RESEARCH ARTICLE

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Postoperative Abscesses in the Liver Resection Plane in Patients with a History of Biliary Tract Treatments: A Multicenter Cohort Study

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Abstract

Objective: The effect of previous biliary reconstruction (BR) or endoscopic sphincterotomy (EST) on post-hepatectomy bile leakage and abscess formation remains controversial. This study aimed to investigate the incidence, clinical findings, and risk factors of postoperative abscesses in the liver resection plane in patients with such histories. **Methods:** This multicenter retrospective study included 5,742 patients who underwent liver resection between 2011 and 2020 (38 with a history of BR, 44 with EST, and 5,660 with no history of biliary treatment). The incidence, clinical characteristics, and risk factors for abscess formation, as well as factors associated with prolonged healing duration (≥45 days), were analyzed. **Results:** Abscess formation was significantly more frequent in the BR (47.4%) and EST (25.0%) groups than in the non-BR/non-EST group (3.5%). Bile leakage was identified as an independent risk factor for abscess formation. Bile leakage and mixed infection both significantly more frequent in the BR group than in the non-BR/non-EST group were independent risk factors for prolonged healing duration. **Conclusion:** Patients with a history of BR or EST are at a higher risk of postoperative abscess formation in the liver resection plane. Bile leakage plays a critical role in both abscess development and prolonged healing.

Keywords: Postoperative abscess- liver resection- biliary treatment

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Introduction

Complications following liver resection include postoperative bleeding, surgical site infections, such as organ or space and wound infections, refractory ascites, pleural effusion, bile leakage, and post-hepatectomy liver failure. Intra-abdominal infection (organ or space infection) occurs in 2.7–11.0% of patients who undergo liver resection without biliary reconstruction (BR) (i.e., without bilioenteric anastomosis) [1-4]. The causes of intra-abdominal infections in these patients include intraoperative contamination, retrograde infection via abdominal drains, and bile leakage. Bile leakage occurs in 4.0–7.2% of patients who undergo liver resection [4-11]. Reoperation is sometimes necessary for patients with intra-abdominal infection associated with bile leakage, and this complication can occasionally be lethal [5, 6, 8, 9, 11].

Several investigators have reported the development of intrahepatic abscesses following ablation therapies, such as radiofrequency ablation and transcatheter arterial embolization, in patients with a history of BR due to bacterial contamination through bilioenteric anastomosis [12-15]. However, there have been no reports on the incidence and characteristics of postoperative abscesses in the liver resection plane in patients with a history of biliary tract treatment, including bilioenteric anastomosis (BR) and endoscopic sphincterotomy (EST). These procedures can lead to contamination of the intestinal flora in the bile via bilioenteric anastomosis or compromised (loosened) papilla of Vater. The aim of this multicenter retrospective study was investigating the incidence and clinical characteristics of postoperative abscesses in the liver resection plane in patients with a history of biliary tract treatment.

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Materials and Methods

Between January 2011 and December 2020, 5,742 patients underwent liver resection without concomitant BR or resection of other organs at six university hospitals (Shiga University of Medical Science, Osaka Metropolitan University, Wakayama Medical University, Osaka Medical and Pharmaceutical University, Nara Medical University, and Kansai Medical University). This multicenter retrospective study conformed to the Clinical Research Guidelines and was approved by the ethics committee of each institution (approval number in principal institution: R2021-115). Informed consent was obtained by opt-out from all patients or their family members at each institution.

Of the 5,742 patients, 38 had a history of BR (BR group), and 44 had a history of EST (EST group). The mean interval between BR and liver resection was 42 months and that between EST and liver resection was 30 months. Another 5,660 patients with no history of BR or EST were classified as the "non-BR or non-EST group." In the BR group, pancreaticoduodenectomy was performed in 24 patients, liver resection with extrahepatic bile duct resection and bile duct reconstruction in three patients, and extrahepatic bile duct resection and bile duct reconstruction in 11 patients. Overall, 212 developed abscesses in the liver resection plane after liver resection. Patients with intra-abdominal infections caused by injury or gastrointestinal tract infections were excluded.

In this study, we investigated the following: (1) comparison of incidence and clinical findings including laboratory results, operative factors, postoperative course, and microorganisms isolated from the postoperative abscess in the liver resection plane among the BR, EST, and non-BR or non-EST groups, (2) risk factors for postoperative abscess formation in the liver resection plane in the BR and EST groups, and (3) factors contributing to prolonged abscess healing (duration from abscess diagnosis to healing ≥45 days, which corresponded to the mean duration in this cohort).

