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Textbook Outcomes and Minimally Invasive Techniques in Resectable Gallbladder Cancer: A Global Cohort Study

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A R T I C L E I N F O

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A B S T R A C T

Introduction: Surgery for resectable gallbladder cancer (GbC) encompasses complex operative management, and evaluating surgical quality through textbook outcome (TO) is crucial. This study aimed to assess TO incidence and impact in a global cohort, identify independent predictors, and evaluate TO rates of minimally invasive (MI) techniques, including robotic (ROB) and laparoscopic (LPS).
Materials and methods: This cohort study included patients undergoing curative-intent hepatectomy and lymphadenectomy for GbC (T1b–T3) from 2012 to 2023 in 41 hospitals. TO was defined as the absence of intraoperative transfusion, major complications, readmission, reoperation, or 90-day mortality, alongside negative margins and ≥6 retrieved lymph nodes. MI-TO additionally required no conversion. A 1:1 propensity score matching compared TO in open (OPEN) and MI approaches. Data were analyzed from July to November 2024.
Results: Among 667 patients (MI, 361; OPEN, 306), TO was achieved in 205 (30.7 %), with no difference between OPEN and MI. ROB independently increased TO (odds ratio, 4.297; p = 0.002), achieving higher MI-TO (37.8 % vs. 23.2 %; p = 0.003), better lymphadenectomy (≥6 nodes: 55.3 % vs. 40.6 %; p = 0.009), and fewer OPEN conversions (1.2 % vs. 13.7 %; p < 0.001) than LPS. TO correlated with lower mortality (HR, 0.506; p = 0.001) and recurrence (HR, 0.682; p = 0.027).
Conclusion: TO in resectable GbC is achieved in one-third of cases, with significant long-term benefits. MI is effective, with ROB outperforming LPS in MI-TO measures. These results establish a benchmark for centers to enhance outcomes.

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1. Introduction

Gallbladder cancer (GbC) is the most common cancer of the biliary system [1,2] and the best potentially curative treatment for GbC is radical resection [3].

The 2018 update of the American Joint Committee on Cancer (AJCC) cancer staging manual guidelines has suggested that cholecystectomy is sufficient for Tis–T1a tumor stages. For all resectable GbC ≥ T1b, cholecystectomy with hepatectomy and lymphadenectomy is indicated, achieving a 5-year survival rate of 35 % [4,5]. Nowadays, despite minimally invasive (MI) approaches for GbC treatment have been increasingly reported, their short-term results and oncological effectiveness remain unclear and poorly reported [6,7].

Classical assessments, focused solely on mortality and morbidity, are increasingly considered inadequate. The use of composite measures, a more comprehensive approach, provides a more accurate evaluation, offering a multidimensional view and patient-centered healthcare assessment. The most frequently used objective composite measure for comparing surgical quality across centers is the textbook outcome (TO) [8].

TO is an “all-or-none” combined outcome tool. Thus, it is achieved only when all desirable surgical outcomes are reached.

To the best of our knowledge, only two previous Eastern World studies have addressed the issue of TO in GbC [9,10]. However, their analyses also encompassed advanced-stage diseases, including T4 and M1, where surgical prognosis benefits are unclear and the impact of MI procedures are not assessed.

Considering the increasing number of MI procedures for GbC, in which the robotic approach is expected to improve the outcomes, evaluating surgical quality across centers is necessary [11].

Therefore, this study aimed to evaluate the TO rate undergoing potential curative-intent resection for GbC from T1b to T3 and assess the impact of the MI approach, including laparoscopic (LPS) and robotic (ROB) techniques, on TO.

2. Material and methods

2.1. Study Design and patient selection

This multicenter international observational cohort study included all patients who underwent curative-intent surgical resection for GbC from January 2012 to March 2023. The coordinating center provided each center with a specific pseudo-anonymized database, which was fulfilled by data from various individual databases.

Each center followed its local clinical protocols, and the coordinating center revised and standardized all the variables of interest. The following were the exclusion criteria: patients with Tis or T1a, for which cholecystectomy was the only surgical indication; those with T4 histopathological staging; and those with metastatic disease (M1), considering them as patients operated with palliative intent and concomitant resections (including adjacent organs).

2.2. Data Collection

Patient demographic and clinicopathologic characteristics, including age, biological sex, body mass index (BMI, kg/m^2), the American Society of Anesthesiologists (ASA), and the Charlson Comorbidity Index (ChI) grades, comprised the variables of interest. The grade of complications was defined according to the Clavien–Dindo classification and Comprehensive Complication Index (CCI) [12,13]. Severe complications were defined as Clavien–Dindo grade ≥ IIIA [12]. Liver wedge resection was defined as a portion of the liver parenchyma from segments S4b to S5, located near the gallbladder fossa. Anatomical and non-anatomical resections and major hepatectomy were defined according to the Tokyo 2020 terminology of liver anatomy and resections [14]. Staging was based on the eighth edition of the AJCC (2018) for GbC [5]. An R0 resection margin was defined when margins exhibited no microscopic disease.

2.3. Definition of textbook outcome

TO for GbC curative resection was defined by the following criteria: the absence of intraoperative blood transfusion, the absence of 90-day major complications (defined as Clavien–Dindo classification ≥ III) [12], absence of 90-day readmission, absence of 90-day reoperation, absence of 90-day mortality, absence of a positive margin resection [14], and lymphadenectomy with ≥6 retrieved nodes. Second TO was defined to address the subanalysis of the MI procedure, adding to the previous variable the absence of conversion to an open approach. Individuals who had achieved all domains at once were considered to have achieved TO.

2.4. Participants

Centers were recruited by emailing all Clinical Robotic Surgery Association members.

A learning curve effect may exist considering the novelty and emergence of MI as an approach. To mitigate this effect, each center was classified according to liver resection volume per year, considering overall caseload (≥40 cases/year), MI procedures (≥20 cases/year), and previous experience in ≥20 cases of robotic liver resection.

Ethical approval

Institutional and ethical approval was obtained from the coordinating center. This study was registered in ClinicalTrials.gov. Owing to the retrospective nature of this study, the requirement for informed consent was waived by the Ethics Committee. Other participating centers obtained additional institutional and national approvals as required. This study was conducted and reported following the STROCSS [15].

2.5. Statistical analysis

Continuous variables were expressed as medians (interquartile ranges [IQRs]), and categorical variables were presented as frequencies (percentages). Categorical variables were compared using the Fisher exact or chi-square test, as appropriate. In contrast, continuous variables were compared using the Student-t test or Kruskal–Wallis test, as appropriate.

