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Comparison Between Outcomes of Laparoscopic Cholecystectomy in Patients With Liver Cirrhosis or With Normal Liver Function

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Objective and Background: The safety of laparoscopic cholecystectomy in patients with Child–Pugh A and B cirrhosis is well-established, but perioperative complications are frequently observed in patients with cirrhosis. Technical challenges of this operation in cirrhotic patients remain in need of resolution.

Methods: Twenty-one patients preoperatively diagnosed as having cirrhosis underwent laparoscopic cholecystectomy mainly using the French approach and were retrospectively reviewed. Their clinicopathologic characteristics were compared with 74 continuous patients with gallstone but no cirrhosis who underwent laparoscopic cholecystectomy using the American approach.

Results: Most cirrhotic patients (19/21, 90.5%) had a chronic liver disease such as hepatitis B/C, alcoholic hepatitis, or primary biliary cholangitis. On imaging, the Chilaiditi sign and gallbladder bed pocket score, previously proposed to be informative in these patients, were significantly higher in the cirrhosis group than in the no cirrhosis group. Although the Child–Pugh score was higher in patients with cirrhosis, the model for end-stage liver disease (MELD) score was similar for the 2 groups. There were no differences in the operation time or the amount of intraoperative blood transfused. Postoperative hospital stay and postoperative morbidity rates were significantly greater in the cirrhosis group, although severe complications with a Clavien–Dindo score $\geq$ IIIa occurred in only 1 patient in each group.

Conclusions: The safety of laparoscopic cholecystectomy in cirrhotic patients was confirmed. Because the gallbladder is completely covered in patients with cirrhosis, the

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French style approach, which enables surgeons to more easily access the gallbladder pocket, is assumed to be one of the operative options.

Key words: Laparoscopic cholecystectomy – Cirrhosis – French approach

Liver cirrhosis is one of the most serious risk factors for intra- and postoperative morbidity and mortality after abdominal surgery: in patients with cirrhosis, 30-day mortality rates were reported as 7%–20%.[1–3] Studies suggested that the Child–Pugh score, the model for end-stage liver disease (MELD) score, and the amount of intraoperative blood transfused are predictive factors for complications and prognosis in cirrhotic patients.

Laparoscopic surgery for cholecystectomy has been shown to have advantages over open surgery regarding intraoperative bleeding,[4] length of hospital stay, time to go back to a full diet, and postoperative complications.[5–7] Laparoscopic cholecystectomy is therefore now accepted as the standard procedure for patients with a benign disease of the gallbladder including acute/chronic cholecystitis and gallbladder polyps. Even in patients with cirrhosis (Child–Pugh A and B), laparoscopic cholecystectomy was reported to be associated with less blood loss, fewer postoperative complications, and shorter hospital stay than open cholecystectomy.[8]

Although bleeding, peri-hepatic adhesion caused by hepatitis and deformed liver can be intraoperatively problematic, few studies have been conducted to develop technical improvements. To address this, the aims of the present study were to assess clinical features associated with laparoscopic cholecystectomy in cirrhotic compared with noncirrhotic patients, and identify technical challenges in the former.

Materials and Methods

Patients

This retrospective study included patients with cirrhosis who underwent laparoscopic cholecystectomy between 1999 and 2015 (designated the cirrhosis group), and patients with normal livers who underwent laparoscopic cholecystectomy for cholelithiasis in 2014 and 2015 (the no cirrhosis group) at Kobe University Hospital. Patients with Child–Pugh C cirrhosis were excluded from the study because they are not candidates for laparoscopic surgery.[9]

Cirrhosis was diagnosed based on the following factors and was confirmed by intraoperative observation (Fig. 1): the presence of concomitant chronic liver disease and preoperative imaging showing irregularities of the liver surface, atrophy of the right lobe, and hypertrophy of the left lobe.[10] Indications for surgery in the cirrhosis group were symptomatic cholelithiasis (15 patients) and prevention of gallbladder necrosis after transarterial embolization (TAE) for hepatocellular carcinoma in the remaining 6. In the no cirrhosis group, all patients underwent surgery for symptomatic cholelithiasis. All operations were elective in both groups.

Preoperative assessment and surgical procedures

Prior to surgery, multidetector-row computed tomography (CT) and magnetic resonance imaging (MRI) were performed to assess the presence or absence of gallstones and common duct stones, location of gallstones, and anomalies of the biliary system. When common duct stones were identified, they were preoperatively removed by endoscopic retrograde cholangiography.

