

Risk Factors of Postoperative Complications in Laparoscopic Cholecystectomy for Acute Cholecystitis

Manabu Sato, MD, PhD, Koujin Endo, MD, PhD, Akihiko Harada, MD, PhD, Masahiro Shijo, MD

ABSTRACT

Introduction: There are often cases with postoperative complications after laparoscopic cholecystectomy (LC), resulting in severe consequences. This study aimed to identify potential risk factors of postoperative complications in cases of LC for acute cholecystitis.

Materials and Methods: A total of 423 patients with cholecystitis underwent LC. We divided the patients into two groups: group without postoperative complications (Group A) and group with postoperative complications (Group B). Pre-operative findings, surgical findings, and the methods for evaluating the risk of peri-operative complications were compared between the two groups with a univariate analysis. Independent risk factors of postoperative complications were then evaluated in a multivariate analysis with the factors shown to be statistically significant in the univariate analysis.

Results: A Physiological and Operative severity Score for enUmeration of Mortality and morbidity (POSSUM) of \geq 48.3 and moderate or severe cholecystitis were independent risk factors of postoperative complications in LC.

Conclusions: This study indicated that POSSUM morbidity and moderate or severe cholecystitis were potential risk factors of postoperative complications. The pre-operative management of the general condition and cholecystitis using antibiotics, infusion, percutaneous transhepatic gallbladder drainage, and other approaches may be significant for the prevention of postoperative complications. Once the POSSUM morbidity reaches the threshold after LC, postoperative management becomes difficult, so

Department of Surgery, JCHO Sendai South Hospital, Sendai, Japan (all authors) Disclosure: none.

Funding/Financial support: none.

Conflicts of Interest: The authors declare no conflict of interest.

Informed consent: Dr. Manabu Sato declares that written informed consent was obtained from the patient/s for publication of this study/report and any accompanying images.

DOI: 10.4293/JSLS.2020.00049

strict control of the general condition should be performed.

Key Words: Cholecystitis, Laparoscopic Cholecystectomy, Postoperative Complications, Risk Factors, Scoring Methods.

INTRODUCTION

Laparoscopic cholecystectomy (LC) is an important approach for treating acute cholecystitis. The Tokyo Guidelines 2018 (TG18) proposed that after the cholecystitis severity has been assessed as mild or moderate, LC should be performed soon after the onset if the general condition of the patient suggests they are able to withstand surgery.^{1–3} In cases of severe acute cholecystitis, the patient's overall status is significantly deteriorated, and treatment should be selected based on a full and careful consideration of the patient's background characteristics, including complications and comorbidities.² Every effort should be made to avoid risks in order to ensure LC is performed safely.

The feasibility and safety of LC for acute cholecystitis in early management have been discussed in several studies, including the short postoperative stay and low morbidity and mortality as medical and economic benefits.4-6 However, there are often cases with postoperative infectious and noninfectious complications after LC for acute cholecystitis, resulting in adverse economic and medical consequences.⁶⁻⁹ It may therefore be useful to assess the risk of early postoperative complications of LC for acute cholecystitis using pre- and intra-operative data. The predictors of postoperative complications after LC discussed in past studies have included the age, gender, body mass index (BMI), total bilirubin, white blood cell (WBC) count, C-reactive protein (CRP) level, renal function, and ultrasound findings.^{4,6–10} In the TG18, early LC is recommended if a patient's general status is evaluated as good according to the criteria of the Charlson comorbidity index (CCI) and American Society of Anesthesiologists (ASA).¹¹ The objective of applying these criteria and the severity grade of acute cholecystitis is the safe management of LC.

Address correspondence to: Dr. Manabu Sato, Department of Surgery, JCHO Sendai South Hospital, 143, Aza-Maeoki, Nakada-machi, Taihaku-ku, Sendai, Miyagi 981-1103, Japan, Telephone: +81-22-306-1711, Fax: +81-22-306-1712, E-mail: mana0609@dg8.so-net.ne.jp

^{© 2020} by JSLS, Journal of the Society of Laparoscopic & Robotic Surgeons. Published by the Society of Laparoendoscopic & Robotic Surgeons, Inc.

Therefore, these scoring systems may be useful for evaluating the risk of early postoperative complications after LC.

However, few studies have evaluated the potential risk factors of early postoperative complications after LC using pre-, intra-, and postoperative factors of the general condition or data, and few scoring systems of risk factors for operative complications have been developed. The present study; therefore, aimed to identify potential risk factors for postoperative complications in LC according to the perioperative condition and scoring systems for postoperative complications.

