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Does minimally invasive anatomical hepatectomy reduce surgical site infections?

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Abstract

Aim: This study aims to clarify the effectiveness of laparoscopic anatomical liver resections (ALRs) in surgical site infections (SSIs).

Methods: We included 95 cases (44.0%) of laparoscopic ALRs (LALRs) and 121 (56.0%) of open ALRs (OALRs). Retrospective comparisons were performed between the two groups.

Results: In preoperative factors, tumor size was significantly smaller in LALRs than in OALRs ($34.4 \pm 23.0 \text{ mm vs.}$ 45.9 ± 35.7 mm, *P* = 0.007). The operative duration was longer in LALRs than in OALRs ($523.0 \pm 186.5 \text{ min vs.}$ 356.3 ± 100.5 min, *P* < 0.001). However, the blood loss and the blood transfusion were fewer in LALRs than in OALRs ($592.1 \pm 911.7 \text{ mL vs.}$ 1,240.6 ± 1,131.8 mL, *P* < 0.001, 26.3% vs. 48.8%, *P* = 0.001, respectively). Postoperative complications above the Clavien-Dindo grade IIIb were one case (1.1%) in LALRs and two in OALRs (*P* = 1.000). The postoperative hospital stay was shorter in LALRs than in OALRs (14.8 ± 16.5 days vs. 20.7 ± 18.9 days, *P* = 0.017). There was one (0.8%) postoperative death within 90 days in OALRs and none (0.0%) in LALRs (*P* = 1.000). Incisional SSIs (ISSIs) were significantly reduced in LALRs than in OALRs (1.1% vs. 7.4%, *P* = 0.045). Organ/space SSIs (OSSIs) were observed in five cases (5.3%) in LALRs and seven cases (5.8%) in OALRs (*P* = 1.000). A strong correlation between bile leakage and OSSIs was found. Although OSSIs (Odds ratio 31.200, *P* = 0.009) were the significant predictive factors for developing ISSIs in OALRs, no risk factors predicting ISSIs were found in LALRs using Multivariate logistic regression analyses.

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Conclusion: Although this is a limited study at a single institution, minimally invasive anatomical hepatectomy can reduce ISSIs.

Keywords: Laparoscopic hepatectomy, surgical site infection, postoperative infectious complications

INTRODUCTION

In recent years, laparoscopic surgery has become widespread for lesions occurring in intraperitoneal organs. In the field of liver surgery, laparoscopic liver resections (LLRs) are performed mainly at high-volume centers, and their application is expanding to more difficult hepatectomies. Laparoscopic surgery, which allows for precise surgery with the effect of magnification, has been reported to be less invasive than open surgery and has been shown to reduce postoperative complications in various organs, such as the stomach^[1] and colon^[2]. However, although there have been some previous reports on the occurrence of postoperative infectious complications, including surgical site infections (SSIs), in liver surgeries, this is still open to debate. On the other hand, systematic anatomical liver resections (ALRs) are more complex and have a higher complication rate than non-systematic partial hepatectomy. Therefore, we compared the treatment outcomes of laparoscopic ALRs (LALRs) and open ALRs (OALRs) performed at our facility and described the effectiveness of minimally invasive surgeries in ALRs in reducing postoperative infectious complications, especially SSIs.

METHODS

Patients and methods

Of the 651 cases of all liver resections performed in our department between January 2006 and May 2022, 216 ALRs were studied [Figure 1], excluding biliary reconstruction, cases of combined resection of other organs, and emergency cases. Of these, 95 cases (44.0%) were LALRs, and 121 (56.0%) were OALRs. By performing a retrospective comparison between these two groups, we verified whether LALRs reduce SSIs. The study was conducted in line with the principles of the Declaration of Helsinki. It was reviewed and approved (No. M22194 21242) by the ethics committee of Toho University Omori Medical Center, Japan. The details about the study were disclosed on the web page of Toho University Omori Medical Center (https://www.lab.toho-u.ac.jp/med/omori/gastro_surgery/patient/crl2160000000ku-att/20230214_M22194_21242.pdf), and the potential participants were given the opportunity to opt-out.

Indications for systematic LLRs

When we first introduced LLRs, the tumor factor was tumors 5 cm or less located on the periphery or superficial surface of the lateral or infero-hepatic segments (S3, S4b, S5, S6). The surgical procedure factor was only partial hepatectomies or left lateral sectionectomy. In addition, the candidates were patients who could tolerate similar open liver resections (OLRs) as host factors, and cases with apparent bleeding tendency or ascites were excluded. By accumulating these cases, standardizing the procedure, and improving surgical outcomes, we gradually expanded the indications for hepatic systemic anatomical resection equivalent to OLRs. Anatomical hepatic resections were planned as segmentectomies, sectionectomies, or two or more section resections from the perspective of tumor size, tumor number, and achieving radical surgery^[3-5].

Perioperative management of LLRs

In preoperative systemic evaluation, the American Society of Anesthesiologists physical status (ASA-PS) and the Charlson comorbidity index (CCI)^[6] were used.



Figure 1. Patient selection. BD: Biliary duct; LALRs: laparoscopic anatomical liver resections; OALRs: open anatomical liver resections.