Multivariable logistic regression models were employed for analyzing factors correlated with TO achievement. Variables with a significance level of $P < 0.05$ in the univariable analysis were included in the multivariable model. Odds ratios (ORs) and hazard ratios (HRs) with 95 % confidence intervals (CIs) were reported, as appropriate.

To address any variable imbalances among groups, propensity score matching (PSM) was performed, which was calculated using a multivariable logistic regression model based on tumor-related factors, patient demographics, and relevant clinical parameters (sex, age, BMI, ASA score, ChI, and albumin). Several propensity score models were developed and compared based on discrimination and calibration. Patients were matched (1:1) using the nearest neighbor method without replacement with a caliper width set at 0.2.

Overall survival (OS) and disease-free survival (DFS) probabilities were estimated using the Kaplan–Meier curve and compared using the log-rank test. To assess the effect of TO on OS and DFS, multivariable Cox regression analyses were employed.

Considering the recommendation of a minimum of six resected nodes being published only in 2018 [5], a period of time of surgery effect may exist. To mitigate this, procedures before and after 2017 were included in the analysis.

3. Results

3.1. Study population

This study involved 41 hospitals across four continents, encompassing 717 patients with resected GbC. Fifty patients were excluded owing to incomplete records or other exclusion criteria; ultimately, 667 patients were included in the final analysis. Of these patients, 361 underwent MI surgery, comprising 181 LPS and 180 ROB, whereas 306 underwent open surgery (OPEN) (Fig. 1).

TO was achieved in 205 patients (30.7 %). The following were the key TO components: no intraoperative transfusions required in 608 patients (91.15 %), tumor-free resection margins achieved in 546 patients (81.9 %), no severe postoperative complications in 606 patients (90.8 %), no reoperations required in 643 patients (96.4 %), no readmissions in 600 patients (90 %), and no < 6 lymph nodes retrieved in 299 patients (44.8 %). Within 90 days of surgery, no deaths were reported in 643 patients (96.4 %) (Fig. 2A).

Patient characteristics stratified by TO achievement are presented in Table 1.

Univariable analysis identified the following factors as associated with achieving TO: female sex (OR, 1.484; 95 % CI, 1.050–2.099; $p = 0.026$), BMI (OR, 1.035; 95 % CI, 1.003–1.067; $p = 0.031$), albumin (OR, 1.022; 95 % CI, 1.000–1.045; $p = 0.049$), CA 19-9 levels (OR, 0.998; 95 % CI, 0.997–1.000; $p = 0.019$), lower AJCC T stage (OR, 1.540; 95 % CI, 1.084–2.189; $p = 0.016$), ROB (OR, 1.480; 95 % CI, 1.003–2.185; $p = 0.048$), prior laparoscopic surgery (OR, 1.519; 95 % CI, 1.084–2.129; $p = 0.015$), and hospitals with previous 20 robotic hepatectomies (OR, 1.858; 95 % CI, 1.026–3.280; $p < 0.001$).

Multivariable logistic regression analysis revealed that ROB (OR, 4.297; 95 % CI, 1.739–10.616; $p = 0.002$) was independently associated with TO achievement (Table 2).

3.2. Comparison between MI and OPEN (before and after PSM)

Patients in the MI group were more likely to have lower CA 19-9 levels (MI, 15.5 [IQR, 34–43] vs. OPEN, 25.2 [IQR, 10–137] U/L; $p = 0.006$), lower AJCC T stages (T1b, 17.2 % for MI vs. 7.2 % for OPEN; $p < 0.001$), and a higher prevalence of pre-existing liver disease (MI, 8.0 % vs. OPEN, 3.9 %; $p = 0.035$).

To balance relevant clinical covariates, PSM was applied, matching 265 patients in each group (Table 3). Following PSM the previous differences were balanced, showing reduced estimated intraoperative blood loss (MI, 100 [IQR, 50–200] vs. OPEN, 200 [IQR, 50–300] mL; $p < 0.001$), shorter operative times (MI, 225 [IQR, 169–300] vs. OPEN, 253 [IQR, 197–354] min; $p < 0.001$), and decreased length of hospital stays (MI, 5 [IQR, 4–8] vs. OPEN, 8 [IQR, 6–13] days; $p < 0.001$).

The MI group had significantly fewer severe complications (CD $\geq$ III) than the OPEN group, both before (40 [13.1 %] vs. 21 [5.9 %]; $p = 0.001$) and following PSM (35 [13.2 %] vs. 16 [6.0 %]; $p = 0.005$). However, no significant difference in treatment outcomes (TO) was observed between the groups following PSM (33.6 % vs. 30.9 %; $p = 0.515$) (Fig. 2B).

3.3. Subanalysis of patients who underwent MI: LPS versus ROB

In the MI cohort, a modified definition of MI-TO was used, including the absence of conversion to open as an additional criterion. MI-TO was achieved in 110 patients (30.5 %), with the ROB group showing a higher rate (37.8 %, n = 68) than the LPS group (23.2 %, n = 42; $p = 0.003$).

Univariable analysis identified the following factors associated with MI-TO achievement: lower CA 19-9 levels (OR, 0.995; 95 % CI, 0.992–0.999; $p = 0.027$), lower AJCC T stage (OR, 1.976; 95 % CI, 1.156–3.378; $p = 0.013$), ROB approach (OR, 2.009; 95 % CI, 1.271–3.177; $p = 0.003$) and hospitals with higher robotic surgery volumes (>20 cases per year, OR, 11.979; 95 % CI, 2.849–50.368; $p < 0.001$). Multivariable logistic regression analysis confirmed that both lower CA 19-9 levels (OR, 0.996; 95 % CI, 0.996–1.000; $p = 0.049$) and the ROB approach (OR, 1.976; 95 % CI, 1.156–3.378; $p < 0.001$) were independently associated with MI-TO achievement (Table 4).

Following PSM, 160 patients were matched in each group (ROB vs. LPS). The ROB group achieved MI-TO at a significantly higher rate (37.5 % vs. 30.9 %; $p = 0.011$) (Table 5). Notably, the following two specific components contributed to this difference: conversion to open (ROB, 98.8 % vs. LPS, 86.3 %; $p < 0.001$) and retrieval of $\geq$6 lymph nodes (ROB, 55.3 % vs. LPS, 40.6 %; $p = 0.009$) (Fig. 2C).

