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Original Article

Relationships of hepatic histopathological findings and bile microbiological aspects with bile duct injury repair surgical outcomes: A historical cohort

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Backgrounds/Aims: To analyze relationships of hepatic histopathological findings and bile microbiological profiles with perioperative outcomes and risk of late biliary stricture in individuals undergoing surgical bile duct injury (BDI) repair.
Methods: A historical cohort study was carried out at a tertiary university hospital. Fifty-six individuals who underwent surgical BDI repair from 2014–2018 with a minimal follow-up of 24 months were enrolled. Liver biopsies were performed to analyze histopathology. Bile samples were collected during repair procedures. Hepatic histopathological findings and bile microbiological profiles were then correlated with perioperative and late outcomes through uni- and multi-variate analyses.
Results: Forty-three individuals (76.8%) were females and average age was 47.2 ± 13.2 years; mean follow-up was 38.1 ± 18.6 months. The commonest histopathological finding was hepatic fibrosis (87.5%). Bile cultures were positive in 53.5%. The main surgical technique was Roux-en-Y hepaticojejunostomy (96.4%). Overall morbidity was 35.7%. In univariate analysis, liver fibrosis correlated with the duration of the operation (R = 0.3; p = 0.02). In multivariate analysis, fibrosis (R = 0.36; p = 0.02) and cholestasis (R = 0.34; p = 0.02) independently correlated with operative time. Strasberg classification independently correlated with estimated bleeding (R = 0.31; p = 0.049). The time elapsed between primary cholecystectomy and BDI repair correlated with hepatic fibrosis (R = 0.4; p = 0.01).
Conclusions: Bacterial contamination of bile was observed in most cases. The degree of fibrosis and cholestasis correlated with operative time. The waiting time for definitive repair correlated with the severity of liver fibrosis.

Key Words: Cholecystectomy; Iatrogenic disease; Cholangitis; Bile duct diseases; Cholestasis

INTRODUCTION

Laparoscopic cholecystectomy was firstly performed by Erich Mühe in 1985 [1]. Since then, it has been performed more than an open approach because it can lead to benefits such as reduction of postoperative pain, shorter hospital stays, and earlier return to daily activities [2]. Nonetheless, Renz et al. [3] have reported that the rate of clinically relevant iatrogenic bile duct injury (BDI) is around 3% in laparoscopic cholecystectomy, higher than that (0.1%–0.5%) in an open surgery. BDI can cause greater operative morbidity, reduce quality of life, and lead to complications such as biliary strictures, which in turn can lead to biliary cirrhosis. It can also generate higher costs associated with hospital admissions and procedures, in addition to costs associated with legal issues [4-7]. BDI is a potentially life-threatening condition, with long-term mortality rate that can reach 1.8%–4.6% [8]. Some factors such as injury site, previous repair attempt, sepsis, postoperative leaks, and corrective operation by a surgeon without required skills are

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associated with a worse prognosis after BDI correction [9-12]. Factors that can lead to a worse prognosis are still under debate. Some studies have reported that vascular injuries and timing of repair are associated with negative outcomes and primary treatment failure [9-11]. However, according to a study by Stewart et al. [12], the incidence of right hepatic artery injury does not influence the mortality or repair success rate. The timing of repair, when performed by a hepatobiliary surgeon, has no impact on outcomes either according to another study carried out by Stewart and Way [13].

At the facility in which this study was conducted, bilobar liver biopsies were routinely performed during surgical treatment of BDI and bile was collected for microbiological analysis. Little is currently known on the potential associations of hepatic histopathological findings, bile microbiological profiles, and biochemical examinations with perioperative outcomes, late outcomes, and risk of late biliary stricture in individuals undergoing surgical BDI repair. Analysis of these associations could predict patients at higher risk of surgical complications and late anastomotic strictures.

Therefore, the aim of this study was to analyze associations of hepatic histopathological findings and bile microbiological profiles with perioperative outcomes and the risk of late biliary stricture in individuals undergoing surgical BDI repair.