In our institution, the American approach is the common procedure,[11] and the French approach is considered for cirrhotic patients on a case-by-case basis. We believe that the French approach has a technical advantage in cirrhotic patients with liver deformation resulting in deep burial of the gallbladder, as described as follows. Intraoperative cholangiography is a routine procedure to detect choledocolithiasis in patients with cholelithiasis, under consideration of the patient's general condition. Before resecting the cystic duct, a catheter is inserted into it and contrast material injected to visualize the bile duct.[11]

Assessment variables

In this study, we surveyed patient data in both groups including imaging findings, the gallbladder bed pocket score (GBPS), and operation-associated variables. We previously described the GBPS, defined as the maximum ratio between the height and width of the gallbladder bed measured on one representative CT or MRI slice (Fig. 2). Because this

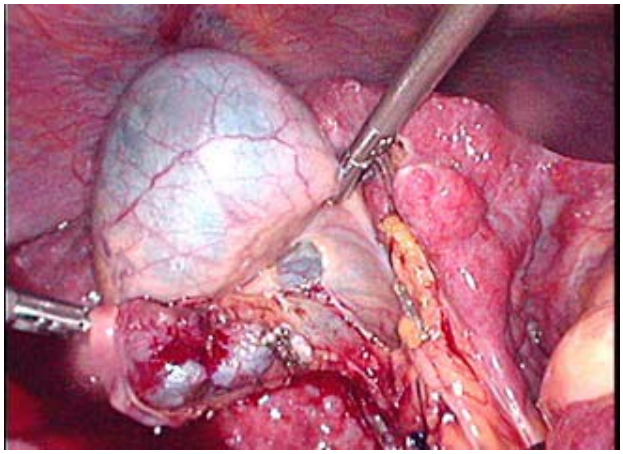

Fig. 1 Intraoperative observation of a cirrhotic patient. Liver deformation and a buried gallbladder were observed.

score reflects the degree to which the gallbladder is buried deep within the gallbladder bed and the difficulty of separating it from the gallbladder bed,[12] we predicted that the cirrhosis group would have a higher GBPS.

Statistical analysis

Continuous variables are shown as median±SD, and were assessed by the unpaired *t* test and the Chi-square test. All categoric results are reported as a number and percentage. The continuous and categoric variables in the cirrhosis and no cirrhosis groups were compared using Fisher's exact test. JMP 12 statistical software (SAS Institute Incorporated, Cary, North Carolina) was used for the statistical analyses.

Fig. 2 Gallbladder bed pocket score (GBPS). The GBPS reflects the degree to which the gallbladder is buried. (GBPS = b/a).

Ethics

This study was approved by the Ethics Committee of Kobe University Graduate School of Medicine (#170084).

Results

Patient characteristics and preoperative data

Twenty-one patients with cirrhosis and 74 patients without met the study criteria and were enrolled. There were 54 men and 41 women with a mean age of 63.6 years. All patients underwent elective laparoscopic cholecystectomy.

Table 1 shows the characteristics of the patients in the cirrhosis and no cirrhosis groups. There were no differences in age and gender between the two. Although none of the patients without cirrhosis had chronic liver disease, 90.5% (19/21) of cirrhotic patients had hepatitis B (n = 3), hepatitis C (n = 9), alcoholic hepatitis (n = 5), primary biliary cholangitis (n = 1), or hepatitis of unknown etiology (n=1). On imaging, the Chilaiditi sign, indicating left liver lobe atrophy,[13] was observed in only 3 patients in the cirrhosis group ($P = 0.002$). Child–Pugh B was seen in 5 patients in the cirrhosis group (5/21, 24%) and in 1 patient in the no cirrhosis group (1/74, 1%); the 1 patient in the no cirrhosis group who had Child–Pugh B was an 80-year-old man who had low serum albumin and slightly elevated serum bilirubin. The MELD score was similar in the 2 groups. The indocyanine green retention rate at 15 minutes (ICG–15R) was 20.3 ± 12.2%, as measured in 17 of the 21 patients with cirrhosis.

Gallbladder Bed Pocket Score

The GBPS was significantly higher in the cirrhosis than in the no cirrhosis group (0.47 ± 0.14 versus 0.28 ± 0.11, $P < 0.01$) (Fig. 3). In this cohort, although patients with higher GBPS had greater intraoperative blood loss (correlation coefficient 0.25, $P = 0.02$), GBPS was not correlated with operation time. Higher GBPS was associated with a higher rate of intraoperative perforation of the gallbladder ($P = 0.04$). Among the cirrhotic patients, there were no differences in GBPS according to the cause of cirrhosis, Child–Pugh classification or MELD score.

