77)	91.97 (30.99)	1.227	< 0.001
ALT on POD3 (mean ± SD)	71.63 (29.44)	76.32 (229.12)	0.029	< 0.001
AST on POD3 (mean ± SD)	58.58 (22.81)	40.01 (53.18)	0.454	< 0.001
Total bilirubin on POD3 (mean ± SD)	21.86 (7.78)	13.04 (6.63)	1.221	< 0.001
GGT on POD3 (mean ± SD)	107.88 (47.32)	53.19 (39.53)	1.254	< 0.001
CRP on POD3 (mean ± SD)	33.71 (21.94)	35.23 (53.31)	0.037	< 0.001

Values are presented as absolute numbers (n) with percentages (%) unless otherwise stated; For variables with coded categories (e.g., number of drains), SMD and p-value refer to the overall test for the

variable.

*Complicated hydatid cyst was defined as the presence of at least one of the following: cystobiliary communication, free rupture into the peritoneal or pleural cavity, abscess formation due to secondary bacterial infection, systemic manifestations (e.g., anaphylaxis, cholangitis), or anatomically unfavorable localization; Laboratory units: ALP, ALT, AST, and GGT are expressed in U/L, total bilirubin levels in μmol/L, CRP in mg/L.

**Leukocytosis was defined as a peripheral blood leukocyte count greater than 10×10^9/L; CRP, C-reactive protein; AST, Aspartate aminotransferase; ALT, Alanine aminotransferase; ALP, Alkaline phosphatase; GGT, Gamma-glutamyl transferase; POD3, postoperative day 3.

Operative management and unadjusted postoperative outcomes

The anatomical distribution of cysts further supported selective use of laparoscopy. Cysts involving segments 5 and 8 were more frequent in the open group than in the laparoscopic group (32.7% vs 14.5%, $p = 0.021$; and 24.2% vs 9.1%, $p = 0.032$, respectively) (Supplementary Table 2).

Table S2
Anatomical distribution and operative details (unadjusted)

Characteristic	Open (n = 1472)	Laparoscopic (n = 55)	SMD	p-value
Segment I involved	29 (2.0%)	0 (0.0%)	0.200	1.000
Segment II involved	198 (13.4%)	8 (14.5%)	0.024	0.804
Segment III involved	249 (16.9%)	16 (29.1%)	0.281	0.071
Segment IV involved	340 (23.1%)	14 (25.5%)	0.061	0.717
Segment V involved	482 (32.7%)	8 (14.5%)	0.446	0.021
Segment VI involved	345 (23.4%)	17 (30.9%)	0.180	0.271
Segment VII involved	676 (45.9%)	19 (34.5%)	0.239	0.172
Segment VIII involved	356 (24.2%)	5 (9.1%)	0.432	0.032
Spleen involvement	25 (1.7%)	0 (0.0%)	0.186	1.000
Bile duct suture performed (Yes)	272 (18.5%)	5 (9.1%)	0.295	0.201
T-drain used (Yes)	69 (4.7%)	2 (3.6%)	0.096	1.000
Type of procedure			0.374	0.053
Marsupialization	6 (0.4%)	0 (0.0%)		
Partial pericystectomy	1271 (86.4%)	39 (70.9%)		
Total cystopericystectomy	155 (10.5%)	12 (21.8%)		
Minor resection	28 (1.9%)	2 (3.6%)		
Major resection	12 (0.8%)	2 (3.6%)		

Values are presented as absolute numbers (n) with percentages (%) unless otherwise stated. Segment variables indicate whether the cyst involved a given liver segment.