MATERIALS AND METHODS

Study design

This was a retrospective, descriptive, observational, and longitudinal study (historical cohort). Individuals undergoing surgical BDI repair by an advanced biliary surgery unit at a tertiary university hospital were enrolled. This study was approved by the local institutional review board under the reference number 3.510.604/UNICAMP.

Study population

Study participants were identified through electronic outpatient spreadsheets. All individuals who consecutively underwent surgical BDI repair from January 2014 to December 2018 regardless of sex with age of at least 18 years were included. Patients who belonged to vulnerable groups, those who had incomplete medical records, and those who were followed-up for less than 24 months were excluded. The flow chart showing the selection of the study population is shown in Fig. 1.

Variables

The following variables were analyzed: age at repair surgery, sex, weight, body mass index (BMI), symptoms, comorbidities, previous data related to primary surgery (elective or emergency procedure; open or laparoscopic approach; reinterventions at the facility of origin), time elapsed between admission and definitive surgical correction, preoperative laboratory tests, type of BDI according to the Strasberg classification, presence

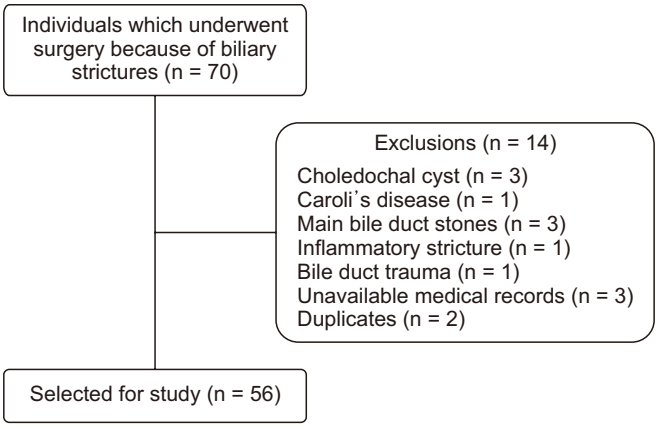

Fig. 1. Flowchart of the study population.

of associated vascular injury, histopathological findings (presence of elementary liver traits in bilobar liver biopsy performed during surgery), bilobar heterogeneity, microbiological aspects (culture of bile collected in the intraoperative period), surgical technique adopted, estimated bleeding, surgical time, length of stay in the intensive care unit (ICU), total length of postoperative stay, 30-day postoperative complications, 30-day mortality, 90-day mortality, and occurrence of biliary stricture detected at least after 24 months (confirmed through imaging or scintigraphy scans).

Elementary hepatic characteristics considered were steatosis (occurrence of more than 5% of fat deposition in hepatocytes), fibrosis (classified according to the Kleiner classification in grades 0 to 4), cholestasis (classified according to its severity in absent, mild, moderate, and severe), acute and chronic cholangitis (classified as absent, mild, moderate, and severe), ductular proliferation (classified as absent, mild, moderate, and severe), and ductopenia (classified as absent or present).

Statistical analysis

Descriptive analysis was performed with presentation of frequency tables for categorical variables and position and dispersion measurements for numerical variables. Data normality was assessed using the Shapiro-Wilk test. To compare proportions, the chi-squared test or Fisher's exact test was used. To compare continuous or ordinal variables between two independent groups, the Mann–Whitney test was used. Continuous variables were compared between three or more groups using the Kruskal–Wallis test. To analyze correlations between continuous variables and continuous or ordinal outcomes, single and multiple logistic regression analyses were performed. The significance level was set at $p < 0.05$. All statistical analyses were performed using SAS System for Windows (Statistic Analysis System), version 9.2 (2002–2008; SAS Institute Inc., Cary, NC, USA).