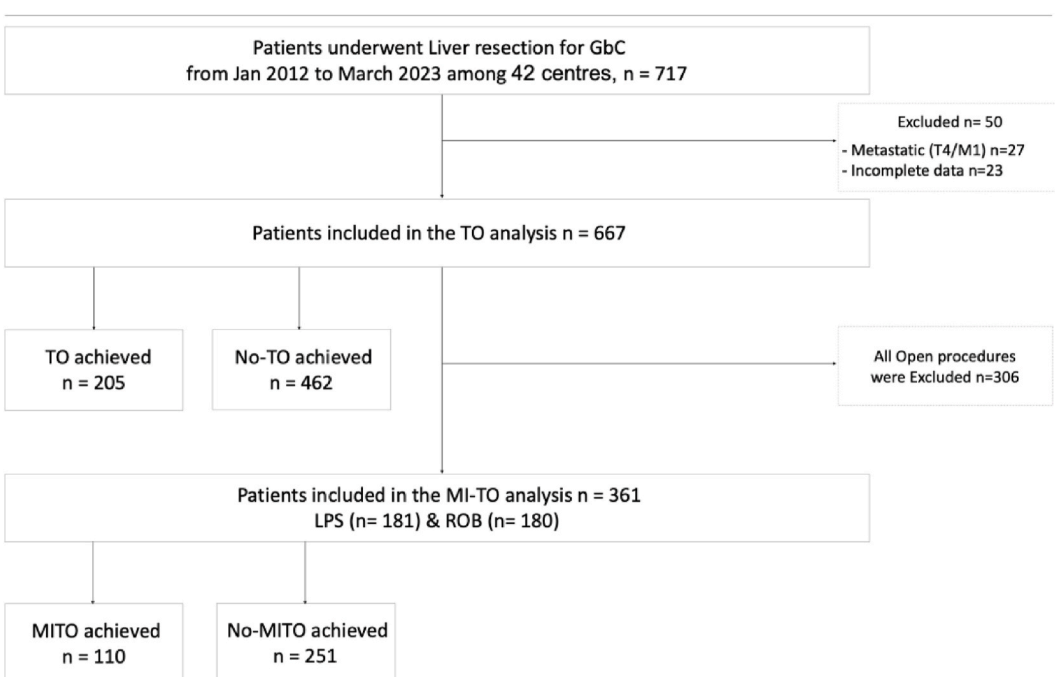

Fig. 1. Study flowchart.

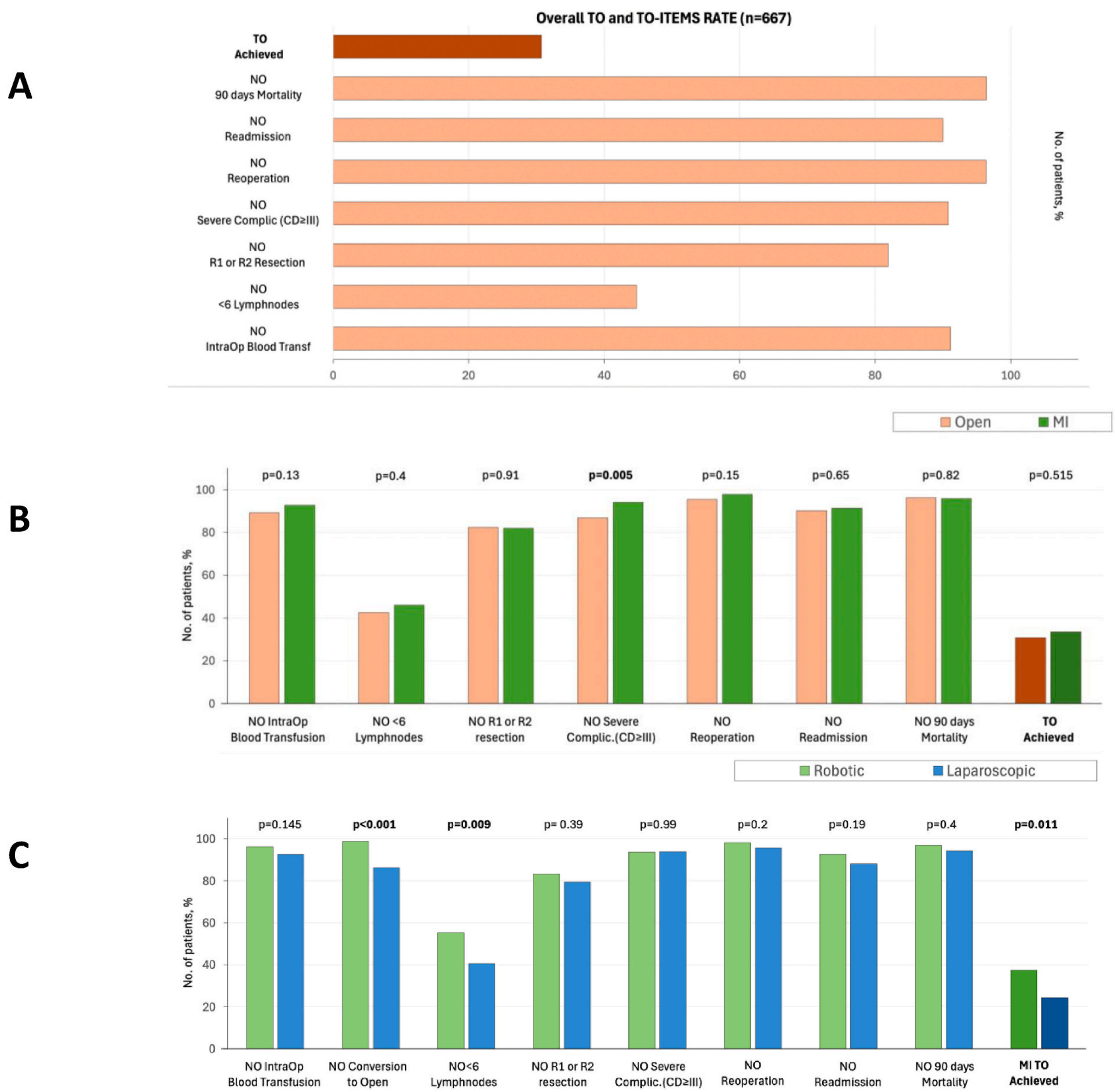

Fig. 2. **A:** Textbook outcome evaluation
B: Distribution of textbook outcome and its components relative to minimally invasive vs open approach.
C: Distribution of minimally invasive textbook outcome and its components relative to the robotic vs the laparoscopic surgical approach.