However, segment 7 involvement was also present in 19 laparoscopic patients (34.5%) and did not differ significantly between groups. This suggests that segmental location alone did not determine the operative approach, but was interpreted together with overall cyst accessibility and expected technical feasibility (Supplementary Table 2). There were no differences in the type of procedure (partial pericystectomy in 86.4% vs 70.9%, total pericystectomy in 10.5% vs 21.8%, minor resection in 1.9% vs 3.6%, major resection in 0.8% vs. 3.6% of patients, p = 0.053) between the open and laparoscopic groups (Supplementary Table 2). No difference was found between the study groups concerning bile duct suture and T-tube placement. Operative characteristics are presented for the full historical cohort, whereas unweighted and overlap-weighted postoperative outcomes in Tables 3 and 4 refer to the minimally invasive-era cohort. The overall morbidity (fever, respiratory complications and wound-related

complications) and liver-related complications (intra-abdominal abscess) were more frequent in patients operated by open approach ($p < 0.001$). The length of hospital stay was longer in the open group (9 vs 4 days, $p < 0.001$). No differences between the study groups were found in the rates of reoperation and recurrence of hydatid disease ($p = 0.433$, $p = 0.375$) (Tables 3 and 4).

Table 2
Outcomes (overlap-weighted effects)

Outcome	Open approach (raw)	Laparoscopic approach (raw)	OW risk Open	OW risk Lap	OW effect (RD/MD, 95% CI)	p value
Length of hospital stay (days), median (IQR)	**9 (8–11)**	**4 (3.5–6.5)**	-	-	MD = -3.49 (-5.05 to -1.92)	< 0.001
Recurrence of hydatid cyst	68/543 (12.52%)	3/55 (5.45%)	10.31%	6.32%	RD = -0.040 (-0.128 to 0.048)	0.375
Reoperation	20/543 (3.68%)	3/55 (5.45%)	2.73%	5.99%	RD = 0.033 (-0.049 to 0.114)	0.433

Unweighted results are shown for the minimally invasive-era cohort (open vs laparoscopic) as n/N (%) for binary outcomes and median (IQR) for length of stay (LOS). **Overlap-weighted treatment effects were estimated in the same minimally invasive-era propensity score analytic cohort, restricted to patients treated from 2003 onward (n = 598; open n = 543, laparoscopic n = 55).** Length of stay is reported as mean difference (MD), and recurrence and reoperation as risk difference (RD) with 95% confidence intervals. RD and MD were calculated as laparoscopic minus open surgery. Negative values indicate lower risk or a shorter hospital stay after laparoscopy. **All p values correspond to the PS/OW analytic sample.**

Table 3

Postoperative complications (raw distribution and overlap-weighted effects)

Variable	Open (raw)	Lap (raw)	OW risk Open	OW risk Lap	OW effect (RD, 95% CI)	P value
General complications						
Fever	5/543 (0.92%)	0/55 (0.00%)	0.31%	0.00%	RD = − 0.003 (− 0.006 to − 0.001)	0.013
Cardiac complications	2/543 (0.37%)	0/55 (0.00%)	0.43%	0.00%	RD = − 0.004 (− 0.011 to 0.002)	0.206
Respiratory complications	26/543 (4.79%)	0/55 (0.00%)	2.07%	0.00%	RD = − 0.021 (− 0.029 to − 0.013)	< 0.001
Wound-related complications	13/543 (2.39%)	0/55 (0.00%)	1.83%	0.00%	RD = − 0.018 (− 0.027 to − 0.009)	< 0.001
Liver-related complications						
Biliary leakage	6/543 (1.10%)	5/55 (9.1%)	0.97%	9.14%	RD = 0.082 (− 0.017 to 0.181)	0.106
Intra-abdominal abscess	12/543 (2.21%)	0/55 (0.00%)	1.39%	0.00%	RD = − 0.014 (− 0.021 to − 0.007)	< 0.001
Postoperative jaundice	1/543 (0.18%)	0/55 (0.00%)	0.02%	0.00%	RD = − 0.000 (− 0.001 to 0.000)	0.318

Raw values are shown as unweighted event counts in the minimally invasive-era cohort (n/N, **%**). **Overlap-weighted risks and treatment effects were estimated in the same propensity score analytic cohort, restricted to patients treated from 2003 onward (n = 598; open n = 543, laparoscopic n = 55).** Postoperative complications are reported as risk differences (RD) with 95% confidence intervals. RD was calculated as laparoscopic minus open surgery. Negative values indicate lower risk after laparoscopy, whereas positive values indicate higher risk after laparoscopy. **All p values correspond to the PS/OW analytic sample.**