MATERIALS AND METHODS

A total of 1026 patients underwent LC for cholecystolithasis or acute cholecystitis from January 2005 to December 2018. We defined "acute cholecystitis" based on the diagnostic criteria for acute cholecystitis in the TG18: (A) local signs of inflammation, including (1) Murphy's sign and (2) right upper abdominal quadrant mass/pain/tenderness; (B) systemic signs of inflammation, including (1) a fever, (2) elevated CRP level, and (3) elevated WBC count; (C) imaging findings characteristic of acute cholecystitis, with a definite diagnosis of acute cholecystitis set as one item in A + one item in B + C. In the present study, "acute cholecystitis" was defined based on the definite diagnosis criteria, which included an elevated CRP level of $\geq 0.2 \text{ mg/}$ dl and elevated WBC count of $\geq 9,000$.

We performed pre-operative biliary tract evaluations for all patients of cholecystitis with magnetic resonance cholangiopancreatography or drip infusion cholangiographic computed tomography. Four hundred twenty-three patients were registered in this study. One hundred thirtynine patients who underwent cholecystectomy with a stone of the common bile duct were excluded. Of the remaining 887 patients, 437 without cholecystitis were excluded. The patients treated with initial open cholecystectomy were also excluded, but those who underwent conversion from laparoscopic to open cholecystectomy were included in this study. Laparoscopic cholecystectomy was performed by the four-port technique. Achievement of clinical view of safety (CVS) was set as a general rule in LC, and if we could not achieve CVS, LC was converted to open cholecystectomy.

The background factors in LC (sex, age, comorbidity, grade of cholecystitis, pre-operative drainage of gallbladder, timing of LC, waiting time from onset to LC, and morbidity and mortality) were obtained from our database.

We assessed the severity of postoperative complications according to the Clavien-Dindo classification. In our study, the patients were divided into two groups: those with Grade I or no complications (Group A) and those with Grade II or more severe postoperative complications (Group B) with regard to independent risk factors for morbidity. Surgical factors (severity of cholecystitis, external gallbladder drainage, cholecystectomy within 72 h from the onset, blood loss, operating time) and methods for evaluating the risk of perioperative complications were compared between the two groups with a univariate analysis. Independent risk factors of postoperative complications were then evaluated in a multivariate analysis using the factors extracted from the univariate analysis.

In the analysis of the independent risk factors of postoperative morbidity and mortality, several scoring systems for predicting the postoperative morbidity and mortality were used. The ASA and Eastern Cooperative Oncology Group Performance Status were measures of the patients'

	Table 1.
	Charlson Comorbidity Index
Assigned Weight Diseases	ts for
1	Myocardial infarction
	Congestive heart failure
	Peripheral vascular disease
	Cerebrovascular disease
	Dementia
	Chronic pulmonary disease
	Connective tissue disease
	Peptic ulcer disease
	Mild liver disease
	Diabetes mellitus
2	Hemiplegia
	Moderate or severe chronic kidney disease
	Diabetes mellitus with end-organ damage
	Any solid tumor
	Leukemia
	Malignant lymphoma
3	Moderate or severe liver disease
6	Metastatic solid tumor
	Acquired immune deficiency syndrome

	Dhuci	ological and Oporativo Sovorit	Table 2. y Score for enUmeration of Mortality Sco	ring System
The Equations for 1		$\ln [R / (1-R)] = -5.91 + (0.16)$		ring System
PS				
	1	2	4	8
Age (years)	≤ 60	61–70	≥ 71	
Cardiac signs, chest radiograph	No failure	Diuretic, digoxin, antiangi- nal, or hypertensive therapy	Peripheral edema, warfarin therapy, borderline cardiomegaly	Raised jugular venouspressure, cardiomegaly
Respiratory history	No dyspnea	Dyspnoea on exertion, Mild COPD	Limiting dyspnoea, Moderate COPD	Dyspnea on rest, Fibrosis or consolidation
Systolic blood pressure (mmHg)	110–130	100–109, 131–170	90–99, ≧ 171	≤ 89
Pulse rate (Beats/ min)	50-80	40-49, 81-100	101–120	$\leq 39, \geq 121$
Glasgow coma score	15	12–14	9–11	≤ 8
Hemoglobin (g/ 100 ml)	13–16	11.5–12.9, 16.1–17.0	10.0–11.4, 17.1–18.0	$\leq 9.9, \geq 18.1$
White cell count (nmol/mm ³)	4,000– 10,000	3,100-4,00010,100-20,000	$\leq 3,000, \geq 20,100$	
Plasma urea (nmol/L)	≦ 7.5	7.6–10.0	10.1–15.0	≧ 15.1
Plasma sodium (nmol/L)	≧ 136	131–135	126–130	≤ 125
Plasma potassium (nmol/L)	3.5–5.0	3.2–3.4, 5.1–5.3	2.9–3.1, 5.4–5.9	$\leq 2.8, \geq 6.0$
Electrocardiogram	Normal		Atrial fibrillation (rate 60-90)	Any other abnormalrhythm or Q waves or ST/T wave changes
OS				
	1	2	4	8
Operation grade	Minor	Moderate	Major	Major +
Multiple procedures	1		2	>2
Blood loss (ml)	≤ 100	101-500	501-999	≥ 1000
Peritoneal soiling	None	Minor (serous fluid)	Local pus	Free bowel content, pus, or blood
Malignancy	None	Primary only	Nodal metastases	Distant metastases
Mode of surgery	Elective		Emergency resuscitation of > 2h possible, Operation < 24h after admission	Emergency (immediate surgery < 2h needed)