Table 1. Demographic, histopathological, and microbiological characteristics of the study population

Variable	Value
Total	56
Sex	
Female	43 (76.8)
Male	13 (23.2)
Age (yr)	47.2 ± 13.2
Body mass index (kg/m^2)	26.6 ± 5.1
Comorbidity profile	
Hypertension	15 (26.7)
Diabetes	8 (14.2)
Dyslipidemia	6 (10.7)
Primary cholecystectomy regimen	
Elective	28 (50.0)
Emergency	14 (25.0)
Not reported	14 (25.0)
Surgical approach of primary operation	
Open	29 (51.8)
Laparoscopic	27 (48.2)
Laparoscopic with conversion to open	13 (23.2)
Re-intervention at the primary facility	30 (53.5)
Abdominal drainage	16 (28.5)
Bilioenterostomy	14 (25.0)
Symptoms	
Jaundice	75.0%
Choluria	41.1%
Fecal acholia	41.1%
Fever	17.8%
Injury degree according to Strasberg classification	
E1	6 (10.7)
E2	22 (39.3)
E3	24 (42.9)
E4	4 (7.1)
Time elapsed between events (mon)	
From cholecystectomy until admission at tertiary hospital	26.02 ± 35.6
From admission at tertiary hospital until surgical repair	3.1 ± 3.7
From cholecystectomy until surgical repair	30.1 ± 40.4
Hepatic histopathological findings	
Fibrosis	
Grade 1	16 (28.5)
Grade 2	13 (23.2)
Grade 3	20 (35.7)
Grade 4/cirrhosis	3 (5.3)
Steatosis	
Mild	8 (14.2)
Moderate	4 (7.1)
Chronic cholangitis	
Mild	10 (17.8)
Moderate	11 (19.6)
Acute cholangitis	
Mild	1 (1.7)
Severe	1 (1.7)
Cholestasis	
Mild	10 (17.8)
Moderate	12 (21.4)
Severe	13 (23.2)
Ductular proliferation	
Mild	16 (28.5)
Moderate	7 (12.5)
Severe	2 (3.5)
Ductopenia	2 (3.5)
Bacteria identified in bile cultures	30 (53.6)
Escherichia coli	16 (53.3)
Klebsiella spp.	12 (40.0)
Klebsiella pneumoniae	9 (30.0)
Klebsiella oxytoca	3 (10.0)
Enterococcus spp.	9 (30.0)
Enterococcus faecalis	6 (20.0)
Pseudomonas spp.	4 (13.3)
Pseudomona aeruginosa	3 (10.0)
Streptococcus spp.	4 (13.3)
Enterobacter spp.	3 (10.0)

Values are presented as number only, number (%), or mean ± standard deviation.

RESULTS

Of 56 individuals included, 43 (76.8%) were females. Of all subjects, the average age was 47.2 ± 13.2 years and the mean follow-up time was 38.1 ± 18.6 months. The average time elapsed between primary cholecystectomy and definitive surgical repair was 30.1 ± 40.4 months. Complete demographic, anthropometric, and clinical characteristics of participants are summarized in Table 1.

Surgical procedures were performed at the origin facility after cholecystectomy in 30 (53.5%) individuals, including 16 (28.5%) who underwent abdominal drainage and 14 (25.0%) who underwent bilioenterostomy. For 16 patients who underwent abdominal drainage, six (37.5%) cases had a T-tube placed, four (25.0%) cases had a simple closure, and the remaining six (37.5%) cases had no other reported procedures. Endoscopic retrograde choangiopancreatography (ERCP) was performed in 50% of the individuals who underwent abdominal drainage. With regard to individuals who underwent bilioenterostomy, four (28.6%) patients underwent choledocoduodenostomy and the remaining ten (71.4%) underwent Roux-en-Y hepaticojejunostomy.

Main histopathological findings identified were hepatic fibrosis (87.5%) and cholestasis (62.5%). Bilobar heterogeneity occurred in five (8.9%) patients, of which three had more severe alterations on the right lobe. The Kappa coefficient of

agreement between findings of the two lobes was 0.82. Nine (16.1%) individuals had associated vascular injury. In all cases, the right hepatic artery was affected.

Positive bile cultures with one or more identified microorganisms were present in 30 (53.5%) patients. Among positive cultures, 18 (60.0%) had two or more microorganisms. Microorganisms from 12 (40.0%) cultures were considered multiresistant. The most prevalent bacteria are presented in Table 1.

The main surgical technique used was the Roux-en-Y hepaticojejunostomy (96.4%). One patient underwent choledocojejunostomy and another underwent left hepatectomy with Roux-en-Y right hepaticojejunostomy. Mean intraoperative bleeding was 509.1 ± 405.5 mL. The mean operative time was 213.4 ± 49.6 minutes.