In intraoperative anesthetic management, maximum airway pressure (MAP) was maintained at 15 cm H_2O or less. In addition to significant hepatectomy and tumor resection near the hepatic vein or inferior vena cava, a central venous catheter (CVC) was placed in cases where monitoring of circulatory and respiratory dynamics was deemed necessary, and central venous pressure (CVP) was managed with a target of 3-8 mmHg.

Standard surgical technique

Pneumoperitoneum pressure (PP) was 8-10 mmHg with CO₂ insufflation to ensure visibility. For hepatectomy, preparation for hepatic portal blockade using the Pringle method was performed in all cases, and portal blockade was performed when necessary. The area of ischemic blood flow was confirmed by securing and ligating the dominant Glissonean sheath on the hepatic portal side, and the anatomical resection area was confirmed using the indocyanine green (ICG) fluorescence method. The vessels were exposed using a cavitron ultrasonic surgical aspirator (CUSA) or clump crushing, and the liver parenchyma was resected using an Ultrasonic Activated Device, Monopolar Device, or Bipolar Device. A stapling device was used to dissect a relatively large Glissonean pedicle and significant hepatic veins. The approach started as pure laparoscopy but was changed to hybrid or hand-assisted laparoscopic surgery (HALS) to ensure safety, such as improving the visual field and controlling bleeding. For LLRs, the specimen was placed in a plastic bag and removed from the body. If bile leakage was observed during surgery, a C-tube was placed through the cystic duct. A closed suction drain was placed in all cases. The wound was closed by irrigating with saline and then suturing the dermis with absorbable sutures.

Standard perioperative antimicrobial management

Prophylactic antibiotics were cefmetazole (CMZ) or cefotiam (CTM). In patients with normal renal function, antibiotics were administered every 3 h during surgery from before the start of surgery.

Postoperative antibiotics were administered continuously for up to 48 h. In cases where a peritoneal drain was inserted, it was generally removed on the third postoperative day after confirming neither bleeding nor bile leakage.

Definition of postoperative complications

SSIs were classified into incisional SSIs (ISSIs) and organ/space SSIs (OSSIs) according to the Centers for Disease Control and Prevention (CDC) guidelines^[7]. ISSIs were defined as cases in which wounds were opened due to signs of wound infection within 30 days after surgery, and drainage cultures were positive. OSSIs were defined as positive when purulent drainage was observed from peritoneal drains within 30 days after surgery or when pathogens were isolated from aseptically collected specimens. Bile leakage was defined as positive according to the International Study Group of Liver Surgery (ISGLS) criteria^[8] when bile leakage continued for three days or more after surgery, containing three times or more the T-Bil value than the blood test in biliary drainage juice, or when surgical or radiological treatment was required for drainage due to bile leakage. According to TG18^[9], cholangitis was considered positive if, in addition to fever or worsening inflammatory symptoms, serum total bilirubin levels were 2 mg/dL or higher, hepatobiliary test results were 1.5 times higher than the reference values or bile duct dilation was observed on abdominal ultrasound (US) or computed tomography (CT) scans. Furthermore, cases of Clavian-Dindo^[10] (CD) grade 3a or higher that required interventional radiology (IVR) or endoscopic treatment were considered positive. Intestinal obstruction was considered positive if symptoms of gastrointestinal obstruction such as nausea and vomiting were present, stomach or small intestine dilation was observed on plain abdominal X-rays or abdominal CT scans, and fasting treatment was required as CD grade 3a or higher. Deep vein thrombus (DVT) was considered positive if, in addition to clinical symptoms such as edema and pain, the coagulation and fibrinolysis levels were elevated, whole-leg venous ultrasound (whole-leg US) was performed on all patients, and the diagnosis was positive if intravenous thrombus was demonstrated. Portal vein thrombosis (PVT) was also considered positive if demonstrated on percutaneous US or contrast CT scans. According to the ISGLS criteria^[11], liver failure was determined to be positive if the prothrombin time was prolonged or the serum total bilirubin level was elevated on the fifth postoperative day or later, and if the patient had ISGLS Grade B or higher, requiring treatment such as blood transfusion. All the above complications were graded according to the CD; cases with CD grade 3a or higher were considered positive.

Statistical analysis

Statistical analysis was performed using EZR on R commander, version 1.55, and the Mann-Whitney *U* test or chi-square test was used to compare the two groups. Univariate and multivariate analyses were performed using a logistic regression model to determine independent risk factors of ISSIs. Each group used receiver operating characteristic curve analysis to calculate cut-off values for logistic regression analysis.