Overlap-weighted analysis in the minimally invasive era

For adjusted comparisons, propensity score analyses were restricted to the minimally invasive era, after laparoscopic surgery had become available at the study center. Detailed balance diagnostics and overlap-weighted outcome estimates are shown in Tables 2–4. After overlap weighting, laparoscopic surgery remained associated with shorter length of hospital stay (LOS), whereas the adjusted estimates

for recurrence, reoperation, overall morbidity, and biliary leakage were less precise and not statistically significant (Tables 2 and 3).

Table 4
Propensity score overlap weighting: covariate balance and effective sample size in the minimally invasive-era cohort

Item	Value
Maximum absolute SMD after OW	4.026e-09
Effective sample size (ESS), Open	454.24
Effective sample size (ESS), Laparoscopic	51.72

OW = overlap weighting. ESS reflects the size of the overlap population and may be substantially smaller than the unweighted sample size.

The post hoc power assessment showed that the study was underpowered for rare binary outcomes. With 543 open and 55 laparoscopic cases, only large differences in recurrence, reoperation, or biliary leakage could be detected with 80% power. Therefore, non-significant findings for these endpoints were interpreted as inconclusive rather than as evidence of equivalent safety.

Sensitivity analysis

The primary comparisons were repeated in predefined sensitivity analysis using propensity score matching (nearest-neighbor 1:1, 1:3, and 1:4) to assess whether the findings depended on the weighting approach. The associations with shorter LOS remained consistent across all matched samples, with a mean difference (MD) of -3.33 days (95% CI -4.96 to -1.70, p = 0.001) in 1:1 matching, -3.25 days (95% CI -4.86 to -1.64, p = 0.002) in 1:3 matching, and − 3.32 days (95% CI -5.02 to -1.62, p = 0.002) in 1:4 matching (Table 5). For binary outcomes (reoperation, recurrence, occurrence of any complications, biliary leakage), point estimates were directionally similar to the overlap-weighted analysis. However, given the small number of events and the reduced matched sample size, confidence intervals were wide and difference were not statistically significant (Table 5).

Table 5
Propensity score matching sensitivity analysis in the minimally invasive-era cohort (ATT; caliper 0.2 SD logitPS) Panel A. Matched sample, covariate balance, and length of stay

Matching ratio	Laparoscopic, n	Open, n	Maximum adjusted SMD	LOS MD (95% CI)	P
1:1	33	33	0.3649	-3.33 (− 4.96 to − 1.70)	0.001
1:3	33	74	0.2049	-3.25 (− 4.86 to − 1.64)	0.002
1:4	33	93	0.2000	-3.32 (− 5.02 to − 1.62)	0.002

Panel B. Binary outcomes after propensity score matching

Matching ratio	Reoperation RD (95% CI), p	Recurrence RD (95% CI), p	Any complication RD (95% CI), p	Biliary leakage RD (95% CI), p
1:1	0.095 (-0.033 to 0.224) p = 0.147	-0.143(-0.347 to 0.062) p = 0.171	0.095 (-0.033 to 0.224) p = 0.147	0.095 (− 0.033 to 0.224) p = 0.147
1:3	0.095 (-0.033 to 0.224) p = 0.147	-0.095(-0.265 to 0.074) p = 0.271	0.063 (-0.033 to 0.160) p = 0.199	0.095 (-0.033 to 0.224) p = 0.147
1:4	0.095 (-0.033 to 0.224) p = 0.147	-0.095(-0.263 to 0.072) p = 0.264	0.071 (-0.031 to 0.174) p = 0.171	0.095 (-0.033 to 0.224) p = 0.147

