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Influence of previous gastrectomy on postoperative bile leakage after laparoscopic liver resection



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Abstract

Background Postoperative bile leakage (POBL) is a common cause of major morbidity following liver resection. Although the use of laparoscopy for liver surgery has expanded rapidly, POBL has been poorly described in patients undergoing laparoscopic liver resection (LLR). This study aimed to identify the risk factors for POBL after LLR.

Methods We enrolled 510 consecutive patients who underwent LLR for hepatic tumors between January 2009 and December 2023. POBL was defined according to the International Study Group of Liver Surgery, and its incidence, consequences, clinicopathological factors, and surgical details were evaluated retrospectively. Risk factors for POBL were determined using a multivariable logistic regression analysis.

Results POBL occurred in nine patients (1.8%). POBL was significantly associated with advanced age (81 vs. 72 years, p = 0.005), history of gastrectomy (3/9 vs. 25/501, p = 0.002), high incidence of postoperative complications (9 vs. 26, p = 0.001), and prolonged hospital stay (57 vs. 8 days, p = 0.001). In the multivariable analysis, POBL was significantly associated with a history of gastrectomy (OR 7.71, 95% CI 1.744–34.043, p = 0.007). In the management of POBL, all patients were successfully treated with percutaneous drainage alone or with additional treatment using endoscopic nasobiliary drainage.

Conclusion Previous gastrectomy was an independent risk factor for POBL in patients undergoing LLR. **Keywords** Postoperative bile leakage, Laparoscopic liver resection, Previous gastrectomy

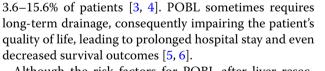
Introduction

Recent advances in surgical techniques and improvements in perioperative management, including strict indication criteria, have enabled the safe performance of liver resection [1, 2]. Nevertheless, postoperative bile leakage (POBL) remains a frequent complication after liver resection, which is reported to occur in approximately

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Although the risk factors for POBL after liver resections remain to be determined, numerous studies have demonstrated patient characteristics such as advanced age, liver dysfunction, diabetes mellitus, higher body mass index, sarcopenia, higher white blood cell count, and type of liver resection as risk factors for POBL [7–9]. Furthermore, in addition to understanding such risk factors for POBL, prevention and perioperative care for this critical condition will be more important [6]. However,



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previous studies have focused on open liver resection (OLR), and there are few reports focused on POBL after laparoscopic surgery.

Since laparoscopic liver resection (LLR) was first performed in the early 1990s, liver surgery via a laparoscopic approach has increased rapidly. Owing to its safety, which has been widely confirmed, LLR is now becoming a popular and standard surgical procedure for treating liver tumors [10]. In addition, several reports have revealed that LLR reduced blood loss, decreased rates of postoperative complications, and shorter hospital stay in comparison to OLR [11–13]. Thus, the opportunity to perform OLR has been gradually decreasing; consequently, further investigations focused on perioperative management, especially for LLR, are required.

Hence, the present study aimed to identify the risk factors for POBL in patients undergoing LLR.

Materials and methods

Study design

The present study was a single-center, non-randomized, observational, and retrospective analysis. A total of 510 consecutive patients underwent purely laparoscopic liver resection for hepatic tumors at Department of Surgery of Saga University Hospital between January 2009 and December 2023. No patient underwent surgery with a planned hand-assisted or hybrid approach. The selection criteria were as follows: Child-Pugh classification A or B, tumor < 10 cm in diameter, number of lesions < 4, no involvement of major vessels, no involvement of hilar structures, and no combined resection of other organs. Patients were categorized into two groups based on the presence or absence of POBL: POBL (+) and POBL (-). Patient demographics, clinicopathological variables, surgical details, and short-term results were compared between the two groups. This study was reviewed and approved by the Ethics Committee of the Saga University Hospital.