The mean length of stay in the ICU was 2.9 ± 6.4 days. The average total postoperative hospital stay was 6.8 ± 3.8 days. Postoperative complications are summarized in Table 2. Overall morbidity was 35.7% (20 patients). The most frequent complications were intracavitary abscesses and biliary fistulas in five (8.9%) patients each. There was one (1.7%) death within 90 days due to multiple organ dysfunction secondary to abdominal sepsis. Late biliary stricture occurred in 12 (21.4%) patients during the follow-up period.

Univariate analysis of perioperative outcomes and continuous variables identified a positive relationship between the value of alanine aminotransferase (ALT) and the length of postoperative hospital stay (R = 0.3; p = 0.04). The degree of BDI estimated by the Strasberg classification (R = 0.3; p = 0.02) and ALT levels (R = 0.3; p = 0.04) were significantly associated with a higher estimated intraoperative bleeding. The degree of liver fibrosis was associated with a longer duration of the surgical procedure (R = 0.3; p = 0.02). Alkaline phosphatase (ALP) levels were associated with a higher rate of late stricture (p = 0.01). Detailed results of univariate analyses are shown in Tables 3 and 4.

Table 2. Morbidity and mortality of bile duct injury repair

Complication	Number (%)
Biliary leaks	5 (8.9)
Intracavitary abscesses	5 (8.9)
Pulmonary complications	4 (7.1)
Wound infection	3 (5.3)
Hepatic abscesso	1 (1.7)
Late stricture	12 (21.4)
90-day surgical morbidity	20 (37.5)
30-day mortality	0
90-day mortality	1 (1.7)

Multivariate analyses of factors associated with length of postoperative and ICU stay, estimated bleeding, and operative time were performed. No variable showed a significant association with the length of postoperative hospital stay or ICU stay. The intensity of liver fibrosis (R = 0.36; p = 0.02) and cholestasis (R = 0.34; p = 0.02) were independently and positively correlated with operative time. Bismuth classification was independently and positively correlated with the estimated bleeding (R = 0.31; p = 0.049). Complete results of multivariate analyses are shown in Table 5.

The time elapsed between primary cholecystectomy and definitive surgical repair was significantly and positively correlated with the severity of hepatic fibrosis (R = 0.4; p = 0.01). The longer the waiting time for repair, the more severe the degree of liver damage. There was no significant correlation between

Table 3. Univariate analysis (simple regression) of continuous or ordinal variables associated with surgical outcomes

Variable	Hospital stay		ICU stay		Estimated bleeding		Operative time	
	R	*p*-value	R	*p*-value	R	*p*-value	R	*p*-value
Age	0.2	0.30	0.2	0.29	0.07	0.59	0.07	0.63
Time elapsed between cholecystectomy and repair	0.03	0.82	0.03	0.82	–0.08	0.64	0.1	0.38
Aspartate aminotransferase	0.3	0.06	0.2	0.18	0.3*	0.05*	0.1	0.32
Alanine aminotransferase	0.3*	0.04*	0.2	0.15	0.3	0.04	0.2	0.25
Alkaline Phosphatase	–0.1	0.62	0.03	0.82	–0.02	0.84	0.05	0.74
Gamma-glutamyl transferase	–0.1	0.58	0.06	0.74	–0.08	0.63	0.1	0.26
Bilirrubin	–0.1	0.62	0.1	0.45	–0.1	0.44	–0.2	0.15
International normatized ratio	0.03	0.83	0.1	0.51	–0.1	0.39	–0.004	0.99
Albumin	–0.1	0.62	0.1	0.49	–0.06	0.64	–0.04	0.84
Strasberg classification degree	0.2	0.09	0.07	0.64	0.3*	0.02*	0.06	0.62
Body mass index	–0.1	0.39	0.1	0.29	–0.02	0.93	–0.3	0.07
Fibrosis severity	0.06	0.64	0.002	> 0.99	0.2	0.18	0.3*	0.03*
Cholestasis severity	0.2	0.17	0.2	0.07	0.2	0.27	–0.1	0.45

R, coefficient of regression; ICU, intensive care unit.
*Statistical significance.