Table 1 Patients' characteristics

	Cirrhosis (n = 21)	No cirrhosis (n = 74)	*P*
Age (yr)	67 ± 2.9	65.5 ± 1.5	0.11
Gender			0.64
M	11 (52%)	43 (58%)	
F	10 (48%)	31 (42%)	
Chronic liver disease			
B	3	0	
C	9		
alcohol	5		
PBC	1		
Chilaiditi sign	3 (15%)	0	0.002
GBPS	0.47 ± 0.14	0.28 ± 0.11	<0.01
Child–Pugh			<0.01
A	16 (76%)	73 (99%)	
B	5 (24%)	1 (1%)	
Child score			<0.01
5	6	63	
6	10	10	
7	4	1	
8	1	0	
MELD score	6.5 ± 1.6	7.0 ± 2.7	0.52
Blood platelet ($10^4/\mu L$)	12.8 ± 6.2	23.3 ± 7.6	<0.01
AST (IU/L)	43.3 ± 4.3	24.1 ± 2.3	<0.01
ALT (IU/l)	31.8 ± 3.8	24.4 ± 2.0	0.09
ALP (IU/l)	378.0 ± 132.1	292.0 ± 152.5	0.02
γ-GTP (IU/l)	89.4 ± 67.8	92.3 ± 143.8	0.93
Total Bilirubin (mg/dL)	0.86 ± 0.09	0.81 ± 0.05	0.57
ICG15R (%)	20.3 ± 12.2*	-	-

ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transaminase; GBPS, gallbladder bed pocket score; ICG15R, indocyanine green retention rate after 15 minutes; MELD, model for end-stage liver disease; PBC, primary biliary cirrhosis; γ-GTP: gamma-glutamyl transpeptidase.

*The ICG15R was measured in 17 of the 21 cirrhosis patients. The mean ± SD in the 17 patients is shown.

Operation-associated variables

Although there were no significant differences in the operation time or the amount of intraoperative blood transfused, the postoperative hospital stay was significantly longer and the postoperative morbidity rate significantly higher in the cirrhosis group (8.0 ± 4.0 versus 5.3 ± 3.5, $P < 0.01$: 29% versus 4%, $P < 0.01$, respectively) (Table 2). Major complications (> Clavien–Dindo III) were observed in 1 case in each group; 1 patient in the cirrhosis group had postoperative bleeding requiring transabdominal drainage, and 1 patient in the no cirrhosis group had wound dehiscence. Postoperative accumulation of ascites was observed in 4 patients in the cirrhosis group (Table 3). Intraoperative gallbladder perforation tended to be more frequent in the cirrhosis group (48% versus 26%, $P = 0.06$). The conversion rate to open surgery was not significantly different in the two groups [3/21, 14% (2 cases of severe adhesion and 1 case of presence of hepatocellular carcinoma close to cystic duct) in the

Table 2 Operation-associated variables

	Cirrhosis (n = 21)	No cirrhosis (n = 74)	*P*
French/American	14/7	0/74	<0.01
Operation time (min)	159.8 ± 11.2	146.9 ± 5.9	0.31
Bleeding (mL)	63.3 ± 120.0	28.2 ± 120.6	0.24
Hospital stay (days)	8.0 ± 4.0	5.3 ± 3.5	<0.01
Morbidity	6 (29%)	3 (4%)	<0.01
Perforation of gallbladder	10 (48%)	19 (26%)	0.06
Conversion to open surgery	3 (14%)	6 (9%)	0.41
Cholangiography	4 (19%)	55 (74%)	<0.01

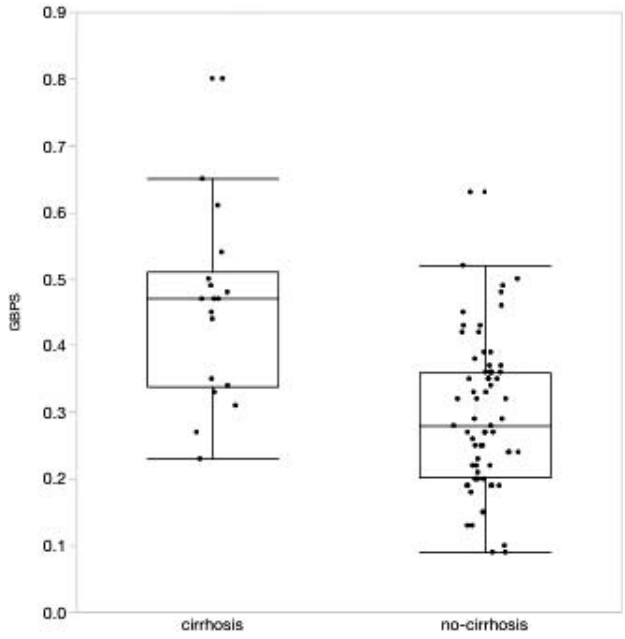

Fig. 3 Comparison of the GBPS between the cirrhotic and no-cirrhotic patients. The 5 horizontal lines represent the maximum value, 75th percentile, median, 25th percentile, and minimum value. There are 2 outliers in each group.

cirrhosis group, and 6/74, 8% (4 cases of severe adhesion, 1 case of uncontrollable bleeding, and 1 case of bile duct injury) in the no cirrhosis group]. Intraoperative cholangiography was performed in 19% of the cases in the cirrhosis group and in 74% in the no cirrhosis group ($P < 0.01$).