POSSUM, Physiological and Operative severity Score for enUmeration of Mortality; R, morbidity; PS, physiological score; OS, operative severity score; COPD, chronic obstructive pulmonary disorder.

functional status and general health.^{12,13} The CCI is used to categorize a patient's comorbidities based on the International Classification of Diseases codes^{2,14} (**Table 1**). The Physiological and Operative severity Score for enUmeration of Mortality and morbidity (POSSUM) is a simple scoring system previously validated for patients

undergoing surgical treatment that estimates the risk of postoperative complications and death.¹⁵ The POSSUM score involves a physiological score (PS), which contains 12 pre-operative physiological variables, and an operative severity score (OS), which contains six operative variables (**Table 2**). The Surgical Apgar Score (SAS) provides

Table 3. Surgical Apgar Score						
Points	0	1	2	3	4	
Estimated blood loss (ml)	> 1000	601-1000	101-600	< 100		
Lowest mean arterial pressure (mmHg)	> 40	40-54	55-69	≥ 70		
Lowest heart rate (/min)	> 85	76–85	66–75	56-65	55 ≧	

surgeons with a simple, objective, and direct rating of the operative performance and risk (**Table 3**).

Continuous parameters were expressed as the median and interquartile range. All statistical analyses were performed with R 3.5.2 (The R Foundation for Statistical Computing). The threshold of continuous data was detected with a receiver operating characteristic (ROC) curve. Fisher's exact test was used for the analysis of categorical data. A logistic regression analysis was used for the multivariate analysis to identify the independent postoperative risk factors.

This study was conducted with the approval of the JCHO Sendai South Hospital Ethics Committee. (2019-11-1)

RESULTS

A total of 423 cholecystitis patients were treated with laparoscopic cholecystectomy during the 14-year study period. The patients were 232 males (54.8%) and 191 females (45.2%), 19–95 years old (median, 65 years old), and 263 (62.2%) were \geq 60 years of age. A total of 268 patients (63.4%) had comorbidities, including hypertension, cardiovascular disease, diabetes mellitus, and neurogenic and mental disorders, but the remaining 155 patients (36.6%) had no comorbidities.

According to the severity grading of the TG18, the severity of 354 patients (83.7%) was Grade I (mild), that of 60 (14.2%) was Grade II (moderate), and that of 9 (2.1%) was Grade III (severe). External gallbladder drainage before cholecystectomy was performed for 19 patients (4.5%). Urgent laparoscopic cholecystectomy within 72 h from the onset was performed for 74 patients (17.5%). Conversion from laparoscopic to open cholecystectomy was needed in 33 patients (7.8%) (**Table 4**). The causes of moderate and severe cholecystitis are shown in **Table 5**.

Eighteen patients (4.3%) experienced Grade \geq 2 postoperative complications. Of these, surgical infectious complications included postoperative bile leak in one case, and subhepatic abscess in one case. Pulmonary complications were noted in five cases and cardiac complications in three cases.

Postoperative cholangitis occurred in three cases (**Table 6**). There were two cases of in-hospital deaths: one due to acute postoperative heart failure the other due to exacerbation of liver failure caused by alcoholic liver cirrhosis (**Table 7**). This analysis indicated that the cause of Grade III (severe) cholecystitis in Group A was only a low platelet count, whereas the causes in Group B included cardiovascular dysfunction and renal dysfunction.