Notably, before and after PSM, the following factors remained significant: estimated intraoperative blood loss (ROB, 100 [IQR, 30–200] vs. LAP, 100 [IQR, 50–300] mL before PSM; $p = 0.016$; and ROB, 90 [IQR, 50–200] vs. LAP, 125 [IQR, 50–300] mL after PSM; $p = 0.016$), conversion to open (ROB, 1.7 % vs. LAP, 13.3 % before PSM; $p < 0.001$; and ROB, 1.2 % vs. LAP, 13.7 % after PSM; $p < 0.001$), retrieval of ≥ 6 lymph nodes (ROB, 56.1 % vs. LAP, 38 % before PSM; $p < 0.001$; and ROB, 55.3 % vs. LAP, 40.6 % after PSM; $p = 0.009$), and shorter lengths of hospital stay (5 [IQR, 4–6] vs. 6 [IQR, 4–9] days before PSM; $p = 0.001$; and 5 [IQR, 4–6] vs. 6 [IQR, 4–10] days after PSM; $p = 0.003$) (Table 5).

3.4. Survival analysis

Following an overall mean follow-up of 51.8 (range, 11–99) months, the median OS in the TO versus non-TO groups was 69 (95 % CI, 39.3–98.6) and 38 (95 % CI, 24.6–51.3) months, respectively ($p = 0.001$). The median DFS in the TO versus non-TO groups was 58 (95 % CI, 21.1–94.8) and 28 (95 % CI, 18.2–37.7) months, respectively ($p = 0.023$) (Fig. 3).

Multivariable Cox regression analysis after adjusting for other demographic and pathologic features revealed that older age (HR, 1.023; 95 % CI, 1.021–1.125; $p = 0.041$) and AJCC-T stage (HR, 0.631; 95 % CI, 0.461–0.938; $p = 0.031$) increased the risk of death, whereas patients who achieved TO (HR, 0.627; 95 % CI, 0.358–0.853; $p = 0.001$) exhibited a decreased risk of death (Supplementary Table 1).

These data were further confirmed in the DFS Cox regression analysis, indicating that TO achievement decreased the risk of recurrence (HR, 0.781; $p = 0.032$) (Supplememtary Table 2).

4. Discussion

Increasing healthcare expenditures and variability in outcomes among hospitals and practitioners have prompted stakeholders to prioritize high-value surgical care. Therefore, accurate assessment of surgical quality care delivery across hospital systems has become

Table 1
Summary of patients' clinical characteristics, comparing patients with achieved and nonachieved textbook outcome.

Clinical characteristics	All patients (N = 667)	TO (N = 205)	Non-TO (N = 462)	p
Age, years	68 (61–75)	70 (63–75.5)	68 (61–75)	0.110
Sex (woman)	410 (61.4 %)	139 (67.8 %)	271 (58.6 %)	**0.025**
BMI	26 (23–29)	26 (23–30)	25 (22–29)	**0.030**
ASA score	2 (2–3)	2 (2–3)	2 (2–3)	0.975
Charlson score	5 (3–6)	5 (3–6)	5 (3–6)	0.541
Preoperative biliary drainage	180 (26.9 %)	63 (30.7 %)	117 (25.3 %)	0.147
Albumin, g/L	39.0 (34–43)	40.0 (35–44)	38.0 (34–44)	0.078
CA 19-9, U/L	20.7 (9–88)	18.3 (8–56)	23.5 (9–112)	0.120
AJCC T stage				0.08
T1b	84 (12.6 %)	37 (18.0 %)	47 (10.1 %)	
T2	336 (50.3 %)	106 (51.7 %)	230 (49.8 %)	
T3	247 (37.0 %)	62 (30.2 %)	185 (40.0 %)	
AJCC N stage				0.837
N0	422 (63.2 %)	130 (63.4 %)	293 (63.4 %)	
N1	197 (29.5 %)	59 (28.7 %)	138 (29.8 %)	
N2	44 (6.6 %)	16 (7.8 %)	31 (6.7 %)	
Hepatectomy type				0.223
Wedge hepatectomy	388 (58.1 %)	112 (54.6 %)	216 (46.7 %)	
Anatomical resection	279 (41.8 %)	93 (45.3 %)	144 (31.1 %)	
Major hepatectomy	9 (1.3 %)	2 (1 %)	7 (1.5 %)	0.31
Biliary resection	15 (2.2 %)	6 (2.9 %)	9 (1.9 %)	0.61
Surgical approach (open-lap-ROB)				0.47
Open	306 (45.8 %)	89 (43.4 %)	217 (46.9 %)	
Laparoscopic	181 (27.1 %)	48 (23.4 %)	133 (28.8 %)	
Robotic	180 (26.9 %)	68 (33.1 %)	112 (24.24 %)	
Pre-existing liver diseases	37 (5.5 %)	10 (4.8 %)	27 (5.8 %)	0.671
Neoadjuvant therapy	36 (5.3 %)	6 (2.9 %)	30 (6.5 %)	0.068

AJCC, American Joint Committee on Cancer Classification; ASA, American Society of Anesthesiologists; BMI, body mass index; CA 19-9, carbohydrate antigen 19-9; TO, textbook outcome; ROB, robotic approach; Bold for significative value.

increasingly significant.

TO is a novel composite tool that offers a comprehensive measure of optimal surgical care and clinical auditing, enabling a more objective assessment of surgical quality among centers [8]. However, few studies have investigated a specific TO among patients with respectable GbC [9,10].

The adoption of MI surgery has significantly increased over the past decade, supported by evidence demonstrating enhanced patient recovery and reduced morbidity. Consequently, ROB and LPS approaches have become widely accepted for hepato–pancreato–biliary (HPB) procedures, leading to an escalating number of MI GbC resections [11,15–20].

Currently, this is the first study to present TO results for both open and MI approaches and compare LPS and ROB techniques.

Although a universal and consensual definition of TO in HPB surgery remains lacking, TO in our study was defined according to the most frequently used criteria in the literature [8]. Several recent studies have proposed TO definitions in liver surgery; however, these definitions require GbC-specific considerations [20–23].

Based on the latest National Comprehensive Cancer Network (NCCN) recommendations, curative-intent resection for GbC includes not only cholecystectomy and hepatectomy but also the removal of at least six lymph nodes [4,5]. For accurate oncological evaluation and treatment in GbC, adequate lymphadenectomy is crucial [24,25]. Unlike previous studies on TO in liver surgery or the two existing papers on TO in GbC, we incorporated this lymph node retrieval criterion into the TO definition. This addition is essential to align with NCCN guidelines and provide a more comprehensive assessment of surgical quality, bridging a critical gap in oncological care previously neglected by traditional TO definitions.