Panel A shows matched sample size, post-matching balance, and length of stay estimates. Panel B shows matched estimates for binary outcomes. Matching was performed in patients treated from 2003 onward, using nearest-neighbor matching on the logit of the propensity score, with a caliper of 0.2 SD. Estimates refer to the ATT population. Length of stay is reported as mean difference (MD), and binary outcomes as risk difference (RD), with 95% confidence intervals and p values. MD and RD are calculated as laparoscopic minus open surgery. Negative MD values indicate shorter hospital stay after laparoscopy, whereas positive RD values indicate higher event risk after laparoscopy. Any complication was defined as the occurrence of at least one recorded postoperative complication. ATT, average treatment effect on the treated; CI, confidence interval; LOS, length of hospital stay; MD, mean difference; RD, risk difference; SD, standard deviation; SMD, standardized mean difference.

DISCUSSION

According to the literature review, this is one of the largest single-center surgical series of patients with HHD, with more than 1500 patients treated over a 60-year institutional period. Such a long study period gives a broad view of surgical practice in an endemic region, but it also introduces unavoidable heterogeneity. For several decades, open surgery was the only established operative approach, while laparoscopy was introduced in our center in 2003, and then gradually adopted in selected patients. For this reason, differences between the open and laparoscopic groups were not unexpected, and the results should not be read simply as a head to head comparison of two equivalent operative approaches, but as a reflection of how laparoscopy entered routine practice and how its use was shaped by cyst anatomy, disease complexity, and surgical judgement. Propensity score adjustment was therefore used not to remove this clinical reality, but to place the outcome comparison on more balanced grounds. The results of the presented study should be interpreted in this context.[6,18,19]

The number of patients operated by laparoscopic approach remained limited because of the surgeons' opinion, in the time when minimally invasive surgery was introduced, that the laparoscopic approach increases the probability of intraoperative spillage of hydatid material. This attitude has already been reported in the literature.[20–22] Gradually, with the acceptance of minimally invasive surgical techniques laparoscopic approach was considered primary treatment modality for patients with HHD.

The unadjusted baseline profile in our cohort clearly supports the presence of selection bias (Table 1). The two groups were comparable concerning the patient gender and age. Female gender was dominant in both open and laparoscopic group without significant difference between the groups ($p = 0.228$). There was no difference between the study groups concerning the patient age either ($p = 0.894$).

Symptomatic disease was more frequent in the open than in the laparoscopic group ($p < 0.001$), mainly reflected by higher rates of abdominal pain and palpable mass. In daily practice, this usually points to a larger or more complex cyst burden, with mass effect, inflammation, infection, or possible biliary involvement.[19,23,24] Therefore, symptoms in this cohort should be considered part of the operative risk profile, not as isolated clinical variables. Interestingly, no difference was found between the two groups in respect to other clinical features, such as jaundice and cholangitis ($p = 1.000$), suggesting that the imbalance between open/laparoscopic approach was driven more by cyst burden and anatomical complexity than by clinically evident biliary sepsis or acute inflammatory presentation.[19,23]

The majority of patients in the laparoscopic group had unilocular cyst while multilocular cyst finding was more common in the open group ($p = 0.029$). While there was no difference between the groups in the number of hydatid cysts, larger cyst diameter was found in the open group ($p = 0.004$). Peripheral cyst localization was a dominant feature in the laparoscopic group and central cyst localization was more common in the open group ($p = 0.029$). These features indicate a selection bias favoring laparoscopic approach for technically less demanding cases with unilocular, peripherally located cysts as it is reported in the available literature.[6,7,19,23,25] Thus, the baseline differences in our series are not unexpected, as they reflect the same operating logic documented in the literature, in which the laparoscopic approach is generally applied initially to anatomically favorable disease.[6,8,11,18,26] The