In accordance with our analysis of postoperative complications, a univariate analysis showed statistically significant differences between Groups A and B in preoperative factors (Grade II [moderate] or Grade III [severe] cholecystitis), surgical factors (conversion to open cholecystectomy, cholecystectomy within 72 h from the onset), and all methodologies for evaluating postoperative risk factors (**Table 7**). We then performed a logistic regression analysis on the factors that were significantly different in the univariate analysis. The multivariate analysis revealed that the occurrence of Grade II (moderate) or Grade III (severe) cholecystitis and a POSSUM morbidity of \geq 48.3 were independent risk factors of postoperative complications. The odds ratio of Grade II (moderate) or Grade III (severe) cholecystitis was 6.32, while that of POSSUM morbidity was 22.60 (Table 8).

DISCUSSION

We investigated the potential risk factors of early postoperative complications in LC. In the study period, 18 patients (4.3%) suffered from early postoperative complications of Grade II or worse. Surgical complications due to the surgical technique only occurred in two cases (bile leak and subhepatic abscess). Postoperative complications in nine cases were attributed to deterioration of the general condition (due to cardiac, pulmonary, or neurogenic diseases). The postoperative morbidity rate of 4.3% was less than or equal to the value in other studies, and the mortality was very low.^{5,10,16-19} Postoperative complications due to the

Table 4. Patient Characteristics, Severity Grad Intraoperative Findings, and Postopera Laparoscopic Cholecystectomy for	ative Complica	tions of
	n	%
Gender		
Male	232	54.8
Female	191	45.2
Age		
< 40	46	10.9
40-49	43	10.2
50–59	71	16.8
60–69	99	23.4
70–79	99	23.4
80–89	60	14.2
> 90	5	1.2
Comorbidity		
Hypertension	179	42.3
Cardiovascular	44	10.4
Respiratory	22	5.2
Neurogenic and mental disorder	45	10.6
Diabetes mellitus	73	17.3
Other	77	18.2
None	155	36.6
Severity grade of cholecystitis		0
Grade I (mild)	354	83.7
Grade II (moderate)	60	14.2
Grade III (severe)	9	2.1
External gallbladder drainage	/	2.1
Yes	19	4.5
No	404	95.5
Urgent cholecystectomy	101	//./
Yes	74	17.5
No	348	82.5
Conversion to open cholecystectomy	540	02.)
Yes	33	7.8
No	390	92.2
Clavien-Dindo classification	390	92.2
No complication	388	91.8
Grade I		91.8 4.0
Grade I Grade II	17	
Grade III Grade III a	9 4	2.1
	-	0.9
Grade III b	0	0.0
Grade IV a	3	0.7
Grade IV b	0	0.0
Grade V	2	0.5
≥ Grade II	18	4.3

	Grou	up A	Group B	
	n	%	n	%
Moderate cholecystitis	48	100.0	12	100.0
WBC count > $18,000/\text{mm}^2$	20	41.6	3	25.0
Marked local inflammation	16	33.3	6	50.0
Duration of complaints > 72h	9	18.8	2	16.7
Palpable tender mass	3	6.3	1	8.3
Severe cholecystitis	6	100.0	3	100.0
Platelet count < 100,000/mm ²	6	100.0	1	33.3
Cardiovascular dysfunction	0	0.0	1	33.3
Renal dysfunction	0	0.0	1	33.3
WBC; white blood cell.				

Breakdown of Postoperative Complications in Laparoscopic Cholecystectomy for Acute Cholecystitis

	n
Surgical infectious	2
Bile leakage	1
Subhepatic abscess	1
Nonsurgical infectious	16
Paralytic ileus	3
Pulmonary	5
Cardiac	3
Cholangitis	3
Neurologic	1
Liver failure	1

surgical technique only occurred in two cases, so issues with our LC technique do not appear to be frequent. Instead, the exacerbation of the postoperative condition was the main concern in this study of complications.

Two cases had Grade V complication in our hospital. Early LC was performed within 96 h for both cases, and the general condition was not improved in either case before LC. These LC procedures were performed prior to 2013, when TG13 was published. After 2013, we initially performed general organ support and conservative therapies with infusion, antibiotics, and percutaneous transhepatic gallbladder

Table 7. Details of Two Mortality Cases					
	Case 1	Case 2			
Age	88	81			
Gender	Male	Male			
Comorbidity	Hypertension, Chronic kidney disease, Diabetes mellitus, Chronic heart failure	Hypertension, Diabetes mellitus,			
		Alcoholic liver cirrhosis			
Cholecystitis grading	Grade III	Grade III			
Gallbladder drainage	No	No			
Early cholecystectomy in 72 h	Yes	No			
Postoperative course	Acute heart failure, Ventricular fibrillation	Liver failure			
American Society of Anesthesiologists	4	4			
Charlson comorbidity index	4	4			
Eastern Cooperative Oncology Group Performance Status	3	3			
POSSUM morbidity	88.8	98.9			
Surgical Apgar Score	6	5			

drainage (PTGBD). Elective cholecystectomy was performed after the improvement of the general condition, according to the flowchart in TG13 and TG18. We have therefore not experienced any cases of postoperative death following cholecystectomy since 2013.