Table 4. Analysis of associations of study variables with surgical complications and late strictures

Variable	Mild to moderate complication (Clavien-Dindo 1-2)	Severe complication (Clavien-Dindo ≥ 3)	*p*-value	Late stricture	No stricture	*p*-value
Number	42 (75.0)	14 (25.0)	NA	12 (21.4)	44 (78.6)	NA
Age (yr)	46.3 ± 13.0	50.0 ± 13.9	0.39	41.3 ± 12.5	48.8 ± 13.0	0.08
Sex	M: 11 (26.2) F: 31 (73.8)	M: 2 (14.3) F: 12 (85.7)	0.42	M: 2 (16.7) F: 10 (83.3)	M: 11 (25.0) F: 33 (75.0)	0.49
Body mass index (kg/m^2)	26.8 ± 5.1	25.9 ± 4.9	0.58	27.1 ± 5.3	25.7 ± 4.7	0.72
Time elapsed between cholecystectomy and repair (mon)	29.58 ± 43.91	22.6 ± 27.0	0.56	27.58 ± 39.45	29.66 ± 40.50	0.88
Aspartate aminotransferase (U/L)	52.2 ± 36.7	72.9 ± 45.9	0.10	73.0 ± 57.3	66.3 ± 40.9	0.62
Alanine aminotransferase (U/L)	69.3 ± 57.4	103.4 ± 78.4	0.12	91.6 ± 48.5	95.7 ± 80.9	0.87
Alkaline phosphatase(U/L)	506.1 ± 595.9	433.4 ± 455.0	0.63	799.5 ± 832.6	402.9 ± 307.0	0.01*
Gamma-glutamyl transferase (U/L)	693.5 ± 856.0	697.1 ± 488.8	0.97	792.7 ± 853.4	667.6 ± 509.5	0.46
Bilirrubin (mg/dL)	5.8 ± 8.1	6.0 ± 6.8	0.92	7.7 ± 7.8	5.4 ± 7.8	0.35
International normatized ratio	1.1 ± 0.2	1.1 ± 0.2	0.48	1.1 ± 0.2	1.1 ± 0.1	> 0.99
Albumin (g/dL)	3.4 ± 0.8	3.8 ± 0.5	0.04*	3.5 ± 0.7	3.8 ± 0.6	0.09
Strasberg E1-E2 vs. ≥ E3	1–2: 22 ≥ 3: 20	1–2: 7 ≥ 3: 7	0.88	1–2: 6 (50.0) ≥ 3: 6 (50.0)	1–2: 22 (50.0) ≥ 3: 22 (50.0)	> 0.99
Fibrosis	Present: 37 (88.1) Ausente: 5 (11.9)	Present: 12 (85.7) Absent: 2 (14.3)	0.79	Present: 11 (91.7) Absent: 1 (8.3)	Present: 38 (86.4) Absent: 6 (13.6)	0.62
Cholestasis	Present: 28 (66.7) Absent: 14 (33.3)	Present: 7 (50.0) Absent: 7 (50.0)	0.27	Present: 8 (66.7) Absent: 4 (33.3)	Present: 27 (61.4) Absent: 17 (38.6)	0.68
Bile culture	Positive: 20 (47.6) Negative: 22 (52.4)	Positive: 10 (71.5) Negative: 4 (28.5)	0.23	Positive: 7 (58.3) Negative: 5 (41.7)	Positive: 23 (52.3) Negative: 21 (47.7)	0.68

Values are presented as number (%), mean ± standard deviation, or number only.
M, male; F, female; NA, not applicable.
*Statistical significance.