Postoperative abscess in the liver resection plane was defined as the presence of fever, elevated inflammatory findings on blood tests, and an abscess-like mass on imaging in the liver resection plane. Abscess healing was defined as the discontinuation of antibiotics, removal of drains, and the absence of infection-related abnormal signs and symptoms. Mixed infection was defined as the detection of multiple bacterial species from drains at the same site. Bile leakage was defined according to the International Study Group of Liver Surgery (ISGLS) grades B and C [16]. Post-hepatectomy liver failure (PHLF) was diagnosed according to the ISGLS criteria: total serum bilirubin level of >50 μmol/L and a prothrombin time index of 50% (corresponding to an international normalized ratio greater than 1.7) on postoperative day 5 or later [17].

Statistical analyses

Categorical variables were compared using the chi-squared test or Fisher's exact test. Continuous variables were compared using the Mann–Whitney U test. When significant differences were observed among the three groups, comparisons were made for each pair via post-hoc analysis via Bonferroni's multiple comparison test. Independent risk factors were evaluated using multiple logistic regression analysis.

Results

Comparison of incidence and clinical findings of postoperative abscesses in the liver resection plane

Postoperative abscesses in the liver resection plane developed in 3.5% of patients in the non-BR or EST group, 25% in the EST group, and 47.4% in the BR group ($p<0.001$, Figure 1). Abscesses developed in nearly half of the patients in the BR group. The incidence of abscesses was significantly higher in the BR group than in the EST and non-BR or non-EST groups, and significantly higher in the EST group than in the non-BR or non-EST group.

A comparison of the clinical findings among the three groups is shown in Table 1. Alanine aminotransferase (ALT) activity and indocyanine green retention rate at 15 min (ICGR15) were significantly lower in the BR group than in the non-BR or non-EST group. The proportion of patients who underwent anatomical resection was significantly lower in the EST group than in the BR and non-BR or non-EST groups. There was no significant difference in the frequency of resection to expose the hilar plate (medial segmentectomy, anterior segmentectomy, or central bisectionectomy) among the three groups. Multiple site resections were also similar among the three groups. The proportion of patients who underwent right subphrenic partial hepatectomy (segments 4, 7, and/or 8) was significantly lower in the EST group than in the non-BR or non-EST group. The operative time tended to be longer in the non-BR or non-EST group than in the BR and EST groups. The proportion of patients who underwent the Pringle maneuver was significantly lower in the BR group than in the EST and non-BR or non-EST groups. The interval between surgery and abscess development was significantly shorter in the EST group than in the non-BR or non-EST group. The frequency of bile leakage did not differ among the three groups. Mixed infections were significantly more frequent in the BR group than in the non-BR or non-EST group. The proportions of patients who required abscess drainage (percutaneous puncture or drainage via a surgically placed drain) did not differ among the three groups. Treatments using intra-abdominal drain placement during the surgery were performed for abscesses in the liver resection plane in 84 of 212 patients (39.6%) (5 of 18 patients in the BR group, 2 of 11 patients in the EST group, and 77 of 183 patients in the non-BR or non-EST group).

Isolated organisms in the three groups

The organisms isolated from the postoperative abscess in the liver resection plane among the three groups are shown in Table 2. Intestinal flora, such as Enterococcus spp., Escherichia coli, Klebsiella spp., and Pseudomonas aeruginosa were mainly isolated from the BR and EST groups. Skin flora (bacteria that are naturally present on the skin), such as Staphylococcus aureus, Staphylococcus

Table 1. Comparison of Clinical Findings among Patients with Biliary Reconstruction, Endoscopic Sphincterotomy, and Those without them in Postoperative Abscess at the Liver Resection Plane.