According to the TG18 severity grading for acute cholecystitis, the severity of 354 patients (83.7%) was Grade I (mild), that of 60 (14.2%) was Grade II (moderate), and that of 9 (2.1%) was Grade III (severe) in our database. However, Yokoe et al. reported in their Japan-Taiwan collaborative epidemiological study of AC that 2,130 patients (39.0%) were classified as Grade I (mild), 2,308 as Grade II (moderate), and 939 as Grade III (severe).²⁰ In our hospital, the rate of Grade I cholecystitis was higher than in that previous report. While the reason for this discrepancy is unclear, it may have been because our hospital was not a high-volume center for LC and did not have an emergency medical care center, so the proportion of patients with severe or moderate cholecystitis might have been relatively small. In Japan, LC is regularly performed for cholecystitis, not only at acute care centers, but also at small or midsize hospitals. The surgical technique and the methodology of perioperative care in LC are largely fixed by TG18 and the other studies. We do not believe there is any marked difference in the technique or quality of care between acute care centers and any other hospitals.

In the present study, moderate (Grade I) or severe (Grade II) cholecystitis and POSSUM morbidity were found to be independent risk factors of postoperative complications. POSSUM is a method of estimating the risk of operative complications, including factors concerning the pre- and postoperative condition and data.¹⁵ The results suggest that the high risk of postoperative complications for LC may be related to the perioperative general condition.

TG18 recommends the general condition be evaluated with the CCI and ASA, in the flowchart of initial medical treatment and organ support, but studies concerning risk factors for postoperative complications in LC have thus far been insufficient.^{11,21}

Gigar et al. reported that an ASA score > 2, conversion to open surgery, emergency surgery, acute cholecystitis, old age, and intervention time were the predictive factors with the highest risk of inducing postoperative systemic complications in their analysis of 22,953 cases from a Swiss database.²² Murphy et al. concluded that the complication rate of LC was 6.8%, and an advanced age, male gender, high CCI, comorbidities, and emergent LC were associated with postoperative complications in their nationwide inpatient sample.^{23,24} Several studies also mentioned that the age, gender, comorbidity, BMI, presence of a fever, and conversion to open cholecystectomy were independent risk factors for

Table 8.

Prevalence of Postoperative Complications and Potential Risk Factors for Postoperative Complications in Laparoscopic Cholecystectomy for Acute Cholecystitis (Univariate and Multivariate Analysis)

	Univariate Analysis		Multivariate Analysis			
	Group A	Group B	P Value	Odds ratio	95% CI	P Value
Moderate or severe cholecystitis						
Yes	54	15	< 0.001	6.32	1.00 - 39.90	0.049
No	351	3				
External gallbladder drainage						
Yes	16	2	0.175			
No	389	16				
Operation within 72 h from onset						
Yes	66	8	0.006	1.31	0.28 - 6.16	0.730
No	339	10				
Conversion to open cholecystectomy						
Yes	26	7	< 0.001	0.95	0.11 - 8.05	0.963
No	379	11				
Blood loss						
\geq 112 ml	44	10	< 0.001	2.45	0.22 – 26.8	0.463
< 112 ml	361	8				
Operating time						
\geq 117 min	155	15	< 0.001	5.28	0.88 - 31.80	0.070
< 117 min	250	3				
ECOG-PS						
≥ 3	4	3	0.002	0.06	0.00 - 8.15	0.261
< 3	401	15				
ASA						
≥ 3	0	4	< 0.001	1.10×10^{10}	$0.00 - \infty$	0.999
< 3	405	14				
CCI						
≥ 3	10	5	< 0.001	5.10	0.09 - 288.00	0.429
< 3	395	13				
POSSUM PS						
≥ 26.0	117	13	< 0.001	0.29	0.02 - 3.65	0.338
< 26.0	288	5				
POSSUM OS						
≥8	77	15	< 0.001	1.04	0.12 - 8.96	0.969
< 8	329	3				

Table 8. Continued							
	Univariate A	Univariate Analysis			Multivariate Analysis		
	Group A	Group B	P Value	Odds ratio	95% CI	P Value	
POSSUM morbidity							
≥ 48.3	36	14	< 0.001	22.60	1.46 - 350.00	0.026	
< 48.3	369	4					
SAS							
≤ 8	188	18	< 0.001	5.06×10^{7}	$0.00 - \infty$	0.992	
> 8	217	0					

ECOG-PS, Eastern Cooperative Oncology Group Performance Status; ASA, American Society of Anesthesiologists; POSSUM, Physiological and Operative severity Score for enUmeration of Mortality; PS, physiological score; OS, operative severity score; SAS, Surgical Apgar Score.

postoperative complications in LC.^{8,9,25,26} As described in these studies and TG18, the assessment of the patient's general condition, which enables the prediction of the potential for postoperative complications, was very important for the perioperative management in LC.