present findings are consistent with earlier comparison series. Bayrak and Altintas similarly reported larger and less favorable cysts among patients treated by open surgery, with significant differences in cyst size and localization between approaches.[23] Their treatment algorithm favored open surgery for cysts in segments I or VII, deeply positioned intraparenchymal cysts, and cysts larger than 14cm, while more accessible lesions favored laparoscopic surgery.[23] The more recent study reported by Zaharie and co-workers also demonstrated significant differences in cyst dimension, localization and the presence of cystobiliary communication between laparoscopic and open groups, concluding that increasing experience with laparoscopy does not remove the need for certain selection criteria to ensure safe practice.[22] The relatively frequent involvement of segment 7 among laparoscopic cases does not imply that posterosuperior cysts are generally ideal for laparoscopy. In conservative surgery for HHD, a segment 7 cyst may still be approachable when superficial, exophytic, or subdiaphragmatic, allowing exposure and evacuation without complex liver transection. This probably explains why selected segment 7 cysts were treated laparoscopically in the presented cohort. In these cases, the decisive factor was likely not the segment itself, but the real operative accessibility of the cyst and the possibility of managing the residual cavity safely. However, extended use of laparoscopic approach in more advanced cases may require additional laparoscopic instruments as reported in the literature.[27] Moreover, the extended use of laparoscopy is associated with increase rate of postoperative complications, mainly bile leaks, although not statistically significant compared to open surgery.[6,22,28]

Leukocytosis was significantly more prevalent in the open group than in the laparoscopic group ($P < 0.001$), and postoperative day 3 bilirubin, AST, ALP and GGT values also were higher after open surgery. Taken together, these findings suggest a more pronounced inflammatory and hepatobiliary burden in patients managed by laparotomy. This trend is clinically relevant in HHD, since inflammatory, infected, cholestatic or biliary communicating cysts are generally less suitable to a minimally invasive approach and more frequently require open exploration. This is in line with prior recommendations to consider MRCP or ERCP when intrabiliary rupture is suspected and use cross-sectional imaging for complex cysts and operative planning.[2,29,23,26]

The overall morbidity (fever, respiratory complications and wound-related complications) and liver-related complications (intra-abdominal abscess) were more frequent in patients operated by open approach ($p < 0.001$), the findings that are similar to results reported by other studies in the literature.[6,7,10,11,19,22–24] This probably reflects both the greater trauma of laparotomy and the fact that the open group included more complex cysts. Similar series have reported less wound-related and general complications and faster recovery after laparoscopic treatment, while 2022 meta-analysis found lower overall morbidity and fewer incision-related infections after laparoscopy.[19,22–25]

No differences were found in the rates of reoperation and recurrence of hydatid disease ($p = 0.433$, $p = 0.375$). This is important because recurrence has long been considered one of the main concerns with laparoscopy, mainly due to the fear of spillage. However, available data suggest that recurrence is uncommon when basic rules of hydatid surgery are respected: controlled aspiration, protection against

spillage, complete evacuation of parasitic material, inspection of the cavity, and management of biliary communications. In line with our findings, previous comparative series and meta-analytic data have not shown a meaningful difference in recurrence between laparoscopic and open surgery. [11,22,26]

The length of hospital stay was longer in the open group (9 vs 4 days, $p < 0.001$). This finding is in accordance with the broader comparative literature, where the benefit of laparoscopy is best demonstrated by faster postoperative recovery. Previous series have reported hospital stays of approximately 4–6 days following laparoscopy against 7–12 days after open surgery, and the recent meta-analysis confirmed a significant reduction in hospital stay after laparoscopic treatment.[6,11,19,22–26]