This international multicenter study observed a 30.7 % TO rate across the whole cohort, consistent with findings from other studies that have investigated TO in various HPB procedures.

Previous studies have assessed TO outcomes in various HPB procedures. The median achievement rate was approximately 38 %; however, it significantly varied, ranging from 15 % to 70 % [21–23].

Our study showed a slightly lower rate of specific GbC TO reported by two previous similar studies by Li. et al. and Liu et al. (54.4 % and 41.3 %, respectively), which is mainly due to the inclusion of the minimum number of resected nodes in our TO definition [9,10].

Table 2
Univariable and multivariable logistic regression analyses for predictors of textbook outcome achievement.

Clinical characteristics	OR (95 % CI)	Univariable analysis (*p*)	OR (95 % CI)	Multivariable analysis (*p*)
Age, years	1.013 (0.997–1.029)	0.111		
Sex (female vs. male)	1.484 (1.050–2.099)	**0.026**	1.712 (0.888–3.303)	0.109
BMI, continuous	1.035 (1.003–1.067)	**0.031**	1.048 (0.991–1.107)	0.1
ASA score (I–II vs. III–IV)	1.038 (0.732–1.474)	0.833		
Charlson score, continuous	1.023 (0.947–1.105)	0.566		
Preoperative biliary drainage (with vs. without drain)	1.308 (0.910–1.881)	0.147		
Albumin, continuous	1.022 (1.000–1.045)	**0.049**	1.021 (0.978–1.067)	0.338
CA 19-9, continuous	0.998 (0.997–1.000)	**0.019**	0.999 (0.997–1.001)	0.323
Eighth AJCC T stage (T1b/T2 vs. T3)	1.540 (1.084–2.189)	**0.016**	1.098 (0.583–2.065)	0.773
Eighth AJCC N stage (N0 vs. N1/N2)	1.026 (0.722–1.458)	0.885		
Hepatectomy type (anatomical vs. wedge)	1.253 (0.872–1.800)	0.224		
Major hepatectomy	1.126 (0.372–2.710)	0.32		
Biliary resection	1.310 (0.522–2.581)	0.29		
Surgical approach (yes vs. no)				
Open	Reference	**0.049**	Reference	**0.001**
Laparoscopic	0.888 (0.583–1.329)	0.543	0.743 (0.328–1.685)	0.477
Robotic	1.480 (1.003–2.185)	**0.048**	4.297 (1.739–10.616)	**0.002**
Hepatic disease (no vs. yes)	1.178 (0.552–2.514)	0.671		
Liver resection experience >40 years (yes vs. no)	1.406 (0.813–2.433)	0.223		
MI liver resection experience >20 years (yes vs. no)	1.858 (1.026–3.365)	**0.041**	3.024 (0.947–9.661)	0.062
Robotic experience >20 years (yes vs. no)	2.171 (1.437–3.280)	**<0.0001**	1.355 (0.673–2.729)	0.395
Year of surgery (2012–2017)	0.91 (0.46–1.65)	0.381		

AJCC, American Joint Committee on Cancer Classification; ASA, American Society of Anesthesiologists; BMI, body mass index; CA 19-9, carbohydrate antigen 19-9. OR, odds ratio; TO, textbook outcome; CI, confidence interval; Bold for significative value.

Table 3
Propensity score matching: OPEN versus minimally invasive (robotic + laparoscopic) approaches.

Clinical characteristics	OPEN (N = 306) Before PSM	MI (N = 361) Before PSM	p	OPEN (N = 265) After PSM	MI (N = 265) After PSM	p
Age, years	70 (62–76)	68 (61–75)	0.081	70 (62–76)	69 (63–76)	0.585
Sex (female)	199 (65.0 %)	211 (58.4 %)	0.082	174 (65.6 %)	172 (64.9 %)	0.855
BMI	25 (22–29)	26 (23–29)	0.080	25 (22–29)	25 (23–28)	0.456
Charlson score	5 (3–6)	4 (3–6)	0.474	5 (3–6)	4 (3–6)	0.190
Preoperative biliary drainage	70 (22.8 %)	58 (16.0 %)	0.329	50 (18.86 %)	31 (1.7 %)	0.23
Albumin, g/L	39.0 (34–42)	39.0 (34–43)	0.998	39 (34–43)	38 (34–42)	0.393
CA 19-9, U/L	25.2 (10–137)	15.5 (34–43)	**0.006**	25 (10–113)	16 (34–42)	0.109
AJCC T stage			**<0.001**			0.161
T1b	22 (7.2 %)	62 (17.2 %)		21 (7.9 %)	40 (15 %)	
T2	141 (46.1 %)	194 (53.7 %)		124 (46.8 %)	138 (52.1 %)	
T3	143 (46.7 %)	105 (29.1 %)		120 (45.3 %)	87 (32.8 %)	
AJCC N stage			0.402			0.254
N0	186 (60.7 %)	238 (65.9 %)		160 (60.4 %)	179 (67.5 %)	
N1	96 (31.3 %)	101 (27.9 %)		86 (32.4 %)	179 (67.5 %)	
N2	24 (7.8 %)	22 (6.1 %)		19 (7.2 %)	16 (6.0 %)	
Hepatectomy type			0.223			0.19
Wedge hepatectomy	162 (52.9 %)	227 (62.9 %)		146 (55.1 %)	175 (66.0 %)	
Anatomical resection	144 (47.0 %)	134 (37.1 %)		119 (44.9 %)	90 (34 %)	
Major Hepatectomy	5 (1.6 %)	4 (1.1 %)	0.841	2 (0.75 %)	2 (0.75 %)	0.91
Biliary resection	9 (2.9 %)	6 (1.7 %)	0.60	5 (1.9 %)	3 (1.13 %)	0.752
Pre-existing liver diseases	12 (3.9 %)	29 (8.0 %)	**0.035**	10 (3.8 %)	9 (3.4 %)	0.461
Intraop estim. blood loss, mL	200 (100–300)	100 (50–200)	**<0.001**	200 (50–300)	100 (50–200)	**<0.001**
Intraop blood transfusion	37 (12.1 %)	22 (6.1 %)	**0.007**	29 (10.9 %)	19 (7.2 %)	0.13
Operative time, min	268 (200–367.5)	240 (180–315)	**<0.001**	253 (197–354)	225 (169–300)	**<0.001**
R0 status n (%)	252 (82.4 %)	294 (81.4 %)	0.781	218 (82.3 %)	217 (81.9 %)	0.910
Retrieving ≥6 lymph nodes	129 (42.2 %)	169 (46.9 %)	0.234	113 (42.6 %)	122 (46.0 %)	0.4
Length of hospital stay, days	8 (6.0–13.0)	5 (4.0–7.25)	**<0.001**	8 (6.0–13.0)	5 (4.0–8.0)	**<0.001**
Severe complic. (CD ≥ III) n (%)	40 (13.1 %)	21 (5.9 %)	**0.001**	35 (13.2 %)	16 (6.0 %)	**0.005**
Reoperation n (%)	13 (4.2 %)	11 (3.1 %)	0.23	12 (4.5 %)	6 (2.3 %)	0.15
Readmission n (%)	33 (10.8 %)	34 (9.4 %)	0.564	26 (9.8 %)	23 (8.7 %)	0.65
Mortality n (%)	11 (3.6 %)	13 (3.6 %)	0.997	10 (3.8 %)	11(4.2 %)	0.82