In the present study, LC for Grade II (moderate) or Grade III (severe) cholecystitis was also a potential risk factor for postoperative complications. The TG18 and several studies showed that the rate of postoperative complications and conversion to open cholecystectomy in LC for moderate or severe cholecystitis was higher than in LC for mild cholecystitis.^{1,25,27} Severe cholecystitis was diagnosed in three patients with complications after LC. The causal parameters for two of those cases were cardiac and renal dysfunction, while the third case had thrombocytopenia (platelet count under 100,000). While patients with severe cholecystitis due to a low platelet count can undergo LC without postoperative complications, cases of severe cholecystitis with organ dysfunction, such as cardiac and renal dysfunction, were noted only in the group with postoperative complications. Both patients with organ dysfunction died after LC. LC for acute cholecystitis with organ dysfunction can be a deadly procedure, so the general condition of the patient needs to be improved before LC is performed. As such, the ideal approach for risk management in cases of LC for severe cholecystitis patients with organ failure should be differentiated from that in patients being treated for severe cholecystitis with a low platelet count.

Given the present findings of POSSUM morbidity and severity of cholecystitis as potential risk factors, these factors may be used to predict and prevent postoperative complications. The prevention of postoperative complications using these factors is particularly important. There are several methods of improving the preoperative condition in cases of cholecystitis. The TG18 recommended antimicrobial therapy and PTGBD be performed for acute cholecystitis patients with a high surgical risk as an alternative to urgent LC.²⁸ Indeed, the pre-operative use of antibiotics for conservative therapy followed by cholecystectomy is reported to be quite effective.²⁹ PTGBD is a method of improving acute cholecystitis, and its therapeutic role in patients with severe or moderate cholecystitis has been discussed in several studies.^{27,29}

The present findings showed that PTGBD was performed for only 4.5% of patients with cholecystitis, and urgent LC in 72 h was performed for only 17.5% of cases. TG18 recommended early LC for Grade I (mild) cholecystitis, and antibiotics and general supportive care initially for Grade II (moderate) cholecystitis, followed by early or elective LC.¹¹ Our study showed that the rate of LC within 72 h from the onset of cholecystitis in Group B was higher than that in Group A. This result, which contrasts with that from the TG18 recommendation of early LC, suggests that conservative treatments for cholecystitis followed by elective LC might not increase complications after LC. LC was not performed for the remaining 78% within 72 h from the onset because many patients did not visit our hospital within 72 h from the onset due to the mild nature of their symptoms, or they had already received conservative treatments at other institutes before their arrival. In addition, our hospital did not have a system for performing emergency operations, so conservative treatments were required before LC could be performed. Our hospital treats many older patients with cholecystitis and accompanying comorbidities. Early LC for older patients without an assessment of the general condition can be dangerous due to the risk of deterioration of the comorbidities and general condition after LC. For these patients, elective LC followed by an adequate assessment of comorbidities is suitable.

While preoperative antibiotics and PTGBD may be useful for preventing postoperative complication, other methods of improving the preoperative condition have rarely been discussed. The POSSUM morbidity score involves the PS, which contains 12 pre-operative physiological variables, and the OS, which contains six operative variables.¹⁵ The PS and OS may be targets for improving the conditions in patients undergoing LC. In the PS of POSSUM, the parameters of hemoglobin, WBC count, urea, sodium, and potassium can be easily improved before LC with appropriate fluid replacement and antibiotics. However, no effective methods for improving the factors associated with the OS have yet been established for LC. Reducing blood loss during LC may be the only viable method, but its effect may be negligible because of the generally small amount of bleeding in LC.

The POSSUM morbidity includes both the pre- and intraoperative condition. Therefore, the pre-operative prediction of postoperative complications in LC might not be feasible. The POSSUM PS reflects the pre-operative condition of patients, so the PS score may vary widely among patients. The POSSUM OS is an intra-operative score that depends on the operative procedure, such as cholecystectomy for cholecystitis. The OS score can be predicted based in part on the severity of cholecystitis. If the POSSUM morbidity exceeds the cut-off point after LC, then the postoperative management of the patient's general condition may be challenging. Intensive medical care should therefore be carried out for patients with a high POSSUM score. Preoperative conservative treatments before LC is very important if the PS is high. Therefore, assessing the POSSUM morbidity before LC is important.