	Biliary reconstruction (BR) n = 18	Endoscopic sphincterotomy (EST) n = 11	Non-BR or non-EST n = 183	p-value
Age (years)	72.2 ± 9.32	70.6 ± 16.2	71.1 ± 10.4	0.904
Gender (men: women)	15:03	7:04	136:47:00	0.49
Body mass index (Kg/m^2)	21.0 ± 1.9	23.1 ± 2.7	22.3 ± 3.4	0.18
Diabetes Mellitus (%)	7	2	61	0.501
Interval between BR or EST, and hepatectomy (months)	42 [26, 72]	30 [6, 60]	N/A	0.27*
Primary disease				
Hepatocellular carcinoma	6	3	120	0.002***, ****
Intrahepatic cholangiocarcinoma	0	4	19	0.008**, ****
Metastatic liver tumor	9	1	39	0.012**, ***
Others	3	3	5	<0.001***, ****
Hepatitis virus infection				
Hepatitis B virus	1	0	17	0.504
Hepatitis C virus	4	1	48	0.426
Laboratory test results				
Albumin (g/dL)	3.9 [3.7, 4.2]	4.0 [3.3, 4.3]	3.9 [3.7, 4.2]	0.859
Aspartate aminotransferase (IU/L)	28 [23, 35]	24 [19.5, 32]	30 [25, 41.5]	0.094
Alanine aminotransferase (IU/L)	18 [16, 21]	15 [12, 32]	25 [18, 36]	0.025***
Total bilirubin (mg/dL)	0.5 [0.4, 0.7]	0.7 [0.5, 0.9]	0.7 [0.5, 0.9]	0.195
Indocyanine green retention rate at 15 min. (%)	7.2 [5.5, 10.1]	10.0 [7.8, 13.9]	12.0 [8.9, 18.4]	0.008***
Operation				
Anatomic: nonanatomic	13:05	1:10	101:82	0.003**, ****
Expose the hilar plate	1	0	41	0.055
Multiple site resection	3	0	16	0.301
Open: laparoscopic	16:02	11:00	136:47:00	0.066
Subphrenic part hepatectomy (S4, S7, S8)	11	3	121	0.033****
Use of Pringle maneuver	5	11	150	<0.001**, ***
Operation time (min)	297 [231, 386]	329 [299, 379]	370 [305, 448]	0.055
Blood loss (mL)	435 [250, 1270]	400 [251, 575.]	685 [316, 1200]	0.311
Drain placement during surgery	5	2	79	0.134
Interval between hepatectomy and abscess development (days)	7 [5, 10]	7 [5, 7]	9 [6, 12]	0.039****
Duration of prophylactic antibiotics (≤1 days)	3 [1, 4]	1 [1, 3]	2 [1, 2]	0.133
Post-hepatectomy liver failure B or C (%)	1	0	17	0.507
Bile leakage (%)	7	4	91	0.509
Postoperative ileus (%)	1	2	11	0.279
Treatments for abscess				
Drainage by abscess puncture	12	6	95	0.487
Drainage using the drain placed during surgery	5	2	77	0.163
No drainage (antibiotic alone)	1	3	11	0.027****
Mixed infection	12	3	39	<0.001***
Duration between abscess development and healing (days)	45 [23, 58]	34 [19, 61]	31 [17, 56]	0.554
Mortality (%)	0	1	4	0.267
Length of hospital stay (days)	37 [22, 53]	35 [24, 65]	43 [27, 71]	0.278

Age and Body mass index are expressed as mean ± standard deviation. Other data are expressed as median with 25th and 75th percentiles. *The periods were compared between the BR group and the EST group. **p<0.05 between the BR group and the EST group, ***p<0.05 between the BR group and the non-BR or EST group, ****p<0.05 between the EST group and the non-BR or EST group by post hoc analysis.

Table 2. Bacteria Isolated from the Drainage Fluid or Ascites

	Biliary reconstruction (BR) n = 18	Endoscopic sphincterotomy (EST) n = 11	Non-BR or non- EST n = 183
Gram-positive			
Enterococcus avium	1 (5.6%)		3 (1.6%)
Enterococcus faecium	4 (22.2%)		11 (6.0%)
Enterococcus faecalis	6 (33.3%)	4 (36.4%)	35 (19.1%)
Enterococcus spp.	2 (11.1%)		13 (7.1%)
Staphylococcus aureus (MSSA)		1 (9.1%)	17 (9.3%)
Staphylococcus aureus (MRSA)			24 (13.1%)
Staphylococcus epidermidis (MSSE)			11 (6.0%)
Staphylococcus epidermidis (MRSE)			6 (3.3%)
Staphyococcus spp.			4 (2.2%)
Coaglase negative staphylococci			8 (4.4%)
Corynebacterium spp.			13 (7.1%)
Streptcoccus spp	1 (5.6%)		5 (2.7%)
Propionebacterium acne			1 (0.55%)
Others			1 (0.55%)
Gram-negative			
Aeromonas hydrophya	1 (5.6%)	1 (9.1%)	
Citrobacter frendii	1 (5.6%)		2 (1.1%)
Citrobcter braakii			1 (0.55%)
Enterobacter aerogenes	1 (5.6%)		4 (2.2%)
Enterobacter cloacae	1 (5.6%)	2 (18.2%)	14 (7.7%)
Escherichia coli	5		5 (2.7%)
Klebsiella pneumoniae	2 (11.1%)		10 (5.5%)
Klebsiella oxytoca			1 (0.55%)
Morgnella morgani			
Pseudomonas aeruginoza	1 (5.6%)	1 (9.1%)	3 (1.6%)
Proteus mirabilis			1 (0.55%)
Searia marcesens	1 (5.6%)		1 (0.55%)
Steronotrophomonas maltophilla			2 (1.1%)
Anaerobes			
Bacteroides fragilis	1 (5.6%)	1 (9.1%)	3 (1.6%)
Bacteroides thetaiotaomicron			2 (1.1%)
Bacteroides spp.			1 (0.55%)
Clostridium perfurings	1 (5.6%)		1 (0.55%)
Fusobacterium mortiferum	1 (5.6%)		
Prevotella spp.			1 (0.55%)
Fungus			
Candida glabrata			2 (1.1%)
Candida spp.			3 (1.6%)