Discussion

The results of this study confirmed that laparoscopic cholecystectomy could be safely performed in patients with the cirrhosis. In a previous study, the mortality rate for patients with cirrhosis who underwent laparoscopic cholecystectomy was 0.8%;[14] there were no in-hospital deaths in either group in the present study. The postoperative complication rate in the cirrhosis group (29%) was similar to other reported studies (18–23),[3,8,14] although postoperative complications were more frequent in the cirrhosis than in the no cirrhosis group. As expected, the most common complication in the cirrhotic group was the accumulation of ascites. All of these patients were treated by diuretics or were observed without treatment, which is defined as Clavien–Dindo I. Postoperative bleeding was found only in the cirrhosis group, and 1 patient needed transabdominal drainage. This

Table 3 Postoperative complications

	Cirrhosis (n = 21)	No cirrhosis (n = 74)
Ascites*	4	0
Impaired liver function	1	1
Impaired renal function	0	1
Bleeding	1	0
Wound dehiscence	0	1
Death	0	0

*All cases were Clavien–Dindo I.

patient had alcoholic liver cirrhosis (Child–Pugh A), with a very high GBPS (0.8) and intraoperative major bleeding (200 mL).

Here, we have highlighted the usefulness of the French approach in cirrhotic patients. The GBPS, which reflects the degree of difficulty in separating the gallbladder from its bed,[12] was significantly higher in the cirrhosis group. The GBPS clearly showed that the cirrhotic gallbladder was more deeply buried in the liver. Thus, the French approach could more easily handle bleeding during gallbladder separation, because vertical compression can be more readily achieved. In the American technique, the surgeon has to approach the gallbladder bed horizontally from the trocar in the epigastric region, and the surgical assistant cannot easily retract the liver. This is especially the case in cirrhotic patients because of liver deformation and fibrotic hardening, which are the main technical challenges in separating the gallbladder from its bed. The French technique enables a more vertical approach from the port inserted from the left lateral region, and may lead to easier gallbladder separation, contributing to reduced operating time, blood loss, and gallbladder perforation rate. However, when perioperative factors including operation time, bleeding, conversion to open surgery, gallbladder perforation and morbidity, were compared between the American and French styles in cirrhotic patients, no significant differences emerged. This may have been due to the small sample size, and further investigation is needed.

In the present study, the rate of intraoperative gallbladder perforation was quite high (48%). Intraoperative gallbladder perforation is a risk factor for postoperative infectious complications and tumor seeding.[15,16] Previous studies reported an intraoperative perforation rate of 9-29% in patients with normal livers.[17,18] Given a higher perforation rate in the cirrhosis group, laparoscopic

cholecystectomy for cirrhotic patients with polypoid disease should be considered carefully.

The rate of conversion to open surgery was no different between the 2 groups (14% in cirrhosis group, 9% in the no cirrhosis group, $P = 0.41$), similar to findings in other studies (5%∼16%).[19–22] The reasons for requiring open surgery were mainly intraabdominal adhesion caused by inflammation including cholecystitis and gallstone pancreatitis (n = 5). Although patients with cirrhosis generally have a lower number of blood platelets and coagulopathy, there were no cases of intraoperative uncontrollable bleeding in either group in the present study. The use not only of an electric scalpel but also ultrasonic or bipolar coagulation may have contributed to the reduction in intra- and postoperative bleeding.

The present study has some limitations: (1) The cirrhosis group was composed of cases from between 1999 and 2015 but the no cirrhosis group was from 2014 and 2015. Considering progress in technique and surgical devices, postoperative factors in the 2 groups may not be identical; (2) Although cholecystectomy for cirrhotic patients was mainly performed by experienced surgeons, noncirrhotic patients were mostly operated on by junior surgeons.

In conclusion, laparoscopic cholecystectomy is feasible in cirrhotic patients (Child–Pugh A/B) even though the gallbladder is deeply buried in its bed (high GBPS). The French style approach may be preferable for separating the gallbladder from its bed in cirrhotic patients.

Acknowledgments

Following are the author contributions. M. Akita was responsible for study design and interpretation of data, as well as drafting of the manuscript. K. Ueno, K. Shinozaki, H. Toyama, M. Kido, and T. Fukumoto were responsible for analysis of clinical features, interpretation of data, and drafting of the manuscript. T. Ajiki handled study supervision and drafting of the manuscript. All the authors have no financial interests or other potential conflicts of interest.

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