Table 5. Multivariate analysis of continuous or ordinal variables with surgical outcomes

Variable	Hospital stay		ICU stay		Estimated bleeding		Operative time	
	R	*p*-value	R	*p*-value	R	*p*-value	R	*p*-value
Age	–0.12	0.52	–0.12	0.53	0.08	0.65	–0.21	0.21
Body mass index	–0.20	0.21	–0.25	0.12	–0.04	0.76	–0.23	0.09
Strasberg classification	0.01	0.93	–0.18	0.27	0.31*	< 0.05*	0.16	0.23
AST	–0.26	0.40	–0.41	0.19	0.10	0.73	0.17	0.50
ALT	–0.09	0.73	0.16	0.55	–0.33	0.19	–0.33	0.15
ALP	0.20	0.37	0.18	0.41	0.13	0.54	0.008	0.96
GGT	0.02	0.90	–0.14	0.49	0.04	0.82	0.17	0.31
Totak bilirubin	0.02	0.93	0.28	0.34	–0.3	0.28	–0.36	0.15
Fibrosis severity	0.09	0.56	0.23	0.16	–0.09	0.57	0.4*	0.02*
Steatosis severity	0.21	0.19	–0.02	0.89	0.3	0.05	0.10	0.44
Acute cholangitis	0.009	0.96	0.12	0.48	–0.04	0.77	0.01	0.91
Chronic cholangitis	–0.09	0.56	–0.05	0.72	0.07	0.63	0.3*	0.02*
Cholestasis	–0.12	0.62	–0.43	0.10	0.18	0.46	0.11	0.61
Ductular proliferation	0.01	0.92	0.09	0.61	0.02	0.86	–0.02	0.88

ICU, intensive care unit; R, coefficient of regression; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; GGT, gamma glutamyl transferase.
*Statistical significance.

waiting time and the degree of cholestasis (R = –0.1; $p = 0.39$).

The positivity of cultures and sensitivity profile in relation to surgical variables were analyzed. No statistically significant association was identified. Detailed results are shown in Table 6.

DISCUSSION

Although cholecystectomy-related BDI is considered an infrequent complication, it can have deleterious impacts on general health, physical condition, and social functioning compared to uncomplicated cholecystectomy [14]. In addition, it can lead to longer hospital stays, increase the risk of 30-day readmission, and result in higher costs [14,15]. Individuals with cholecystectomy-related BDI are subjected to recurrent cholangitis and liver cirrhosis. They may eventually require a liver transplant. Patients with bile leaks and BDI present higher one-year mortality than those who undergo uncomplicated cholecystectomy [7].

In the current study, 25% of individuals underwent an unsuccessful BDI repair at the facility of origin. Roy et al. [16] have found that patients undergoing repair by non-specialist surgeons have higher long-term complication rates, in addition to higher costs associated with treatment and legal litigation. Stewart and Way [13] observed that patients undergoing repair by the same surgeon who performed the cholecystectomy had significantly lower success rates than those reoperated on by a hepatobiliary surgeon.

In the current study, it was found that 53.5% of patients had positive bile culture for one or more microorganisms, of which 60% were polymicrobial and 40% of cultures were found to have multi-resistant microorganisms, albeit these findings were not statistically related to surgical outcomes. In the literature, few studies have analyzed intraoperative bile culture and its relationship with outcomes. Würstle et al. [17] have analyzed patients with bilomas mostly associated with surgical procedures (65.6%) and ERCP (21.9%). They found that 93.9% of samples

Table 6. Correlation of positivity and sensitivity profile of bile cultures with perioperative outcomes

Variable	Positive	Negative	*p*-value	Positive		*p*-value
				Multirresistant	Multissensitive	
Operative time (min)	220 ± 51.4	206.5 ± 47.6	0.29	211 ± 63.9	225.3 ± 43.7	0.53
ICU stay (day)	2.9 ± 6.1	2.8 ± 6.9	0.92	4.9 ± 9.3	1.6 ± 1.9	0.16
Hospital stay (day)	8.2 ± 7	8.3 ± 8.5	0.98	9.4 ± 9.9	7.4 ± 4.4	0.46
Estimated bleeding (mL)	513.8 ± 363.2	503.8 ± 455.4	0.83	605.9 ± 427.9	383.3 ± 194.6	0.07
Overal morbidity	10 (33.3)	10 (38.5)	0.79	6 (50.0)	4 (22.2)	0.08

Values are presented as mean ± standard deviation or number (%).
ICU, intensive care unit.