RESULTS

Table 1 shows a comparison of preoperative factors. Age was 64.0 ± 13.0 years in the LALRs compared with 67.6 ± 10.0 years in the OALRs, with the LALRs being statistically significantly younger (P = 0.022). There were 66 male cases (69.5%) compared with 85 male cases (70.2%) in the OALRs, and body mass index (BMI) was 23.2 ± 3.6 kg/m² in the LALRs compared with 22.8 ± 3.5 kg/m² in the OALRs, with no statistically significant difference between the two groups (P = 1.000 and P = 0.460, respectively). Alcohol consumption was 35 (36.8%) in LALRs and 34 (28.1%) in OALRs. Smoking history was 63 (66.3%) in LALRs and 84 (69.4%) in OALRs, with no statistically significant differences between the two groups (P = 0.188, P = 0.661, respectively). Regarding comorbidities, insulin use was 34 (35.8%) in LALRs and 33 (27.3%) in OALRs. Chronic kidney disease was 26 (27.4%) in LALRs and 34 (28.1%) in OALRs. Steroid use before surgeries was 2 (2.1%) in LALRs and 2 (1.7%) in OALRs, with no statistically significant differences between the two groups (P = 0.186, P = 1.000, P = 1.000, respectively). In evaluating the physical condition, the ASA

	Variables	OALRs (n = 121)	LALRs (n = 95)	P-value
Age, years		67.6±10.0	64.0 ± 13.0	0.022
Gender	Female, %	36 (29.8)	29 (30.5)	1.000
	Male, %	85 (70.2)	66 (69.5)	
Body mass index, kg/m ²		22.8 ± 3.5	23.2 ± 3.6	0.460
Comorbidity	Alcohol, %	34 (28.1)	35 (36.8)	0.188
	Smoking, %	84 (69.4)	63 (66.3)	0.661
	Diabetes mellitus, %	33 (27.3)	34 (35.8)	0.186
	Chronic renal disease, %	34 (28.1)	26 (27.4)	1.000
	Steroid use, %	2 (1.7)	2 (2.1)	1.000
ASA score	l, %	6 (5.0)	7 (7.4)	0.568
	II, %	100 (82.6)	81 (85.3)	0.711
	III, %	15 (12.4)	7 (7.4)	0.263
	IV, %	0 (0.0)	0 (0.0)	NA
	V, %	0 (0.0)	0 (0.0)	NA
CCI	Low (0), %	13 (10.7)	19 (20.0)	0.081
	Medium (1-2), %	46 (38.0)	33 (34.7)	0.670
	High (3-4), %	21 (17.4)	17 (17.9)	1.000
	Very high (≥5), %	41 (33.9)	26 (27.4)	0.374
Liver function	Cirrhosis, %	10 (8.4)	11 (11.6)	0.492
	ICG R15, %	9.8 ± 6.3	9.2 ± 6.4	0.462
	Child Pugh grade A, %	119 (98.3)	94 (98.9)	1.000
	В, %	2 (1.7)	1 (1.1)	1.000
	С, %	0 (0.0)	0 (0.0)	NA
Tumor factor	Malignant disease, %	108 (89.3)	79 (83.2)	0.229
	Hepatocellular carcinoma, %	56 (46.3)	55 (57.9)	0.101
	Metastatic caricinoma, %	36 (29.8)	22 (23.2)	0.354
	Intrahepatic cholangiocarcinoma, %	10 (8.3)	2 (2.1)	
	Gallbladder carcinoma, %	4 (3.3)	0 (0.0)	
	Neuroendocrine carcinoma, %	1(0.8)	0 (0.0)	
	Benigin disease, %	13 (10.7)	16 (16.8)	
	Tumor size, mm	45.9 ± 35.7	34.4 ± 23.0	0.007
	Preoperative chemotherapy, %	35 (28.9)	16 (16.8)	0.052

Data are expressed as number (percentage) of patients or as mean ± standard deviation. LALRs: Laparoscopic anatomical liver resections; OALRs: open anatomical liver resections; ASA: american societry of anesthesiologisis; CCI: Charlson comorbidity index; ICG %15: indocyanine green retention rate at 15 min; NA: not available.

classification showed no statistically significant difference between the two groups. On the other hand, the number of cases with a low CCI was 19 (20.0%) in LALRs and 13 (10.7%) in OALRs, showing a tendency for the LALRs to have a higher CCI score (P = 0.081). In terms of preoperative hepatic functional reserve, the number of cases with cirrhosis was 11 (11.6%) in LALRs and 10 (8.4%) in OALRs, showing no statistically significant difference between the two groups (P = 0.492). The preoperative ICG R15 values were 9.2% ± 6.4% in LALRs and 9.8% ± 6.3% in OLRs, and there was one case (1.1%) of Child-Pugh Grade B in LALRs and two cases (1.7%) in OALRs, with no statistically significant difference between the two groups (P = 0.462 and P = 1.000, respectively). Regarding tumor factors, the proportion of malignant disease was 79 cases (83.2%) in LALRs and 108 cases (89.3%) in OALRs, with a tendency for malignant disease to be more prevalent in OALRs (P = 0.229). Hepatocellular carcinoma (HCC) was in 55 cases (57.9%) in LALRs and 56 cases (46.3%) in OALRs, with no statistically significant difference between the two groups (P = 0.101).