Surgical procedures

The details of the surgical procedure have been reported previously [14]. Laparoscopic ultrasonography was routinely used to confirm the tumors and guide resection. Liver parenchymal transection was performed using a clamp-crushing technique and/or Cavitron Ultrasonic Surgical Aspirator (CUSA, Valleylab, Boulder, CO, USA) on operator preference. If bile leakage was observed intraoperatively, the leak point was closed using a 5-0 polypropylene suture. The complete Pringle maneuver was performed at 15-min intervals during liver parenchymal transection. Abdominal drains were placed along the cut surface of the liver only in cases of anatomical liver resection or when there was concern about intraoperative bile control.

Definitions

Liver cirrhosis was defined as a fibrosis score of 4 using the new Inuyama classification [15]. Anatomical liver resection included Couinaud segmentectomy, sectionectomy, hemihepatectomy, and central bi-sectionectomy. Major liver resection was defined as the resection of three or more Couinaud segments of the liver. Postoperative complications were graded according to the Clavien-Dindo classification system [16], and defined as grade II or higher. POBL was diagnosed and graded according to the criteria of the International Study Group of Liver Surgery (ISGLS) [17], then defined as grade B or C, which requires additional diagnostic or interventional procedures. Postoperative mortality was defined as death within 90 days of surgery or at any time during the postoperative hospital stay.

Statistical analysis

All statistical analyses were performed using JMP Pro 17 (SAS Institute Inc., Cary, NC, USA). Continuous variables were summarized as the median and range, and categorical variables were summarized as frequencies and percentages. Continuous variables were compared using the Mann-Whitney U-test, and categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. Variables that had relevant associations with the occurrence of POBL on univariate analyses (P < 0.05) were included in a multivariate model. A multivariable analysis was performed using logistic regression analysis. *P* values of <0.05 were considered to indicate statistical significance.

Results

Patient characteristics

POBL occurred in 9 of the 510 patients (1.8%). All POBLs were graded as grade B ISGLS. In POBLs, surgical procedures were non-anatomical resection in six cases and anatomical resection in three cases. The baseline characteristics of the POBL (+) and POBL (-) groups are shown in Table 1. POBL was significantly associated with advanced age (81 vs. 72 years, p = 0.005) and a history of gastrectomy (3/9 vs. 25/501, p = 0.002). There were no significant differences in sex, American Society of Anesthesiologists Physical Status Classification System (ASA), Performance Status (PS), body mass index (BMI), diabetes mellitus, hemodialysis, steroid use, history of upper abdominal surgery including cholecystectomy, or history of colorectal surgery between the two groups.

Regarding the laboratory data and pathological findings, the two groups showed, no significant differences in platelet count, serum total bilirubin, serum albumin, prothrombin activity, ICG-R15, diagnosis, positive rate of HBs-Ag positivity, rate of positive HCV-Ab positivity, tumor size, number of tumors or liver cirrhosis (Table 2).

Table 1 Patient characteristics

Variables	POBL (+) (n=9)	POBL (-) (<i>n</i> = 501)	<i>p</i> value
Age, median (range), yr	81 (62–88)	72 (21–91)	0.005
Sex			0.559
Male	7 (77.8)	344 (68.7)	
Female	2 (22.2)	157 (31.3)	
ASA			0.865
1–2	4 (44.4)	264 (52.7)	
3 or more	5 (55.6)	237 (47.3)	
PS			0.182
0	9 (100)	418 (83.4)	
1	0 (0)	83 (16.6)	
BMI, median (range), kg/m ²	22.4	22.7	0.450
	(17.1–24.8)	(13.9–37.4)	
Diabetes mellitus	3 (33.3)	154 (30.7)	0.867
Hemodialysis	0 (0)	12 (2.4)	0.639
Steroid use	0 (0)	14 (2.8)	0.611
Medical history			
Upper abdominal surgery	5 (55.6)	162 (32.3)	0.139
Gastrectomy	3 (33.3)	25 (4.9)	0.002
Colorectal surgery	4 (44.4)	121 (24.2)	0.524

Data are presented as number (%) unless specified

ASA indicates American Society of Anesthesiologists Physical Status; PS, performance status, BMI, body mass index