These findings should be interpreted in light of non-random treatment allocation. Many of the features that led surgeons to choose open surgery, such as a larger cyst size, central localization, multilocular morphology, or inflammatory and biliary complexity, are also features that may worsen postoperative outcomes.[11,22,23,26] Propensity score analysis was therefore used to place the comparison on more balanced clinical grounds.[28] After the previously described imbalance was reduced, shorter length of hospital stay remained the main finding associated with laparoscopic approach (Table 3). In the overlap-weighted analysis, covariate balance was excellent, and laparoscopy remained associated with a clinically relevant reduction in length of stay. The same direction and magnitude of effect were reproduced in all propensity-score matching sensitivity analyses. This is important because it suggests that shorter recovery was not only a consequence of the more favorable unadjusted laparoscopic cohort, but the most stable advantage of the minimally invasive approach in this series (Table 5). This finding is also the one most consistently supported by the literature. Previous comparative studies and the 2022 meta-analysis have generally associated laparoscopy with shorter hospital stay and faster early recovery, whereas differences in recurrence, biliary leakage, and residual cavity infection have been less consistent or not statistically significant.[11,22,23,29] Majority of this data is derived from non-randomized cohort studies, and the meta-analysis itself points up the need for additional rigorous comparative evidence.[11]

In contrast, the adjusted figures for recurrence, reoperation, overall morbidity, and biliary leakage require more cautious interpretation. These results were limited by a small number of laparoscopic cases and by rare events, so the absence of a significant difference should not be interpreted as evidence of equivalence (Table 4). While propensity score analysis helps improve comparability between groups, it is not a replacement for randomization, nor can it account for all aspects of surgical judgment, cyst complexity, and surgeon preference.

A comprehensive assessment of the impact of minimally invasive approach should include features beyond traditional parameters of postoperative morbidity. However, this data is scarce. In the study by Marshall and co-workers patient satisfaction and cosmetic outcome was assessed 3 months after the surgery by the quality of life assessment questionnaire and patients in the laparoscopic group demonstrated superior satisfaction, faster return to daily activity and improved cosmetic perception.[30]

The present study has certain limitations. The first is a selection bias due to retrospective study design, although data were collected prospectively. The second is the extended study period, because diagnostic modalities, perioperative management and surgical techniques evolved over time. The third is the incomplete availability of morphological classification data (WHO classification was unavailable for a great proportion of the historical cohort). Fourth, the small number of laparoscopic cases limited the precision of propensity score-based estimates, particularly for rare binary outcomes such as recurrence, reoperation, biliary leakage, and other postoperative complications. Finally, recurrence data must be analyzed cautiously due to lack of uniformity in follow up documentation and imaging techniques across the study period. In certain instances, differentiating between true recurrence, residual surgical fluid collections, and potential reinfection in an endemic area may have proven challenging.

In conclusion, laparoscopy was used in a small but selected group of patients with HHD. This was expected, since most of the cohort belongs to the period before laparoscopy was introduced, and later cases were chosen according to cyst morphology and location. The clearest postoperative difference was shorter hospital stay after laparoscopy. For recurrence, biliary leakage, and reoperation, data remain limited by the small laparoscopic cases and low number of events. Taken together, the results support laparoscopy as a useful approach when the cyst is accessible and the residual cavity can be treated safely, with the operative decision still based on the individual anatomy of the cyst.

Declarations

Ethics approval:

The study was approved by the Ethics Committee of the University Clinical Center of Serbia (Approval No. 1500/43).

Consent for publication:

Not applicable

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Author Contribution

Author Contributions: Danijel Galun: study conceptualization, methodology, supervision, and manuscript review. Marko Zivanovic: study design, data collection, data interpretation, and manuscript drafting. Nikolina Vasilijevic: data collection, data curation, statistical analysis and manuscript drafting. Teodor

Vasic: data collection and manuscript review. Ivana Milosevic: data curation and manuscript review. Nikica Grubor: supervision and critical revision of the manuscript. All authors read and approved the final manuscript..

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Data availability statement:

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to restrictions e.g. their containing information could compromise the privacy of research participants.

Competing interests:

The authors declare that they have no competing interests.

Clinical trial number: Not applicable.