Variables		OALRs (n = 121)	LALRs (n = 95)	P-value
Initial resection,	%	105 (86.8)	91 (95.8)	0.032
Approach	open	121 (100.0)		
	pure		67 (70.5)	
	hybrid		17 (18.5)	
	HALS		7 (7.6)	
	conversion		4 (4.2)	
Procedure	Hemihepatectomy, %	47 (38.8)	30 (31.6)	0.317
	left hepatectomy, %	21 (17.4)	15 (15.8)	0.855
	Right hepatectomy, %	26 (21.5)	15 (15.8)	0.301
	Sectionectomy, %	30 (24.8)	27 (28.4)	0.641
	Anterior sectionectomy, %	10 (8.3)	1 (1.1)	0.025
	Medial sectionectomy, %	6 (5.0)	2 (2.1)	0.471
	Posterior sectionectomy, %	8 (6.6)	6 (6.3)	1.000
	Left lateral sectionectomy, %	7 (5.8)	18 (18.9)	0.005
	Segmentectomy, %	48 (39.7)	38 (40.0)	1.000
Operative durati	ion, min	356.3 ± 100.5	523.0 ± 186.5	< 0.001
Blood loss, mL		1,240.6 ± 1,131.8	592.1±911.7	< 0.001
Intraoperative transfusion, %		59 (48.8)	25 (26.3)	0.001

Data are expressed as number (percentage) of patients or as mean ± standard deviation. LALRs: Laparoscopic anatomical liver resections; OALRs: open anatomical liver resections; HALS: hand assisted laparoscopic surgery.

Metastatic carcinoma (Mets) was 22 cases (23.2%) and 36 cases (29.8%) in OALRs, with no statistically significant difference between the two groups (P = 0.354). The tumor diameter was 34.4 ± 23.0 mm in LALRs and 45.9 ± 35.7 mm in OALRs, significantly smaller in LALRs (P = 0.007). Preoperative chemotherapy was administered in 16 cases (16.8%) compared to 35 cases (28.9%) in OALRs, with a tendency for preoperative chemotherapy to be more frequent in OALRs (P = 0.052).

A comparison of intraoperative factors is shown in Table 2. The initial hepatectomy was performed in 91 cases (95.8%) in LALRs and 105 cases (86.8%) in OALRs, with a statistically significant difference between the two groups (P = 0.032). The approach in LLRs was pure in 67 cases (70.5%), hybrid in 17 cases (18.5%), HALS in 7 cases (7.6%), and conversion to conventional open procedure in 4 cases (4.2%). The surgical procedures performed were hemi-hepatectomies in 30 cases (31.6%) in LALRs and 47 cases (38.8%) in OALRs, sectionectomies in 27 cases (28.4%) in LALRs and 30 cases (24.8%) in OALRs, and segmentectomies in 38 cases (40.0%) in LALRs and 48 cases (39.7%) in OALRs, with no difference between the two groups (P = 0.317, P = 0.641, and P = 1.000, respectively). In the LALRs, the operative duration was 523.0 ± 186.5 min, the blood loss was 592.1 ± 911.7 mL, and 25 cases (26.3%) required intraoperative blood transfusion. In contrast, in the OALRs, the operative duration was 356.3 ± 100.5 min, the blood loss was 1,240.6 ± 1,131.8 mL, and 59 cases (48.8%) required intraoperative blood transfusion, resulting in a statistically significantly longer operative time, lower blood loss, and fewer cases of blood transfusion in the LALRs (P < 0.001, P = 0.001, respectively).

In terms of postoperative complications, there was one 30-day postoperative death in the OALRs (0.8%) and one 90-day postoperative death in the OALRs (0.8%) compared with none in the LALRs (P = 1.000 and P = 1.000, respectively) [Table 3]. Regarding infectious complications, ISSIs were observed in 1 case (1.1%) in LALRs and 9 cases (7.4%) in OALRs, which was statistically significantly less in LALRs (P = 0.045). OSSIs were observed in 5 cases (5.3%) in LALRs and 7 cases (5.8%) in OALRs (P = 1.000). There were no

Variables		OALRs (n = 121)	LALRs (n = 95)	P-value
30-day mortality, days	5	1 (0.8)	0 (0.0)	1.000
90-day mortality, days	5	1 (0.8)	0 (0.0)	1.000
Incisional SSIs, %		9 (7.4)	1 (1.1)	0.045
Organ/space SSIs, %		7 (5.8)	5 (5.3)	1.000
Bile leakage, %		10 (8.3)	6 (6.3)	0.794
Cholangitis, %		0 (0.0)	0 (0.0)	NA
Gastro-intestinal bleed	ding, %	0 (0.0)	0 (0.0)	NA
Intraabdominal bleedir	ng, %	1 (0.8)	0 (0.0)	1.000
Ascites, %		2 (1.7)	0 (0.0)	0.505
Pleural effusion, %		2 (1.7)	1 (1.1)	1.000
Heart failure, %		0 (0.0)	0 (0.0)	NA
Renal dysfunction, %		2 (1.7)	0 (0.0)	0.505
lleus, %		0 (0.0)	0 (0.0)	NA
Deep vein thrombosis,	%	0 (0.0)	0 (0.0)	NA
Portal vein thrombosis	i, %	0 (0.0)	0 (0.0)	NA
Liver failure, %		2 (1.7)	0 (0.0)	0.505
Pneumonia, %		0 (0.0)	0 (0.0)	NA
CRBSI, %		1 (0.8)	0 (0.0)	1.000
Enteritis, %		0 (0.0)	0 (0.0)	NA
UTI, %		0 (0.0)	0 (0.0)	NA
AMR bacteria, %		2 (1.7)	2 (2.1)	1.000
Clavian-Dindo	< IIIa, %	119 (98.3)	94 (98.9)	1.000
clasification	IIIb, %	0 (0.0)	1 (1.1)	0.440
	IVa, %	1 (0.8)	0 (0.0)	1.000
	IVb, %	0 (0.0)	0 (0.0)	NA
	V, %	1 (0.8)	0 (0.0)	1.000
Hospital stay, days		20.7 ± 18.9	14.8 ± 16.5	0.017