 Table 2
 Laboratory data & pathological findings

Variables	POBL (+)	POBL (-)	р.
	(n=9)	(<i>n</i> =501)	value
Platelet count, median (range),	18.8	16.6	0.103
x10 ⁴ /µl	(10.3–47.2)	(3.3–51.8)	
Serum total bilirubin, median (range), mg/dl	0.7 (0.4–1.2)	0.8 (0.3–3.7)	0.128
Serum albumin, median (range), g/dl	3.8 (2.7–4.7)	3.9 (1.8-5)	0.656
Prothrombin activity, median	89.1	90	0.434
(range), %	(13.4–119)	(3.8–165)	
ICG-R15, median (range), %	17.5	15.3	0.655
	(10-34.8)	(0.4–89)	
Diagnosis			0.422
Hepatocellular carcinoma	5 (55.6)	367 (73.3)	
Intrahepatic cholangiocarcinoma	0 (0)	18 (3.6)	
Liver metastasis	4 (44.4)	110 (21.9)	
Others	0 (0)	6 (1.2)	
Positive HBs-Ag	0 (0)	58 (11.6)	0.227
Positive HCV-Ab	5 (55.6)	221 (44.1)	0.521
Tumor size, median (range), mm	22 (10–27)	22 (10–100)	0.413
Number of tumors			0.421
Solitary	8 (88.9)	389 (77.6)	
Multiple	1 (11.1)	112 (22.3)	
Liver cirrhosis	2 (22.2)	146 (29.1)	0.651

Data are presented as number (%) unless specified

ICG-R15 indicates indocyanine green dye retention test at 15 min

Surgical and short-term results

The surgical and short-term results of the POBL (+) and POBL (-) groups are shown in Table 3. POBL was significantly associated with a high incidence of postoperative

Table 3 Surgical and short-term results

Variables	POBL (+) (n=9)	POBL (-) (<i>n</i> = 501)	p value
Surgical procedure	((0.742
Anatomical resection	3 (33.3)	194 (38.7)	
Non-anatomical resection	6 (66.7)	307 (61.3)	
Major liver resection	0 (0)	44 (8.8)	0.352
Transection technique			0.977
Clamp-crush	2 (22.2)	124 (24.8)	
CUSA	7 (77.8)	377 (75.2)	
Repeat liver resection	1 (11.1)	113 (22.6)	0.414
Concomitant procedure			0.915
Cholecystectomy	4 (44.4)	297 (59.3)	
Operation time, median (range),	260	251 (133–894)	0.491
min	(209–467)		
Blood loss, median (range), ml	348	150	0.979
	(108–632)	(10-15879)	
Transfusion	0 (0)	16 (3.2)	0.586
Conversion to open surgery	0 (0)	3 (0.6)	0.816
Drain placement	2 (22.2)	198 (39.5)	0.765
Postoperative complication	9 (100)	26 (12.9)	< 0.001
Mortality	0 (0)	2 (0.3)	0.816
Hospital stay, median (range),	57	8 (3–30)	< 0.001
days	(44–106)		

Data are presented as number (%) unless specified

CUSA indicates Cavitron Ultrasonic Surgical Aspirator

 Table 4
 Multivariable logistic regression analysis of risk factors for POBL

Variables	Odds ratio	95% confidence interval	p value
Age≧75	1.05	0.971-1.136	0.216
History of gastrectomy	7.71	1.744-34.043	0.007

complications (9 vs. 26, p = 0.001) and prolonged hospital stay (57 vs. 8 days, p = 0.001). There were no significant differences in the surgical procedure, major liver resection, transection technique, repeat liver resection, chole-cystectomy as concomitant procedures, operation time, blood loss, transfusion, conversion to open surgery, drain placement or mortality between the two groups. Three of 501 patients without POBL had conversion to open surgery with an emergent hand-assisted or hybrid approach. Two of 501 patients without POBL died. The cause of death in these patients was acute myocardial infarction and liver failure, respectively. The details of postoperative complications are shown in Table S1.