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Figures

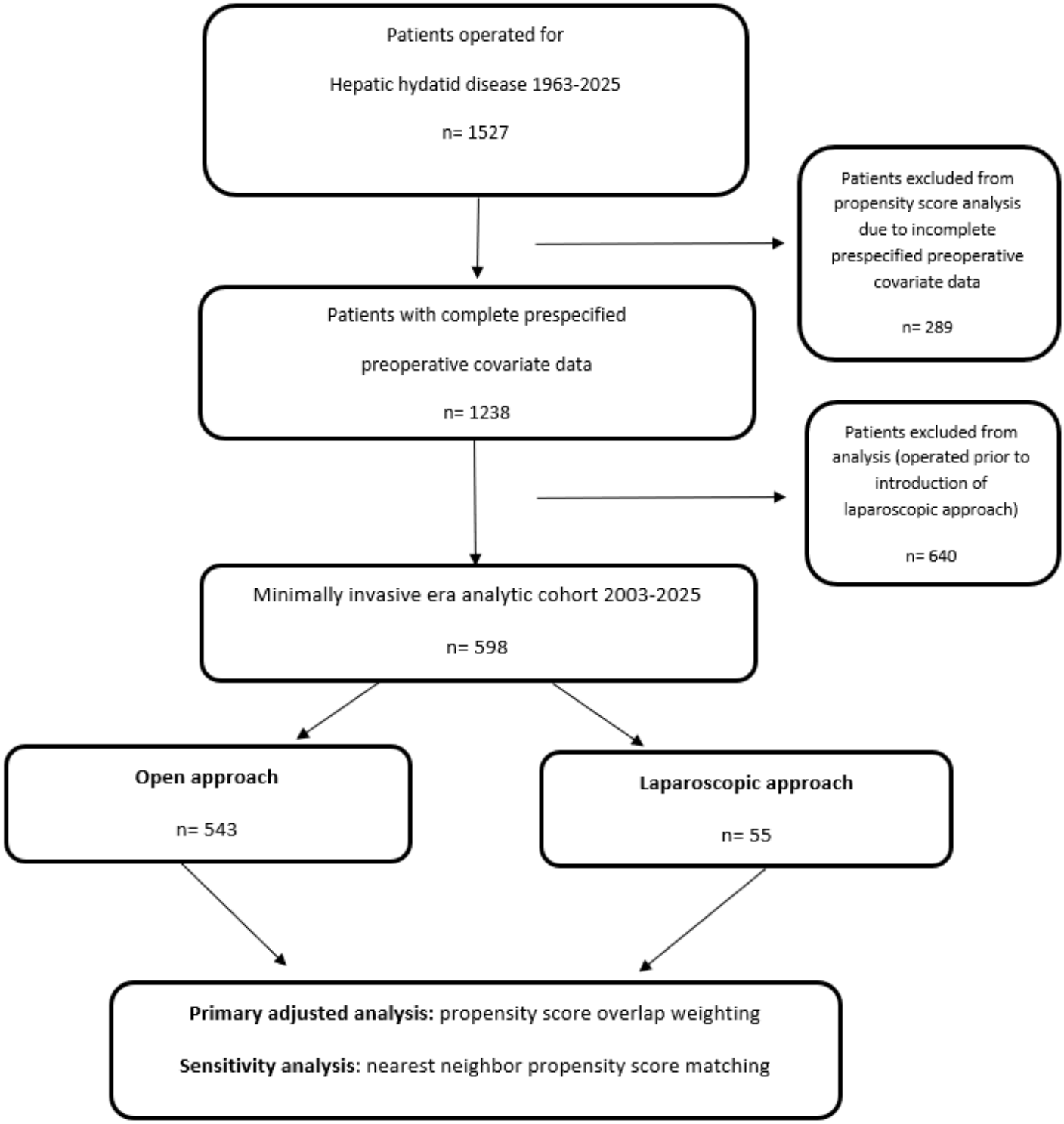


Figure 1

Flowchart of study population and analytic cohorts. The full historical cohort included 1527 patients surgically treated for hepatic hydatid disease between 1963 and the end of 2025. Complete prespecifiedpreoperative covariate data were available for 1238 patients. Propensity score analyses were restricted to the minimally invasive era, resulting in a final analytic cohort of 598 patients, including 543 open and 55 laparoscopic cases.

Supplementary Files

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- GraphicalAbstract.jpg