AJCC, American Joint Committee on Cancer Classification; ASA, American Society of Anesthesiologists; BMI, body mass index; CA 19-9, carbohydrate antigen 19-9. CD, Clavien–Dindo classification; MI, minimally invasive; PSM, propensity score matching; ROB, robotic approach; LPS, laparoscopic approach; Bold for significative value.

Table 4
Univariable and multivariable logistic regression analyses for predictors of minimally invasive textbook outcome achievement.

Clinical characteristics	OR (95 % CI)	Univariable analysis (*p*)	OR (95 % CI)	Multivariable analysis (*p*)
Age, years	1.014 (0.993–1.035)	0.189		
Sex (female vs. male)	1.527 (0.959–2.431)	0.075	1.926 (0.810–4.470)	0.14
BMI, continuous	1.017 (0.978–1.058)	0.406		
ASA score (I–II vs. III–IV)	1.157 (0.725–1.848)	0.541		
Charlson score, continuous	0.996 (0.904–1.098)	0.942		
Preoperative biliary drainage (with vs. without drain)	1.421 (0.875–2.308)	0.156		
Albumin, continuous	1.022 (0.996–1.050)	0.103		
CA 19-9, continuous	0.995 (0.992–0.999)	**0.027**	0.996 (0.992–1.000)	**0.049**
Eighth AJCC T stage (T1b/T2 vs. T3)	1.976 (1.156–3.378)	**0.013**	1.123 (0.358–3.516)	0.843
Eighth AJCC N stage (N0 vs. N1/N2)	1.598 (0.955–2.675)	0.075	1.448 (0.513–4.090)	0.485
Hepatectomy type (anatomical vs. wedge)	1.442 (0.861–2.414)	0.164		
Major hepatectomy	0.995 (0.403–1.965)	0.29		
Biliary resection	0.631 (0.45–2.561)	0.581		
Robotic surgical approach (yes vs. no)	2.009 (1.271–3.177)	**0.003**	5.428 (2.192–13.445)	**<0.001**
Laparoscopic surgical approach (yes vs. no)	2.009 (1.271–3.177)	**0.003**	0.184 (0.074–0456)	**<0.001**
Hepatic disease (no vs. yes)	1.524 (0.582–3.990)	0.39		
Liver resection experience >40 years (yes vs. no)	0.890 (0.403–1.965)	0.774	0.202 (0.031–1.291)	0.091
MI liver resection experience >20 years (yes vs. no)	3.604 (0.813–15.970)	0.091	3.404 (0.228–50.880)	0.375
Robotic experience >20 years (yes vs. no)	11.979 (2.849–50.368)	**0.001**	1.994 (0.207–19.238)	0.551

AJCC, American Joint Committee on Cancer Classification; ASA, American Society of Anesthesiologists; BMI, body mass index; CA 19-9, carbohydrate antigen 19-9; OR, odds ratio; MI-TO, minimally invasive textbook outcome; CI, confidence interval; bold for significant value.

Notably, in the present study, multivariable analysis confirmed that ROB was independently associated with TO achievement (OR, 4.297; p = 0.002), and the experience of MI surgery tended to be associated with TO achievement (p = 0.062).

Our study validated the prevailing view that advanced expertise in technically demanding HPB MI surgery improves the delivery of high-quality surgical care among patients with resectable GbC [25,26].

As we specifically evaluated MI approaches, we included the ”absence of conversion“ as a criterion to fulfill the specific MI-TO, in line with recommendations from previous expert consensus for MI procedures [21,22]. Conversion is typically associated with worse short-term outcomes; therefore, its inclusion in the TO is crucial for an accurate evaluation.

Involving only LPS and ROB procedures, the analysis exhibited an overall rate of 30.5 % MI-TO achievement.

In this subgroup of patients, multivariable analysis revealed that the ROB approach had a greater likelihood of MI-TO achievement than the LPS approach (OR, 5.428; p < 0.001).

Table 5
Propensity score matching: laparoscopic versus robotic approaches.