Risk factors for POBL

Table 4 presents the multivariate analysis of the risk factors for POBL. Two of the 34 factors that were analyzed showed significant differences in the univariate analysis. The cut-off points of age at 75 was defined as advanced age patients in this study. In the multivariable logistic regression analysis, a history of gastrectomy was

identified as an independent risk factor for POBL (OR 7.71, 95% CI 1.744–34.043, p = 0.007).

Details of POBL in patients with a history of gastrectomy

In this study, POBL occurred in one of the 7 patients with a history of gastrectomy for benign disease (14.3%) and 2 of the 21 patients with a history of gastrectomy for gastric cancer (9.5%). There were no significant differences in the occurrence rate of POBL between patients with a history of gastrectomy for benign disease and gastric cancer. The details of POBL in patients with a history of gastrectomy are summarized in Table 5. Among the three patients with POBL, the primary diseases requiring gastrectomy were gastric cancer in two patients and a duodenal ulcer in one patient. Two total gastrectomies and one distal gastrectomy were performed; these were reconstructed by the Roux-en Y (n=2) and the Billroth II method (n = 1). In contrast, most of the reconstruction methods were the Billroth I method in the POBL (-) groups. A laparoscopic approach was applied in all but one case. In the management of POBL, 2 patients were successfully treated using percutaneous drainage alone, and the other patient required additional treatment, which included endoscopic nasobiliary drainage.

Discussion

In our series of 510 patients who underwent LLR between 2009 and 2023, POBL occurred in 9 patients (1.8%). In "simple" liver resection without biliary and/or vascular reconstruction, we could keep the incidence rate of POBL much lower in comparison to previous reports, even though several studies showed a benefit of laparoscopy in decreasing the incidence of postoperative complications [11–13]. These findings may be attributed to appropriate indication criteria, careful perioperative management and established surgical procedures in our institute. Nevertheless, POBL has not been eradicated, indicating that it remains an unsolved problem, and attempts have been made to identify patients at high risk for POBL in order to improve their postoperative outcomes.

Interestingly, the potential risk factors regarding as patient characteristics and surgical details, which were previously reported in OLR, had no correlation with the occurrence of POBL in this study. However, our multivariate analysis identified that a history of gastrectomy was an independent risk factor for POBL in patients undergoing LLR. Few studies have referred to a previous medical history of abdominal surgery as an independent predictor of postoperative hepatobiliary complications. Although most cases in the present study were managed using an open approach, Harimoto et al. revealed that patients with a history of gastrectomy were at risk for postoperative pneumonia and bile leakage [18]. They finally suggested that these high-risk cases, which often

	Table 5	Details of POBL	in patients with I	nistory of gastrectomy
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Gastrectomy related factors				Manage-	
Primary disease	Surgical procedure	Reconstruction	Approach	ment of POBL	
Gastric cancer	Total gastrectomy	RY	Laparos- copy	Percu- taneous drainage	
Gastric cancer	Total gastrectomy	RY	Laparos- copy	Percu- taneous drainage	
Duode- nal ulcer	Distal gastrectomy	BII	Open	Percutane- ous drain- age + ENBD	

RY indicates Roux-en Y; BII, Billroth II; ENBD, Endoscopic nasobiliary drainage

involve elderly patients, require intensive surgical care as well as nutritional support [18]. On the other hand, a rapidly aging society and improved patient prognosis with medical progress have increased the number of surgical interventions for further malignancies and other diseases [19]. Indeed, some researchers reported that liver resection in patients with a history of abdominal surgery were safe and feasible, regardless of approach (open or laparoscopy) [19]. Furthermore, laparoscopic surgery generally produces less adhesion in the abdominal cavity in comparison to open surgery [20]. In accordance with these reports, our study also showed that a history of upper abdominal surgery was not significantly associated with the incidence of postoperative complications or POBL, indicating that the presence or absence of adhesion around the cut surface of the liver seemed to have no relationship with POBL. Thus, we wondered whether specific postoperative conditions accompanied by gastrectomy caused POBL after liver resection.