epidermidis, coagulase-negative staphylococci, Corynebacterium spp., and Propionibacterium acnes, were isolated from the non-BR or EST group. The proportion of patients with skin flora infections was significantly higher in the non-BR or non-EST group (79 of 183 patients) than in the BR group (0 of 18 patients; $p < 0.001$). In contrast, the proportion of patients with anaerobes was higher in the BR group (3 of 18 patients) than in the non-BR or non-EST group (8 of 183 patients, $p = 0.063$).

Clinical findings and risk factors for abscesses in the BR group

The clinical findings of patients with postoperative abscesses in the liver resection plane and those without abscesses were compared (Table 3). Patients with postoperative abscesses were significantly older than those without ($p = 0.046$). There were no differences in sex, body mass index (BMI), association of diabetes mellitus, primary disease, hepatitis virus infection, period between BR and hepatectomy, history of cholangitis, laboratory

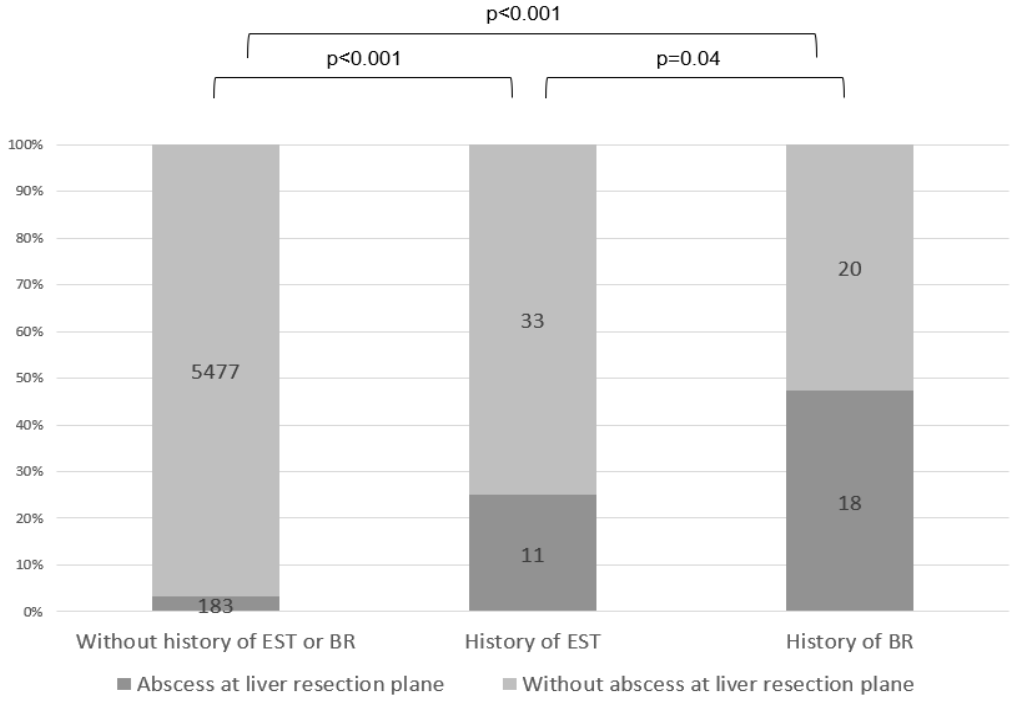

Figure 1. Comparison of the Development of Postoperative Abscess in the Liver Resection Plane in Patients with a History of Biliary Reconstruction (BR) and Endoscopic Sphincterotomy (EST) and in Those without such Histories. The incidences of postoperative abscesses in the liver resection plane are 3.5%, 25 %, and 47.4% in the non-BR or non-EST, EST, and BR groups, respectively. The BR group shows the highest incidence, significantly exceeding that of both the EST and non-BR or non-EST groups. The EST group also has a significantly higher incidence rate than the non-BR or non-EST group.