The POSSUM is used to analyze the risk of postoperative complications in many operative procedures. However, such analyses for LC have been rare. Tambyraja et al. showed that the POSSUM score performed well for predicting morbidity after LC in patients ≥ 80 years old.³⁰

In the present study, a total of 33 cases of LC were converted to open cholecystectomy during surgery in our hospital. The reason for conversion to open cholecystectomy in almost all cases was difficulty performing LC due to advanced inflammation, fibrosis, and adhesion of the gallbladder. Difficulty performing LC may lead to postoperative complications. Several studies have found that conversion to open cholecystectomy in LC was a risk factor for postoperative complications.^{7,8,22} In the present study, however, conversion to open cholecystectomy was not a risk factor of postoperative complications after LC, although why this was true was unclear. In addition, no study has yet described the usefulness of conversion to open cholecystectomy. We suspect that conversion to open cholecystectomy is not necessarily a risk factor for postoperative complications after LC, as morbidity due to the surgical technique was shown to be rare in our hospital. An appropriate conversion strategy may help prevent postoperative complications. Future reports on the appropriate timing and indications for conversion to open cholecystectomy are awaited.

Our study on the potential risk factors of postoperative complications associated with LC is expected to improve the management of the perioperative condition of such patients. However, this study has several limitations that should be considered when interpreting the results. First, this study was a retrospective study using information obtained from the database of operations in our hospital. Second, there were likely several sources of selection bias due to the exclusion of cases in which open cholecystectomy was performed from the start. These cases may have had more severe cholecystitis than those involving LC (with or without conversion). Another limitation was probably the heterogeneity of the operators, but all of the operators had seven or more years of surgical experience in our institution, so the heterogeneity was likely small.

CONCLUSION

According to the present study, POSSUM morbidity and moderate or severe cholecystitis were potential risk factors of postoperative complications. The preoperative management of the general condition and cholecystitis using antibiotics, infusion, and PTGBD may therefore help prevent postoperative complications. Once the POSSUM morbidity reaches the threshold after LC, postoperative management becomes difficult, so strict control of the general condition should be performed.

References

1. Yokoe M, Hata J, Takada T, et al. Tokyo Guidelines 2018: diagnostic criteria and severity grading of acute cholecystitis (with videos). *J Hepatobiliary Pancreat Sci.* 2018;25(1):41–54.

2. Okamoto K, Suzuki K, Takada T, et al. Tokyo Guidelines 2018: flowchart for the management of acute cholecystitis. *J Hepatobiliary Pancreat Sci.* 2018;25(1):55–72.

3. Wakabayashi G, Iwashita Y, Hibi T, et al. Tokyo Guidelines 2018: surgical management of acute cholecystitis: safe steps in laparoscopic cholecystectomy for acute cholecystitis (with videos). *J Hepatobiliary Pancreat Sci.* 2018;25(1):73–86.

4. Pessaux P, Tuech JJ, Rouge C, Duplessis R, Cervi C, Arnaud JP. Laparoscopic cholecystectomy in acute cholecystitis: a

prospective comparative study in patients with acute vs. chronic cholecystitis. *Surg Endosc.* 2000;14(4):358–361.

5. Gourgiotis S, Dimopoulos N, Germanos S, Vougas V, Alfaras P, Hadjiyannakis E. Laparoscopic cholecystectomy: a safe approach for management of acute cholecystitis. *JSLS J Soc Laparoendosc Surg.* 2007;11(2):219–224.

6. Eldar S, Sabo E, Nash E, Abrahamson J, Matter I. Laparoscopic cholecystectomy for acute cholecystitis: prospective trial. *World J Surg.* 1997;21(5):540–545.

7. Brodsky A, Matter I, Sabo E, Cohen A, Abrahamson J, Eldar S. Laparoscopic cholecystectomy for acute cholecystitis: can the need for conversion and the probability of complications be predicted? A prospective study. *Surg Endosc.* 2000;14(8):755–760.

8. Terho PM, Leppäniemi AK, Mentula PJ. Laparoscopic cholecystectomy for acute calculous cholecystitis: a retrospective study assessing risk factors for conversion and complications. *World J Emerg Surg.* 2016;11(1):54.

9. Radunovic M, Lazovic R, Popovic N, et al. Complications of laparoscopic cholecystectomy: Our experience from a retrospective analysis. *Open Access Maced J Med Sci.* 2016;4(4):641–646.