Gallstone formation is widely known as one of the long-term postoperative complications of gastrectomy [21]. Recently, a national clinical database study in Korea showed an increased risk of symptomatic gallstones in patients undergoing gastrectomy [22]. Despite the fact that the mechanism underlying the increased rate of gallstone formation after gastrectomy is not completely understood, gastrectomy is considered to bring about physiological changes in the biliary system, such as the gallbladder and sphincter of Oddi [21, 23]. Above all, the potential causes of these changes might consist of dissecting the nerve system and transecting the duodenum during gastrectomy. In the gallbladder, the hepatic branch of the vagus nerve and hepatic plexus are dissected, which introduces decreased contraction ability due to suppressed sensitivity to cholecystokinin (CCK) [24–26]. In addition, dissection of such nerve systems is reported to promote dysfunction of the sphincter of Oddi [24-26]. Transection of the duodenum also introduces decreased contraction and cyclic motor ability of the gallbladder due to changes in the pattern of CCK secretion

[27]. Several studies revealed that duodenal transection disturbed motility of the sphincter of Oddi, leading to increased internal pressure of the bile duct [27, 28]. Moreover, a blind end of the duodenum might increase the internal pressure of the intestine as well as the bile duct, although this depends on the method of reconstruction that is applied after gastrectomy. This may be related to the bacterial overgrowth in the biliary system. In our study, POBL patients with a history of gastrectomy underwent reconstruction using the Roux-en Y or Billroth II methods, which made a blind end in the duodenum. Thus, disruption of coordination between the alimentary tract and biliary system after gastrectomy seems to not only cause biliary stasis, but also lead to retrograde biliary infection. This mechanism might have an effect on the increased POBL after liver resection in patients with a history of gastrectomy.

On the other hand, the prevention of POBL after liver resection is demanded in perioperative management. In fact, an intraoperative bile leakage test, development of a cystic duct tube (C-tube) for biliary decompression, and the use of various topical hemostatic agents for the resected surface of the liver have been suggested for avoiding this critical condition [7, 8]. Arita et al. also recommended no drain placement after uncomplicated hepatic resection in order to reduce severe postoperative complications including POBL [1]. Although there is no established preventative method for POBL, the development of C-tubes for biliary decompression might be effective, especially in patients with a history of gastrectomy which is reconstructed using the Roux-en Y or Billroth II methods for the reasons mentioned above. Further prospective studies and randomized trials are warranted to clarify their prophylactic effects.

This is the first report to focus on POBL, especially laparoscopic surgery, in patients with a history of gastrectomy. However, this study was associated with several limitations. First, it was a retrospective and non-randomized study that was performed at a single institute. As such, it was subject to a potential selection bias. Second, the number of POBL events might be too small to identify the causes under the conditions of well-established liver surgery at our institute. Third, this study focused on the short-term outcomes and lacked long-term followup data. Despite these limitations, the statistical analyses clearly demonstrated a relationship between a history of gastrectomy and the development of POBL. We are confident that this study is meaningful in considering the prevention of POBL after liver resection.

In conclusion, previous gastrectomy was an independent risk factor for POBL in patients undergoing LLR. Careful surgical procedures and intensive perioperative management are required to minimize the incidence of POBL in high-risk cases.

Supplementary Information

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Supplementary Material 1

Author contributions

Study conception and design: TI, NH. Acquisition of data: TI, KI, TT. Analysis and interpretation of data: TI, KI, TT. Drafting of manuscript: TI, NH. All authors read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the Institutional Review Board of Saga University Hospital (2021-02-R-01). The requirement for informed consent was waived because the patient's data were retrieved from their medical charts. Nevertheless, all patients signed the informed consent form for surgery before the surgery. This research was not registered in an independent, institutional registry (N/A). This research was not an animal study (N/A).

Consent for publication

All the authors have approved the manuscript and agree with submission. The manuscript does not contain any individual person's data in any form.

Competing interests

The authors declare no competing interests.

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