test results, operative methods such as anatomical and laparoscopic resections, operative time, blood loss, period between surgery and abscess development, duration of antibiotic administration, or PHLF. In patients with postoperative abscesses, there was a tendency for multiple site resections to be performed, however, this difference was not significant (p=0.097). The proportions of patients who underwent right subphrenic partial hepatectomy (S4, S7, and S8) and those with bile leakage were significantly higher among patients with abscesses than those without (p = 0.047 and 0.016, respectively). Therefore, older age, right subphrenic partial hepatectomy, and bile leakage are significant risk factors for postoperative abscesses in the liver resection plane on univariate analysis. Multivariate analysis of risk factors for postoperative abscess in the liver resection plane showed that bile leakage was an independent risk factor for abscess formation (risk ratio, 10.60; 95% confidence interval (CI), 1.07-105.00; p = 0.044) in the BR group. The length of hospital stay was significantly longer in patients with abscesses than in those without (p < 0.001).

Clinical findings and risk factors for the abscess in the EST group

The clinical findings of patients with postoperative abscesses in the liver resection plane and those without abscesses were compared (Table 4). There were no differences in age, sex, BMI, association of diabetes mellitus, primary disease, hepatitis virus infection, period between EST and hepatectomy, history of cholangitis, laboratory test results except for ALT, operative methods such as anatomical resection and right subphrenic partial hepatectomy, operative time, blood loss, duration of antibiotic administration, or PHLF. ALT activity was significantly lower in patients with abscesses than in those without (p = 0.045). The proportions of patients who underwent open hepatectomy and those with bile leakage were significantly higher in those with abscesses than in those without (p = 0.003 and 0.01, respectively). Therefore, low ALT activity, open hepatectomy, and bile leakage are significant risk factors for postoperative abscesses in the liver resection plane on univariate analysis. Multivariate analysis of the risk factors for the postoperative abscess in the liver resection plane showed that bile leakage is an independent risk factor for the abscess (risk ratio, 15.40; 95% CI, 1.38-173.00; p = 0.026) in the EST group. The length of hospital stay was significantly longer in patients with abscesses than in those without (p < 0.001).

Factors contributing to prolonged abscess healing

The factors contributing to prolonged abscess healing (duration from abscess diagnosis to healing ≥45 days) were investigated using univariate and multivariate analyses (Table 5). The factors examined were duration of prophylactic antibiotics (≤1 day), post-hepatectomy liver failure B or C, bile leakage, postoperative ileus, drainage by abscess puncture, mixed infection, history of biliary reconstruction, and history of endoscopic sphincterotomy. These factors were selected based on the possibility that they may inhibit abscess healing. In univariate analysis, bile leakage (risk ratio, 3.89; 95% CI, 2.12-7.14; p < 0.001), mixed infection (risk ratio,

Table 3. Comparison of Clinical Findings between Patients with and without Postoperative Abscess at Liver Resection Plane in Biliary Reconstruction Group

	With postoperative abscess n=18	Without postoperative abscess n=20	p-value
Age (years)	72.2±9.32	63.2±14.6	0.046
Gender (men: women)	15:3	14:6	0.454
Body mass index (Kg/m^2)	21.0±1.9	22.3±3.23	0.148
Diabetes mellitus	7	7	>0.999
Primary disease			
Hepatocellular carcinoma	6	5	0.721
Intrahepatic cholangiocarcinoma	0	2	
Metastatic liver tumor	9	9	
Others	3	4	
Hepatitis virus infection			
Hepatitis B virus	1	1	0.838
Hepatitis C virus	4	3	
Interval between biliary reconstruction and hepatectomy (months)	42 [26, 72]	34 [15, 90]	0.759
History of cholangitis	8	4	0.164
Laboratory test results			
Albumin (g/dL)	3.9 [3.7, 4.2]	4 [3.9, 4.1]	0.953
Aspartate aminotransferase (IU/L)	28 [23, 35]	32 [23, 43]	0.629
Alanine aminotransferase (IU/L)	18 [16, 21]	24 [18, 45]	0.098
Total bilirubin (mg/dL)	0.5 [0.4, 0.7]	0.7 [0.4, 1.1]	0.139
Indocyanine green retention rate at 15 min. (%)	7.2 [5.5, 10.1]	11.6 [5.2, 16.0]	0.432
Operative methods			
Anatomic: nonanatomic	13:5	9:11	0.112
Expose the hilar plate	1	0	0.474
Multiple site resection	3	0	0.097
Open: laparoscopic	16:2	19:1	0.595
Subphrenic part hepatectomy (S4, S7, S8)	11	5	0.047
Pringle maneuver	5	5	>0.999
Operative time (min)	297 [231, 386]	287 [220, 434]	0.826
Blood loss (mL)	435 [250, 1270]	638 [149, 1099]	0.807
Duration of prophylactic antibiotics (≤1 day)	3 [1, 4]	1 [1, 3]	0.227
Bile leakage	7	1	0.016
Post-hepatectomy liver failure (B or C)	1	1	>0.999
Length of hospital stay (days)	37 [21, 53]	14 [10, 17]	<0.001