Table 3. Comparison of postoperative factors between OALRs and LALRs

Data are expressed as number (percentage) of patients or as mean ± standard deviation. LALRs: Laparoscopic anatomical liver resections; OALRs: open anatomical liver resections; SSIs: surgical site infection; CRBSI: catheter related blood stream infection; UTI: urinary tract infection; AMR: antimicrobial resistance; NA: not available.

significant differences between the two groups. Details of cases with OSSIs are shown in Table 4. In the OSSI cases, bile leakage was observed in 4 cases (57.1%) in OALRs and 4 cases (80.0%) in LALRs. In Table 3, bile leakage was observed in 6 cases (6.3%) in LALRs and 10 cases (8.3%) in OALRs, with no difference between the two groups (P = 0.794). On the other hand, it showed a strong correlation between bile leak and OSSIs in Table 5 (P < 0.001). No cases of cholangitis were observed in either group. Catheter-related bloodstream and urinary tract infections were observed in 1 case (0.8%), respectively, in OALRs, but none in LALRs (all P = 1.000). No cases of pneumonia and enteritis were observed in either group. Sepsis was observed in 1 case (0.8%) in OALRs, but none in LALRs (P = 1.000). Antimicrobial resistance bacteria were detected postoperatively in 2 patients (1.7%) in OALRs and two patients (2.1%) in LALRs (P = 1.000). MRSA was detected in all four cases and found in the bile juice and wound in LALRs [Table 6]. There were no cases of steroid use, liver cirrhosis, or preceding chemotherapy in these four cases. In Table 3, no cases of gastrointestinal bleeding were observed in either group. Intraperitoneal bleeding occurred in 1 patient (0.8%) in OALRs, not LALRs (P = 1.000). No cases of ileus, DVT, and PVT were observed in either group. Liver failure was detected in 2 patients (1.7%) in OALRs; one patient expired due to liver failure, but none in LALRs (P = 0.505). In the CD, 3b or higher cases were observed, with one case (1.1%) performed reoperation for biliary peritonitis due to accidental removal of a biliary drainage tube in LALRs and 2 cases

Table 4. Details of cases with OSSIs

Case	Diagnosis	Inslin use	CRD	Steroid use	LC	Preceding chemotherapy	Approach	Procedure	ISSIs	Bile leakage
1	Mets	Negative	Positive	Negative	Negative	Positive	OALRs	Sectionectomy (Post)	Positive	Positive
2	ICC	Negative	Negative	Negative	Negative	Negative	OALRs	Sectionectomy (Ante)	Positive	Positive
3	ICC	Negative	Positive	Negative	Negative	Negative	OALRs	Segmentectomy (S6)	Positive	Negative
4	HCC	Negative	Negative	Negative	Negative	Negative	OALRs	Hemihepatectomy (Lt)	Negative	Negative
5	HCC	Negative	Positive	Negative	Positive	Positive	OALRs	Hemihepatectomy (Rt)	Positive	Negative
6	HCC	Negative	Negative	Negative	Negative	Negative	OALRs	Segmentectomy (S7)	Negative	Positive
7	HCC	Negative	Negative	Negative	Negative	Negative	OALRs	Sectionectomy (Ante)	Negative	Positive
8	HCC	Positive	Positive	Negative	Negative	Negative	LALRs	Segmentectomy (S4a + S5)	Negative	Positive
9	HCC	Negative	Negative	Negative	Negative	Negative	LALRs	Segmentectomy (S5)	Negative	Positive
10	HCC	Positive	Negative	Negative	Negative	Negative	LALRs	Sectionectomy (Ante)	Negative	Negative
11	HCC	Negative	Negative	Negative	Negative	Negative	LALRs	Hemihepatectomy (Rt)	Negative	Positive
12	HCC	Positive	Positive	Negative	Negative	Negative	LALRs	Hemihepatectomy (Rt)	Negative	Positive

Mets: Metastatic carcinoma; OSSIs: organ/space SSI; HCC: hepatocellular carcinoma; ICC: intrahepatic cholangiocarcinoma; CRD: chronic renal disease; LC: liver cirrhosis; LALRs: laparoscopic anatomical liver resections; OALRs: open anatomical liver resections; ISSIs: incisional SSI.

Table 5. Relationship between bile leakage and OSSIs

			Bile leakage				
		negative	positive	P-value			
OSSIs	negative	196	8	< 0.001			
	positive	4	8				

Data are expressed as number of patients. OSSIs: Organ/space SSI.