10. Suter M, Meyer A. A 10-year experience with the use of laparoscopic cholecystectomy for acute cholecystitis: is it safe?. *Surg Endosc.* 2001;15(10):1187–1192.

11. Miura F, Okamoto K, Takada T, et al. Tokyo Guidelines 2018: initial management of acute biliary infection and flowchart for acute cholangitis. *J Hepatobiliary Pancreat Sci.* 2018;25(1):31–40.

12. Owens WD, Felts JA, Spitznagel EL. ASA physical status classifications: a study of consistency of ratings. *Anesth.* 1978;49 (4):239–243.

13. Oken MM, Creech RH, Tormey DC, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. *Am J Clin Oncol.* 1982;5(6):649–655.

14. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. *J Chronic Dis.* 1987;40(5):373–383.

15. Copeland GP, Jones D, Walters M. POSSUM: a scoring system for surgical audit. *BrJ Surg.* 1991;78(3):355–360.

16. Thompson MH, Benger JR. Cholecystectomy, conversion and complications. *HPB Surg*, 2000;11(6):373–378.

17. Brazzelli M, Cruickshank M, Kilonzo M, et al. Clinical effectiveness and cost-effectiveness of cholecystectomy compared with observation/conservative management for preventing recurrent symptoms and complications in adults presenting with uncomplicated symptomatic gallstones or cholecystitis: a systematic review and economic evaluation. *Health Technol Assess.* 2014;18(55):1–101.v-vi.

18. Kais H, Hershkovitz Y, Abu-Snina Y, Chikman B, Halevy A. Different setups of laparoscopic cholecystectomy: conversion and complication rates: a retrospective cohort study. *Int J Surg.* 2014;12(12):1258–1261.

19. Hayama S, Ohtaka K, Shoji Y, et al. Risk factors for difficult laparoscopic cholecystectomy in acute cholecystitis. *JSLS*. 2016; 20(4):e2016.00065.

20. Yokoe M, Takada T, Hwang TL, et al. Descriptive review of acute cholecystitis: Japan-Taiwan collaborative epidemiological study. *J Hepatobiliary Pancreat Sci.* 2017;24(6):319–328.

21. Mayumi T, Okamoto K, Takada T, et al. Tokyo Guidelines 2018: management bundles for acute cholangitis and cholecystitis. *J Hepatobiliary Pancreat Sci.* 2018;25(1):96–100.

22. Giger UF, Michel J-M, Opitz I, et al. Risk factors for perioperative complications in patients undergoing laparoscopic cholecystectomy: analysis of 22,953 consecutive cases from the Swiss Association of Laparoscopic and Thoracoscopic Surgery Database. *J Am Coll Surg.* 2006;203(5):723–728.

23. Murphy MM, Ng S-C, Simons JP, Csikesz NG, Shah SA, Tseng JF. Predictors of major complications after laparoscopic cholecystectomy: surgeon, hospital, or patient?. *J Am Coll Surg.* 2010;211(1):73–80.

24. Murphy MM, Shah SA, Simons JP, et al. Predicting major complications after laparoscopic cholecystectomy: a simple risk score. *J Gastrointest Surg.* 2009;13(11):1929–1936.

25. Ambe PC, Christ H, Wassenberg D. Does the Tokyo guidelines predict the extent of gallbladder inflammation in patients with acute cholecystitis? A single center retrospective analysis. *BMC Gastroenterol.* 2015;15(1):142.

26. Halachmi S, DiCastro N, Matter I, et al. Laparoscopic cholecystectomy for acute cholecystitis: how do fever and leucocytosis relate to conversion and complications?. *Eur J Surg.* 2000;166(2):136–140.

27. Endo I, Takada T, Hwang T-L, et al. Optimal treatment strategy for acute cholecystitis based on predictive factors: Japan-Taiwan multicenter cohort study. *J Hepatobiliary Pancreat Sci.* 2017;24(6):346–361.

28. Gomi H, Solomkin JS, Schlossberg D, et al. Tokyo Guidelines 2018: antimicrobial therapy for acute cholangitis and cholecystitis. *J Hepatobiliary Pancreat Sci.* 2018;25(1):3–16.

29. Shinke G, Noda T, Hatano H, et al. Feasibility and safety of urgent laparoscopic cholecystectomy for acute cholecystitis after 4 days from symptom onset. *J Gastrointest Surg.* 2015;19(10):1787–1793.

30. Tambyraja AL, Kumar S, Nixon SJ. POSSUM scoring for laparoscopic cholecystectomy in the elderly. *ANZ J Surg.* 2005; 75(7):550–552.