Age and Body mass index are expressed as mean ± standard deviation. Other data are expressed as median with 25th and 75th percentiles.

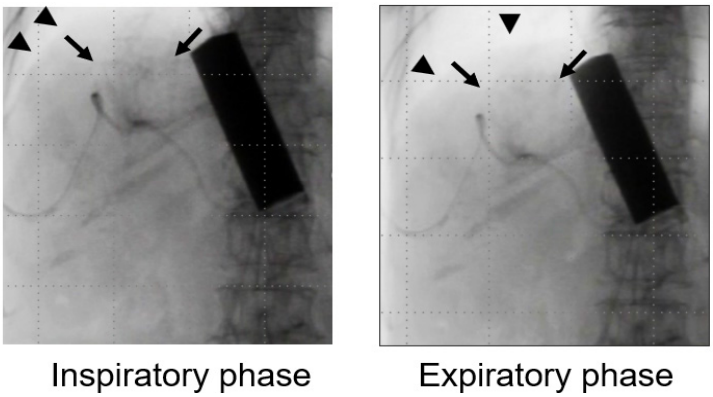

Figure 2. Pumping Effects of the Diaphragm for the Contrast Medium in the Abscess in the Liver Resection Plane. The contrast medium (arrows) flows into the abscess cavity owing to decreased pressure in the abscess cavity during the inspiratory phase and flows out of the abscess cavity owing to the increased pressure in it during the expiratory phase. Arrowhead; diaphragm

Table 4. Comparison of Clinical Findings between Patients with and without Postoperative Abscess at Liver Resection Plane in Endoscopic Sphincterotomy Group

	With postoperative abscess n=18	Without postoperative abscess n=20	p-value
Age (years)	70.6 ±16.2	71.8 ±11.1	0.776
Gender (men: women)	7:4	21:12	>0.999
Body mass index (Kg/m^2)	23.1 ± 2.7	23.7 ± 3.5	0.572
Diabetes mellitus	2	7	>0.999
Primary disease			
Hepatocellular carcinoma	3	18	0.201
Intrahepatic cholangiocarcinoma	4	4	
Metastatic liver tumor	1	5	
Others	3	6	
Hepatitis virus infection			
Hepatitis B virus	0	1	0.428
Hepatitis C virus	1	10	
Interval between endoscopic sphincterotomy and hepatectomy (months)	30 [6, 60]	28 [3, 180]	0.693
History of cholangitis	4	6	0.237
Laboratory test results			
Albumin (g/dL)	4.0 [3.3, 4.3]	4.1 [3.8, 4.4]	0.369
Aspartate aminotransferase (IU/L)	24 [19.5, 32]	30 [22, 42]	0.139
Alanine aminotransferase (IU/L)	15 [12, 32]	25 [17, 46]	0.045
Total bilirubin (mg/dL)	0.7 [0.5, 0.9]	0.6 [0.6, 0.9]	0.66
Indocyanine green retention rate at 15 min. (%)	10.0 [7.8, 13.9]	13.7 [10.2, 18.7]	0.108
Operative methods			
Anatomic: nonanatomic	1:10	13:20	0.076
Expose the hilar plate	0	2	>0.999
Multiple site resection	0	4	0.558
Open: laparoscopic	11:0	17:16	0.003
Subphrenic part hepatectomy (S4, S7, S8)	3	8	>0.999
Pringle maneuver	11	24	0.085
Operative time (min)	329 [299, 379]	315 [202, 417]	0.839
Blood loss (mL)	400 [251, 575.]	480 [50, 1046]	0.776
Duration of prophylactic antibiotics (days)	1 [1, 3]	1 [1, 3]	0.975
Bile leakage	4	1	0.01
Post-hepatectomy liver failure (B or C)	0	2	>0.999
Length of hospital stay (days)	35 [24, 65]	12 [10, 17]	<0.001

Age and Body mass index are expressed as mean ± standard deviation. Other data are expressed as median with 25th and 75th percentiles.