Clinical characteristics	LPS (N = 181) Before PSM	ROB (N = 180) Before PSM	p	LPS (N = 160) After PSM	ROB (N = 160) After PSM	p
Age, years	68 (61–75)	67 (60–74)	0.440	68 (61–75)	68 (61–75)	0.094
Sex (female)	111 (61.3 %)	100 (55.5 %)	0.266	92 (57.5 %)	92 (57.5 %)	0.074
BMI	26 (23–29)	26 (23–29)	0.423	26 (24–29)	26 (23–29)	0.203
Charlson score	4 (3–6)	5 (4–7)	**<0.001**	4 (3–6)	4 (3–6)	0.942
Preoperative biliary drainage	33 (18.2 %)	25 (13.9 %)	0.934	8 (5.0 %)	4 (2.5 %)	0.155
Albumin, g/L	39 (34–43)	39 (34–43)	0.906	39 (33–43)	40 (35–43)	0.942
CA 19-9, U/L	15 (6–55)	16 (10–33)	0.855	15 (6–65)	15 (8–32)	0.592
AJCC T stage			0.663			**<0.001**
T1b	33 (18.2 %)	29 (16.1 %)		28 (17.5 %)	28 (17.5 %)	
T2	93 (51.3 %)	101 (56.1 %)		80 (50.0 %)	87 (54.4 %)	
T3	55 (30.4 %)	50 (27.8 %)		52 (32.5 %)	45 (28.1 %)	
AJCC N stage			0.409			0.230
N0	121 (66.8 %)	117 (65.0 %)		107 (66.8 %)	105 (65.6 %)	
N1	51 (28.2 %)	47 (26.1 %)		44 (27.5 %)	40 (25 %)	
N2	9 (4.9 %)	16 (8.9 %)		9 (5.6 %)	15 (9.4 %)	
Hepatectomy type			0.682			0.163
Wedge hepatectomy	113 (62.4 %)	117 (65.0 %)		102 (63.8 %)	102 (63.8 %)	
Anatomical resection	68 (37.5 %)	63 (35.0 %)		58 (36.2 %)	58 (36.2 %)	
Major hepatectomy	2 (1.1 %)	2 (1.1 %)	0.92	1 (0.6 %)	1 (0.6 %)	0.95
Biliary resection	6 (3.3 %)	9 (5 %)	0.71	1 (0.6 %)	2 (1.25 %)	0.86
Pre-existing liver diseases	9 (4.9 %)	20 (11.1 %)	**0.049**	9 (5.6 %)	21 (13.1 %)	0.388
Intraop estim. blood loss, mL	100 (50–300)	100 (30–200)	**0.016**	125 (50–300)	90 (50–200)	**0.016**
Intraop blood transfusion	14 (7.7 %)	8 (4.4 %)	0.191	12 (7.5 %)	6 (3.7 %)	0.145
Conversion to OPEN	24 (13.3 %)	3 (1.7 %)	**<0.001**	22 (13.7 %)	2 (1.2 %)	**<0.001**
Operative time, min	243 (180–320)	230 (170–300)	0.437	245 (180–319.25)	234 (660–300)	0.466
R0 status n (%)	146 (80.7 %)	148 (82.2 %)	0.703	127 (79.4 %)	133 (83.1 %)	0.390
Retrieving ≥6 lymph nodes	69 (38 %)	101 (56.1 %)	**<0.001**	65 (40.6 %)	88 (55.3 %)	**0.009**
Length of hospital stay, days	6 (4–9)	5 (4–6)	**0.001**	6 (4–10)	5 (4–6)	**0.003**
Severe complic. (CD > or = III) n (%)	11 (6.1 %)	10 (5.6 %)	0.863	10 (6.3 %)	10 (6.3 %)	0.99
Reoperation n (%)	7 (3.9 %)	4 (2.3 %)	0.378	7 (4.4 %)	3 (1.9 %)	0.2
Readmission n (%)	21 (11.6 %)	13 (7.2 %)	0.154	19 (11.9 %)	12 (7.5 %)	0.19
Mortality n (%)	8 (4.4 %)	5 (2.8 %)	0.402	9 (5.7 %)	5 (3.2 %)	0.4

AJCC, American Joint Committee on Cancer Classification; ASA, American Society of Anesthesiologists; BMI, body mass index; CA 19-9, carbohydrate antigen 19-9; PSM, propensity score matching; CD, Clavien–Dindo classification; ROB, robotic approach; LPS, laparoscopic approach.

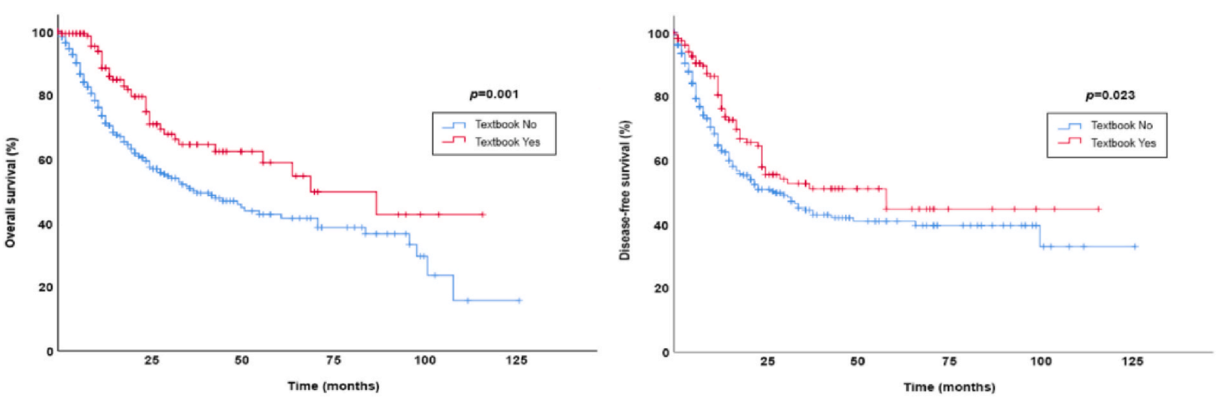

Fig. 3. Kaplan–Meier curves demonstrating better overall and disease-free survival for the textbook outcome achieved group.

To better assess which variables could influence TO achievement, we performed a subgroup analysis of the open versus MI approaches and the differences between the LPS and ROB approaches within the MI approach. Consequently, we performed PSM to better balance the bias of the groups on the basis of clinically relevant preoperative characteristics.

The comparison showed that, consistent with previous series, the MI approach demonstrated a lower rate of severe complications, decreased intraoperative blood loss, shorter operative times, and shorter lengths of hospital stay than the open approach. However, concerning TO, the complication rate was the only TO variable with a significant difference in favor of the MI approach. Notably, the overall TO achievement rate between the open and MI approaches remained similar, confirming the safety and efficacy of MI resection of GbC and its noninferiority compared with the open approach.

A remarkable finding of the MI subgroup analysis was the significantly higher TO achievement rate in the ROB group than that in the LPS group. The ROB approach showed lower estimated intraoperative blood loss and shorter lengths of hospital stay, along with higher TO rates. The most crucial limiting factors included conversion to the open approach and the ability to retrieve a minimum of six lymph nodes. Previous studies have reported that LPS is less likely to achieve an adequate lymphadenectomy in patients undergoing GbC resection [25,27].

This result is not surprising, and it has already been highlighted by the IRON study [28], which demonstrated that ROB resections had a higher median number of resected lymph nodes than LPS, supporting the advantages of the ROB approach in complex procedures, including GbC resection. This finding reflects the improved dexterity of ROB instruments and image magnification, thereby overcoming some of the limitations of LPS, especially in cases requiring a challenging oncological lymphadenectomy.

The authors believe that the higher the complexity of the surgery, the more the ROB approach offers advantages over LPS.