Table 6. Details of cases with antimicrobial resistance bacteria

Case	1	2	3	4
Diagnosis	НСС	ICC	НСС	Intrahepatic calculosis
Inslin use	Negative	Negative	Positive	Negative
CRD	Negative	Negative	Positive	Negative
Steroid use	Negative	Negative	Negative	Negative
LC	Negative	Negative	Negative	Negative
Preceding chemotherapy	Negative	Negative	Negative	Negative
Approach	OALRs	OALRs	LALRs	LALRs
Procedure	Rt. hepatectomy	Sectionectomy (Ante)	Segmentectomy (S4a + 5dor)	Lt. hepatectomy
ISSIs	Positive	Positive	Negative	Positive
OSSIs	Negative	Positive	Positive	Negative
Bile leakage	Negative	Positive	Positive	Negative
Detected bacteria	MRSA	MRSA	MRSA	MRSA
Detected site	Wound	Drain	Bile	Wound

HCC: Hepatocellular carcinoma; ICC: intrahepatic cholangiocarcinoma; CRD; chronic renal disease; LC: liver cirrhosis; LALRs: laparoscopic anatomical liver resections; OALRs: open anatomical liver resections; ISSIs: incisional SSI; OSSIs: organ/space SSI; MRSA: methicillin resistant *Staphylococcus Aureus*.

Variables	No potionto $(n = 0E)$	Univariate analy	sis	Multivariate analysis				
variables	No. patients (n – 95)	Odds ratio (95%CI)	P-value	Odds ratio (95%CI)	P-value			
Age (years)								
≥76/<76	15/80	infimum (0.137-infimum)	0.158					
Gender								
male/female	66/29	infimum (0.011-infimum)	1.000					
Body mass index								
\geq 29.2 kg/m ² /< 29.2 kg/m ²	4/91	infimum (0.583-infimum)	0.04	infimum (0.295-infimum)	0.999			
Malignant disease								
yes/no	79/16	0.000 (0.000-7.899)	0.168					
Smoke								
yes/no	63/32	0.000 (0.000-19.810)	0.337					
Diabetes mellitus								
yes/no	23/72	0.000 (0.000-121.856)	1.000					
Chronic renal disease								
yes/no	26/69	0.000 (0.000-103.335)	1.000					
Steroid use								
yes/no	2/93	0.000 (0.000-1763.556)	1.000					
Cirrhosis								
yes/no	11/84	0.000 (0.000-296.443)	1.000					
Tumor size (mm)								
≥15/<15	79/16	0.000 (0.000-7.899)	0.168					
Preoperative chemotherapy								
yes/ no	16/79	0.000 (0.000-191.988)	1.000					
Initial resection								
yes/no	91/4	infimum (0.001-infimum)	1.000					
Operative duration (min)								
≥ 871/< 871	3/92	infimum (0.786-infimum)	0.032	infimum (0.295-infimum)	0.999			
Blood loss (mL)								
≥ 1,100/< 1,100	15/80	infimum (0.137-infimum)	0.158					
Transfusion								
yes/no	25/70	0.000 (0.000-109.016)	1.000					
Organ/ space surgical site infec	tion							
yes/no	5/90	0.000 (0.000-694.394)	1.000					
Bile leakage								
yes/no	6/89	0.000 (0.000-573.327)	1.000					

Table 7. Univariate and multivariate analyses of the predictive factors for incisional surgical site infection in laparoscopic anatomical liver resections

CI: Confidence interval.

(1.6%) in OALRs. The postoperative hospital stay was 14.8 ± 16.5 days in LALRs and 20.7 ± 18.9 days in OALRs, with significantly shorter hospitalization in LALRs (P = 0.017). Univariate and multivariate analyses were used to reveal those factors predicting ISSIs. In Table 7, univariate analysis of LALRs on the incidence of ISSIs showed that two factors were extracted and identified as being useful for discriminating between those who would develop ISSIs: BMI ≥ 29.2 kg/m² (P = 0.042), Operative duration ≥ 871 min (P = 0.032). Multivariate logistic regression analysis revealed no predictive factor for developing ISSIs. On the other hand, in univariate analysis of OALRs, four factors were extracted and identified as being useful for discriminating between those who would develop ISSIs: Operative duration ≥ 388 min (P = 0.001), Blood loss ≥ 1,786 mL (P < 0.001), Transfusion yes (P = 0.015), and OSSIs yes (P < 0.001) [Table 8]. Multivariate