were positive for any bacterial infection and 25% of study patients had bacterial infections with advanced resistance. The most frequently isolated microorganisms were *Enterococcus faecium*, *Enterobacter* spp., *Escherichia coli*, *Klebsiella* spp. and *Candida* spp. [17]. A 2020 Chinese study analyzed 1,339 patients whose bile samples were collected during endoscopic procedures by radiointervention or surgically. Samples were positive in 55.12% of cases. The most frequently isolated microorganisms were *E. coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *E. faecium*. Age over 60 years, fever, benign diseases or a history of biliary tract diseases, and surgical procedures were associated with a higher positivity rate [18]. The same study detected high levels of bacterial resistance to ceftriaxone, quinolones, and ampicillin commonly used in the treatment of biliary tract infections. This finding could be due to inappropriate use of antibiotics. Routine microbiological analysis of intraoperatively collected bile can contribute to rational prescription of antimicrobials. These previous reported data and findings of the present study highlight the severity of BDI cases, considering the high rate of infections by multidrug-resistant germs. Thus, upon admission of patients with BDI, adequate infectious screening and careful evaluation of antibiotic therapy initiation are of great relevance.

In liver biopsies, more than 80% of patients had some degree of liver fibrosis, although only three (5.3%) individuals had liver cirrhosis on biopsy. Our findings are comparable with those of Negi et al. [19] who identified liver fibrosis or cirrhosis in 92% of patients. Although most histological changes are reversible after stricture repair in experimental studies, the presence of liver cirrhosis is an important risk factor for postoperative morbidity and mortality, in addition to being a predictor of surgical repair failure [20-24].

Despite the high overall morbidity rate (35.7%), complications generally did not cause serious repercussions. However, 21.4% of individuals had some degree of late stricture, a rate close to that found in the literature [8], with most being managed conservatively. There were no deaths in the early postoperative period. There was only one death within 90 days. One of the leading multicenter studies has reported a 30-day postoperative morbidity rate of 26.3% and a 30-day mortality rate of 2% [25].

ALT, but not aspartate aminotransferase, canalicular enzymes, or bilirubin, was associated with longer postoperative hospital stay. Lower albumin values had positive correlations with higher rates of severe complications. Serum albumin has been described in the literature as a predictor of morbidity and mortality within 30 days after surgery. It is an important marker of comorbidities and malnutrition [25,26]. ALP was related to higher rates of late strictures. There is an extensive literature analyzing preoperative clinical data (type of injury, timing of repair, presence of associated infections, use of abdominal drain) as predictors of repair success. However, the literature on the relationship between perioperative laboratory tests and surgical outcomes is scarce. Duration of biliary obstruction, baseline preoperative ALT level, and time until normalization of ALT levels after surgery have been identified as independent predictors of grades 2 and 3 liver fibrosis in patients with post-cholecystectomy stricture [19]. The timing of definitive repair is highly important considering that the waiting time is significantly correlated with the degree of liver fibrosis, pointing that these patients should be referred to tertiary facilities as soon as possible.

The current study has some limitations that should be taken into consideration. First, this was a retrospective, single-center study with a small sample of patients. Data related to individuals' previous hospitalizations were not always complete or detailed. BDI is usually underdiagnosed. It is often initially diagnosed at the facility of origin, which can contribute to a severity bias because only patients with more complex injuries are referred to the tertiary service. On the other hand, many patients who firstly underwent repair in the facility of origin and evolved with treatment failure and strictures were referred to this reference hospital with more severe and complex injuries than they would have initially. Likewise, as only patients undergoing surgical repair were included, individuals with partial injuries and leaks, treated exclusively by ERCP or radio intervention, and those who would have a better prognosis and lower late stricture rates were not included in the sample.

In conclusion, fibrosis and cholestasis were the most frequent histopathological abnormalities. Bacterial contamination of bile was observed in most cases. The Strasberg degree of injury was positively correlated with the estimated bleeding. Degrees of fibrosis and cholestasis were correlated with the operative time. The waiting time for definitive repair was directly correlated with the severity of liver fibrosis.

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CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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