This finding is consistent with that of a recently published study by Pawlik et al., demonstrating that sufficient lymphadenectomy rates are strongly associated with TO achievement rates for perihilar cholangiocarcinoma, wherein ROB surgery more frequently achieved an adequate lymphadenectomy than LPS surgery [22]. Ratti et al. stated similar conclusions, reporting that more than six lymph node samples led to superior results in the ROB approach compared with LPS [29].

However, these potential benefits of the ROB approach should be balanced against its high costs, which can only be evaluated through a prospective cost-effectiveness analysis [30].

Furthermore, our study showed that composite metric attainment was associated with better long-term outcomes. The TO group had better median OS and DFS than the non-TO group.

This finding agrees with previous literature on TO, including the study by Endo et al., which showed survival benefits among patients who achieved TO in liver resection [31].

To elucidate its effects on survival and mitigate bias, we performed a multivariable Cox analysis, which confirmed that non-achievement of TO was an independent risk factor for the recurrence of resected GbC.

Assessing the influence of single composite metric factors associated with the survival benefits of the TO group is difficult and should be evaluated in a comprehensive investigation. However, along with the fundamental parameter, such as the R0 radical resection, another significant determinant is retrieving a minimum of six lymph nodes. The understanding of the role of lymphadenectomy in the surgical treatment of GbC was beyond the scope of the present study. However, considering the survival results presented herein, adequate nodal clearance is not primarily aimed at improving survival but rather at ensuring precise nodal staging. This, in turn, improves the accuracy of pathological examination, informs prognostication, and guides the consideration of adjuvant therapies.

To confirm further and elucidate this group of patients' survival advantages, future clinical trials employing comprehensive quality metrics for assessing long-term outcomes are required.

In the current literature, TO studies in HPB surgery are limited. Only two previous studies focused on GbC resection, which posed significant limitations [9,10]. These studies were conducted in Eastern countries, potentially limiting their generalizability and effectiveness as a globally accepted clinical benchmark. In contrast, the present study is more representative, incorporating data from centers across different countries and continents, thereby increasing the generalizability of the findings.

The inclusion of locally advanced GbC and M1-stage diseases, which require extended surgery, thereby warranting more tailored TO measures, constitutes another significant drawback of the previous studies.

Conversely, this study included only potentially curative cases, excluding T4 and M1 stages, and concomitant organ resections, because these are associated with high rates of R1 resections, complications, and reoperations, which could significantly influence TO outcomes. Furthermore, more advanced stages are typically managed through an open approach, which complicates comparisons within the minimally invasive group.

This is the first study to include a sufficient number of resected lymph nodes in the TO and a subgroup analysis of open versus MI approaches and LPS versus ROB techniques. Nonetheless, this study represents the largest cohort assessing the TO of patients undergoing GbC resection, being the first to include several representative centers and continents.

5. Limitations

This study had several limitations that should be considered when interpreting the results.

First, despite applying rigorous statistical methods to account for residual confounders, the potential for bias due to unmeasured confounders remains an inherent limitation of retrospective studies. Although long-term results were not part of the scope of this study, different postoperative regimens and strategies delivered in the several included centers may have influenced OS and DFS. Moreover, while PSM was employed to minimize confounding, T staging was not included in the matching process owing to the challenges in preoperative differentiation and its limited effect on the surgical approach, which potentially introduced some imbalance in T staging between groups, further influencing the survival analysis; it was deemed acceptable because the primary focus of this study was to assess TO rates rather than oncological outcomes.

Second, the extended study duration of 13 years encompassed a period marked by evolving perioperative management, advancements in patient care practices, and improvements in surgical techniques, all of which could affect the observed outcomes.

Although we accounted for experience of the centers, due to the study's time frame, we failed to specifically assess the experience of each surgeon in liver resection.

Finally, the study sample included surgeries performed since 2012, before the publication of the 2018 AJCC recommendation, to retrieve at least six lymph nodes. To address potential bias related to the year of surgery and its effect on the number of resected nodes, the year of surgery (before and after 2017) was included in our multivariable analysis. This analysis revealed no significant effect of the year of surgery on the number of nodes retrieved.

6. Conclusion

This multicenter international study offers the first worldwide perspective on quality indicators through the TO on resectable GbC. Furthermore, the results of this study show that the MI approach is an excellent tool for providing adequate TO, with ROB likely to achieve better MI-specific TO than LPS.

CRediT authorship contribution statement

Simone Cremona: Study Concept, Data Collection, Data Analysis, Data Interpretation, Writing. **Benedetto Ielpo:** Study Concept, Data Collection, Data Analysis, Data Interpretation, Writing. **Marcello di Martino:** Data collectio, Data Analysis, Data interpretation. **Mauro Podda:** Study Concept, Data Collection, Data Analysis, Data Interpretation, Writing. **Gregorio Di Franco:** Data Collection; Data interpretation; Revision; Approval. **Niccoló Furbetta:** Data Collection; Data interpretation; Revision; Approval. **Annalisa Comandatore:** Data Collection; Data interpretation; Revision; Approval. **Felice Giuliante:** Data Collection; Data interpretation; Revision; Approval. **Luca Aldrighetti:** Data Collection; Data interpretation; Revision; Approval. **John Martinie:** Data Collection; Data interpretation; Revision; Approval. **Francesco Izzo:** Data Collection; Data interpretation; Revision; Approval. **Iswanto Sukandy:** Data Collection; Data interpretation; Revision; Approval. **Fabrizio di Benedetto:** Data Collection; Data interpretation; Revision; Approval. **Roberto Troisi:** Data Collection; Data interpretation; Revision; Approval. **Matteo Donadon:** Data Collection; Data interpretation; Revision; Approval. **Andrea Ruzzenente:** Data Collection; Data interpretation; Revision; Approval. **Guido Torzilli:** Data Collection; Data interpretation; Revision; Approval, TO Study group: Data collection, Data interpretation, Revision, Approval. **Pier Cristofo Giulianotti:** Data Analysis, Data Interpretation. **Luca Morelli:** Study Concept, Data Collection, Data Analysis, Data Interpretation, Writing.

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Declaration of competing interest

Authors declare no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejso.2025.110284.

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Erratum to "Textbook outcomes and minimally invasive techniques in resectable gallbladder cancer: A global cohort Study" [Eur J Surg Oncol 51 10 (2025) 110284]

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The publisher regrets the misspelt name of the author, Iswanto Sucandy. The publisher would like to apologise for any inconvenience caused.

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