Verieblee	No. patients	Univariate analys	sis	Multivariate analysis				
Variables (n = 121) Odds ratio (95%CI) P-val			P-value	Odds ratio (95%CI)	P-value			
Age (years)								
≥75/<75	27/94	3.060 (0.561-15.511)	0.111					
Gender								
male/female	85/36	3.607 (0.454-165.775)	0.277					
Body mass index								
\geq 20.1 kg/m ² /< 20.1 kg/m ²	99/22	infimum (0.442-infimum)	0.362					
Malignant disease								
yes/no	108/13	0.960 (0.111-46.103)	1.000					
Smoke								
yes/no	84/37	0.873 (0.174-5.707)	1.000					
Diabetes mellitus								
yes/no	32/89	0.329 (0.007-2.628)	0.442					
Chronic renal disease								
yes/no	34/87	2.171 (0.403-10.845)	0.267					
Steroid use								
yes/no	2/119	0.000 (0.000-69.190)	1.000					
Cirrhosis								
yes/no	10/109	1.398 (0.028-12.713)	0.559					
Tumor size (mm)								
≥ 15/< 15	105/16	infimum (0.295-infimum)	0.605					
Preoperative chemotherapy								
yes/no	35/86	1.248 (0.190-6.276)	0.717					
Initial resection								
yes/no	105/16	infimum (0.295-infimum)	0.605					
Operative duration (min)								
≥ 388/< 388	44/77	16.520 (2.085-755.923)	0.001	8.250 (0.647-105.000)	0.104			
Blood loss (mL)								
≥1,786/<1,786	28/93	14.701 (2.561-154.736)	< 0.001	3.670 (0.400-33.600)	0.250			
Transfusion								
yes/no	59/62	9.425 (1.197-430.474)	0.015	6.710 (0.217-208.000)	0.277			
Organ/ space surgical site infection	on							
yes/no	7/114	26.792 (3.557-238.232)	< 0.001	31.200 (2.380-409.000)	0.009			
Bile leakage								
yes/no	10/111	3.652 (0.320-24.225)	0.162					

Table 8. Univariate and multivariate analyses of the predictive factors for incisional surgical site infection in open anatomical liver resections

CI: Confidence interval.

logistic regression analysis of OALRs revealed that OSSIs (Odds ratio 31.200, 95%CI: 2.380-409.000, P = 0.009) were the significant predictive factors for developing ISSIs.

DISCUSSION

For malignant liver tumors, there are a wide variety of treatments, including local ablation therapy, systemic chemotherapy, and trans-arterial chemo-embolization therapy, in addition to hepatectomy. Individuals have tailor-made these treatment strategies in recent years^[12]. Therefore, there have been more opportunities to experience cases of liver resection after local therapy or chemotherapy in clinical practice. In addition, the number of elderly patients with coexisting major organ diseases is increasing due to the aging society, and

the environment surrounding liver surgery is rapidly diversifying. On the other hand, gastrointestinal surgery has a higher incidence of postoperative infectious complications than surgery in other fields, and there are particularly many cases of SSIs in the hepato-biliary-pancreatic field^[13]. Therefore, hepato-biliary-pancreatic surgeons must respond to various cases, including judging surgical suitability, dealing with major coexisting organ diseases, and taking perioperative infection control measures more than ever before.

Seventeen previous studies comparing LLRs and OLRs for SSIs, including our study, were found and presented in Table 9^[14-29]. LLRs reduced ISSIs in six studies^[15,19,20,28,29]. Five of these studies did not find that LLRs reduced OSSIs^[15,19,20,29]. Two reports could suggest that LLRs can reduce the incidence of OSSIs^[16,28]. Only one study showed that LLRs reduce both ISSIs and OSSIs^[28]. These differences might be due to factors such as anatomical or non-anatomical procedures, HCC or other diseases, primary or recurrence, the number of patients, and selection bias between LLRs and OLRs. Data from this study showed that LALRs reduce ISSIs, which is the same as suggested in the report targeting ALRs by Takahara *et al.*^[20].

OSSIs are considered to be related to ISSIs^[30]. However, LALRs have smaller wounds and can also achieve sufficient drainage of the surgical site by drains in our LALRs. In univariate analysis of LALRs, the ISSIs showed statistically significant differences in BMI and operative duration as predictive factors for ISSIs. However, no significant predictive factors were found in multivariate analysis. Therefore, no association was found between ISSIs and OSSIs in LALRs; that is a rationale for LALRs to reduce the ISSIs in our study.

Although our study showed no significant difference in the reduction of OSSIs due to minimally invasive anatomical hepatectomy, eight reports of non-anatomical hepatectomy showed a tendency to reduce OSSIs^[14-16,18,22,25,28,29]. In general, risk factors for OSSIs include obesity^[31], smoking^[32], and cirrhosis^[33,34]. In addition, diseases and surgical procedures include intrahepatic stones, repeat hepatectomy, long-duration surgery^[13], bi-lobal resections, and excessive bleeding^[33]. In addition, postoperative factors, including long-term placement of abdominal drains^[35], liver failure^[36], and bile leakage^[35,36], are suggested to be the risk factors for OSSIs. While cases are becoming more diverse, bile leakage is still considered to be the most essential factor associated with OSSIs in clinical practice. Although the risk factors for bile leakage are similar to those for OSSIs, difficult anatomical hepatectomies such as central bi-sectionectomy, anterior sectionectomy, medial segmentectomy, and caudate lobectomy are also considerable for high-risk procedures for bile leakage. Therefore, we considered that OSSIs were not improved by LALRs due to bile leakage.