Table 5. Uni- and Multivariate Analyses for Factors Cntributing to Prolonged Abscess Healing

	Univariate analysis		Multivariate analysis	
	Risk ratio (95%CI)	p-value	Risk ratio (95%CI)	p-value
Duration of prophylactic antibiotics (≤1 day)	0.67 (0.37-1.21)	0.18		
Post-hepatectomy liver failure B or C	2.10 (0.79-5.54)	0.14		
Bile leakage	3.89 (2.12-7.14)	0.000012	3.82 (2.02-7.22)	0.000038
Postoperative ileus	2.06 (0.69-6.12)	0.19		
Drainage by abscess puncture	0.88 (0.50-1.55)	0.65		
Mixed infection	3.10 (1.64-5.88)	0.00052	2.33 (1.16-4.69)	0.018
History of biliary reconstruction	2.68 (1.01-7.13)	0.048	2.43 (0.80-7.43)	0.12
History of endoscopic sphincterotomy	1.13 (0.32-3.98)	0.85		

3.10; 95% CI, 1.64-5.88; P < 0.001), and a history of BR (risk ratio, 2.68; 95% CI, 1.01-7.13; p = 0.048) were risk factors for prolonged abscess healing. Multivariate analysis showed that bile leakage (risk ratio, 3.82; 95% CI (2.02-7.22); p <0.001) and mixed infection (risk ratio, 2.33; CI, 1.16-4.69; p = 0.018) were independent risk factors for prolonged abscess healing.

Discussion

The incidence of postoperative abscesses in the liver resection plane was significantly higher in the BR and EST groups than in the non-BR or non-EST, with abscesses occurring in nearly half of patients in the BR group. Microbiological findings indicated that intestinal flora (e.g., Enterococcus spp., Escherichia coli, Klebsiella spp., and Pseudomonas aeruginosa) were predominant in the BR and EST groups, whereas skin flora were frequently isolated in the non-BR or non-EST group. Anaerobes and mixed infections were more common in the BR group. The interval between surgery and abscess development was shorter in the EST group than in the non-BR or non-EST group. Although the incidence of bile leakage did not differ among the three groups, bile leakage was an independent risk factor for abscess formation in both the BR and EST groups. These findings suggest that contamination of bile with intestinal flora via bilioenteric anastomosis or papillary dysfunction after sphincterotomy contributes to abscess formation and prolonged healing.

The clinical findings differed among the three groups. ALT activity and ICGR15 were significantly lower in the BR group, possibly reflecting a higher proportion of patients with metastatic liver tumors and relatively preserved liver function in this group. Anatomical resection was less frequent in the EST group than in the other groups. The proportion of patients who underwent right subphrenic partial hepatectomy (segments 4, 7, and/or 8) was significantly lower in the EST group than in the non-BR or non-EST group. The pringle maneuver was less frequently used in the BR group, likely because it can be technically difficult in patients with BR (bilioenteric anastomosis). However, these factors were not independent risk factors for postoperative abscesses formation in the BR and EST groups.

Intra-abdominal infection associated with bile leakage after liver resection is often refractory and may require prolonged treatment, reoperation, or may be fatal [5-9]. In this study, bile leakage and mixed infection were independent risk factors for prolonged healing (≥45 days). Bile contaminated with intestinal flora is persistently supplied into the abscess via bile leakage and bilioenteric anastomosis, which causes mixed infections and refractory abscesses. In abscesses after right subphrenic partial hepatectomy, a dead space between the liver cut surface and the diaphragm may serve as a culture medium for bacteria, and the diaphragm's pumping effect during respiration (decreased pressure during the inspiratory phase and increased pressure during the expiratory phase in the cavity; Figure 2) may facilitate inflow of contaminated bile, contributing to refractory abscess formation. In patients with an abscess in the non-BR or non-EST group, skin flora such as Staphylococcus aureus, Staphylococcus epidermidis, coagulase-negative staphylococci, Corynebacterium spp., and Propionibacterium acnes were frequently isolated. The longer operative time and later onset of abscesses suggest that prolonged intraoperative contamination and retrograde infection via drains during a longer postoperative course may contribute to the high prevalence of skin-flora infections in the non-BR or non-EST group.