In recent years, in the field of hepatectomies, as well as advances in various surgical techniques and perioperative management, improvements in equipment have been made in liver surgery. As a result, postoperative complications and surgical outcomes have been improving. The superiority of laparoscopic surgery, including its minimal invasiveness, has already been reported compared to laparotomy, and the magnified vision effect allows for precise surgery. However, bile leakage still occurs at a specific frequency in liver surgery. Further expansion of the indications for minimally invasive hepatectomies is expected for the highly complex procedure in the future; efforts to reduce the incidence of bile leakage are encouraged to take advantage of minimally invasive surgery. Standardizing the surgical procedure for the surgical team, identifying the actual anatomy with a good field of view during surgery, and reducing the surgery duration and blood loss are the bandle to do for the reduction of bile leakage.

Although this study is limited by its single center, we conclude that minimally invasive anatomical hepatectomy can reduce ISSIs. Further investigation with multicenter studies should be needed in the

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				Patient number					ISSIs (%)					OSSIs (%)					
Author	Year	Disease	Procedure			Propensity s	score analysis				Prope	nsity sco	re analysis				Prope	nsity sco	re analysis
				LLRs	OLRs	LLRs	OLRs	LLRs	OLRs	P-value	LLRs	OLRs	P-value	LLRs	OLRs	P-value	LLRs	OLRs	P-value
Kanazawa et al. ^[14]	2013	rHCC	nAR	20	20			0.0	15.0	0.231				0.0	15.0	0.231			
Kanazawa et al. ^[15]	2013	HCC	nAR	28	28			0.0	17.9	0.019				0.0	3.6	0.313			
López-Ben et al. ^[16]	2014	All	AR + nAR	50	100			0.0	7.0	0.054				2.0	12.0	0.033			
Takahara et al. ^[17]	2015	HCC	AR + nAR	436	2,969	387	387				0.3	1.0	NA				1.0	1.0	NA
Tanaka et al. ^[18]	2015	HCC	nAR	28	57	20	20	0.0	4.0	1.000	0.0	5.0	1.000	0.0	5.0	0.550	0.0	5.0	1.000
Han et al. ^[19]	2015	HCC	NA			88	88				1.1	5.7	< 0.050				0.0	4.5	NA
Takahara et al. ^[20]	2016	All	AR	929	1,4262	929	929	1.6	3.4	0.004	1.6	3.9	0.004	2.9	4.6	0.021	2.9	4.3	0.135
Cheung et al. ^[21]	2016	HCC	NA	110	330			3.6	2.1	NA				NA	NA	NA			
Noda et al. ^[22]	2018	rHCC	AR + nAR	20	48			0.0	4.2	NA				0.0	4.2	NA			
Tanaka et al. ^[23]	2019	HCC	AR + nAR	117	117	193	314	0.5	3.5	0.031	0.9	3.4	0.370	1.6	5.1	0.042	1.7	1.7	1.000
Onoe et al. ^[24]	2020	rHCC	AR + nAR	30	42			0.0	2.4	NA				6.7	2.4	NA			
Shirai et al. ^[25]	2022	HCC	AR + nAR	252	194	100	100	NA	NA	NA	1.0	2.0	0.568	NA	NA	NA	1.0	6.0	0.091
Bao et al. ^[26]	2022	rHCC	AR + nAR	30	22	19	19	3.3	0.0	0.577	5.3	0.0	0.311	NA	NA	NA	NA	NA	NA
Monden et al. ^[27]	2022	HCC	AR + nAR	133	145	75	75	NA	NA	NA	NA	NA	NA	NA	NA	NA	1.3	0.0	NA
Pu et al. ^[28]	2023	HCC	AR + nAR	845	3031	845	845	1.8	6.3	<0.001	1.8	8.4	<0.001	1.8	4.6	<0.001	1.8	5.2	<0.001
Shinkawa et al. ^[29]	2024	HCC	nAR	193	123	304	304	NA	NA	NA	1.8	7.6	0.025	NA	NA	NA	6.4	9.7	0.380
Maeda	2024	All	AR	95	121			1.1	7.4	0.045				5.3	5.8	1.000			

Table 9. Comparison the incidence of SSIs between OLRs and LLRs on the previous reports

LLRs: Laparoscopic liver resections; OLRs: open liver resections; ISSIs: incisional SSI; OSSIs: organ/space SSI; NA: not available; HCC: hepatocellular carcinoma; rHCC: recurrent hepatocellular carcinoma; AR: anatomical resection; nAR: non anatomical resection.

future.

DECLARATIONS

Authors' contributions

Made substantial contributions to conception and design of the study and performed data acquisition, analysis and interpretation: Maeda T, Otsuka Y Performed data acquisition and provided administrative, technical, and material support: Ito Y, Hosaka H, Yamazaki S, Kajiwara Y, Onishi K, Okada R, Matsumoto Y, Kimura K, Ishii J, Tsuchiya M

Availability of data and materials

The raw data supporting the conclusions of this article will be made available by the authors.

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Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

This study was reviewed and approved (No. M22194 21242) by the ethics committee of Toho University Omori Medical Center, Japan. The details about the study were disclosed on the web page of Toho University Omori Medical Center (https://www.lab.toho-u.ac.jp/med/omori/gastro_surgery/patient/ crl2160000000ku-att/20230214_M22194_21242.pdf), and the potential participants were given the opportunity to opt-out. Informed consent from participants in the study has been waived by the ethics committee of Toho University Omori Medical Center due to the retrospective study.

Consent for publication

Not applicable.

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