Bile leak tests have been reported to reduce postoperative bile leakage [18-20]. These tests are typically performed using a biliary tube inserted during cholecystectomy; therefore, they are difficult to perform in patients with prior BR because the gallbladder has already been removed. In patients after EST, injected fluids (e.g., saline or ICG solution) may easily flow out into the duodenum through a loosened papilla unless a balloon catheter is used [21]. Difficulty in performing effective bile leak tests in BR and EST patients may have contributed to the higher incidence of abscesses in these groups. ICG fluorescence imaging represents a promising adjunct for intraoperative detection of occult bile leakage, particularly in BR and EST patients. However, its use may be limited by availability, cost, and lack of standardized protocols. In EST patients, injected solutions may readily drain into the duodenum unless papillary outflow is controlled. Prospective studies are required to establish whether routine ICG use reduces bile leakage–related abscess formation in high-risk populations.

Regarding intra-abdominal drainage, routine drainage is generally unnecessary after liver resection without BR [10, 22], although drains may be helpful in patients at high risk of bile leakage or bleeding [9, 23]. Drains may also facilitate early detection and treatment of bile leakage and fluid collections, especially in patients with cirrhosis [24–26]. In our cohort, treatment via surgically placed drains was useful for abscess management in 39.6% (84 of 212 patients) of cases. Given the high incidence of abscesses in patients with prior biliary tract treatment, intraoperative drain placement may be considered, although its use did not significantly differ among the three groups in this retrospective analysis.

For prophylactic antibiotic in liver resection without BR, first- or second-generation cephalosporins or flomoxef within 24h are recommended for both open and laparoscopic surgery [27–30]. Although intestinal flora (including anaerobes) was predominantly isolated in the BR and EST groups, prophylactic antibiotics cannot prevent reflux contamination via bilioenteric anastomosis or bacterial influx associated with bile leakage. Therefore, prophylactic antibiotic like that used for liver resection without BR may be reasonable; however, routine postoperative bacterial surveillance of drainage fluid in patients with prior biliary treatment may help guide early, appropriate antimicrobial therapy. The higher rate of cure with antibiotics alone in the EST group compared with the non-BR or non-EST group may be related to a higher proportion of partial resections in the EST group.

From a practical standpoint of clinical implications, patients with a history of BR or EST should be regarded as a high-risk population. Careful intraoperative assessment

for bile leakage, consideration of intra-abdominal drain placement especially when dead space is anticipated and early microbiological evaluation of drainage fluid are recommended. Timely adjustment of antimicrobial therapy based on culture results may improve clinical outcomes.

As international perspective reported rates of post-hepatectomy infectious complications vary globally due to differences in case mix and perioperative management. While the abscess incidence in non-BR/EST patients in this study aligns with international reports, the markedly higher incidence in BR/EST patients highlights a high-risk subgroup that may be under-recognized. These findings are particularly relevant to developing countries, where limited access to advanced imaging or interventional drainage emphasizes the importance of early risk recognition and culture-guided antibiotic strategies.

The main limitation of this study was the differences in the indication and methods of liver resection among hospitals, given that this was a multicenter retrospective study. Therefore, the indications for open or laparoscopic resection, intra-abdominal drain placement, and the selection of prophylactic antibiotics might differ among hospitals. However, this multicenter study clearly showed that a history of biliary tract treatments, such as BR and EST, was a high-risk factor for postoperative abscesses in the liver resection plane. Therefore, attention should be paid to the development of postoperative abscesses in the liver resection plane in patients with a history of biliary tract treatment.

Author Contribution Statement

HI and SK designed the study and analyzed the patient data. HI, HS, HK, MU, HM, KK, SY, MKi, SH, MT, MKa, and SK collected the data. HI and SK drafted the manuscript. All the authors have read and approved the final version of this manuscript.

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Scientific/Academic approval / Thesis

This work was conducted as a multicenter collaborative study and was not part of an approved student thesis.

Ethics approval and consent to participate

This multicenter retrospective study conformed to the Clinical Research Guidelines and was approved by the ethics committee of each institution (approval number in principal institution: R2021-115). Informed consent was obtained by opt-out from all patients or their family members at each institution.

Data Availability

The datasets analyzed during the current study are available from the corresponding author upon reasonable request.

Study registration

This study was not registered in a public registry because of its retrospective observational design.

Conflict of interest

The authors declare no conflicts of interest.

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