Int Surg 2017;**102:**145–150
DOI: 10.9738/INTSURG-D-16-00014.1

Prediction of Surgical Difficulty in Laparoscopic Cholecystectomy for Acute Cholecystitis Performed Within 24 Hours After Hospital Admission

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The objective of this study was to identify preoperative factors predicting operative difficulty in patients who underwent laparoscopic cholecystectomy for acute cholecystitis within 24 hours after hospital admission. Many reports have described the superiority of performing laparoscopic cholecystectomy in the early phase of acute cholecystitis. Recently, even earlier cholecystectomy within 24 hours after hospital admission has been recommended. However, the factors that influence surgical difficulty in this patient population have not been well scrutinized. We analyzed patients who underwent laparoscopic cholecystectomy for acute cholecystitis within 24 hours of hospital presentation from 2007 to 2015. The primary outcome was the operation time. We also analyzed the amount of blood loss and the rate of conversion to open surgery. Seventy-three patients were enrolled. Mean age at surgery was 66 ± 16 years, and 52 patients were male. The mean operation time was 128 ± 59 minutes. Body mass index ≥25 kg/m^2 [odds ratio (OR) = 3.6; 95% confidence interval (CI): 1.4–30.9] and dirty fat sign on preoperative computed tomography (OR = 5.3; 95% CI: 1.0–34.2) were significantly associated with

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increased operative time. Dirty fat sign was also significantly associated with increases in the amount of blood loss and conversion rate. Surgery should be performed more carefully in patients with these risk factors in laparoscopic cholecystectomy for acute cholecystitis performed within 24 hours of hospital presentation.

Key words: **C**holecystitis – Acute cholecystitis – Early phase – Immediate – Laparoscopic cholecystectomy – Emergency surgery

Various reports have proven the feasibility and benefits of performing laparoscopic cholecystectomy in the early phase of acute cholecystitis. Recently, emergent cholecystectomy within 24 hours of hospital presentation—immediate laparoscopic cholecystectomy (ILC)—has been recommended for patients with acute cholecystitis.[1] However, severe inflammatory tissue reaction around the gallbladder, especially in Calot's triangle, tends to make dissection difficult in early-phase acute cholecystitis. This gives rise to increases in the length of the operation, the amount of blood loss, and the rate of conversion to open surgery. Although many reports have described the superiority of performing laparoscopic cholecystectomy in the early phase compared with the late phase, the early phase has generally been defined as within 1 week after hospital admission.[2–6] Few reports have analyzed only cases in which ILC was performed for acute cholecystitis, and little is known regarding predictors of surgical difficulty in ILC. In terms of preoperative risk factors associated with surgical difficulty in laparoscopic cholecystectomy for all gallbladder diseases, diabetes mellitus, previous history of acute cholecystitis, and gallbladder wall thickness > 4 mm have been significantly associated with longer operation times.[7] In this study, we focused on cases in which ILC was performed for acute cholecystitis to identify preoperative factors predicting operative difficulty that could influence the surgical plan (selection of a surgical team, preparation for possible conversion). Moreover, the identification of these factors makes it possible to accurately inform patients regarding the predicted operation time and likelihood of conversion.

Materials and Methods

We analyzed consecutive patients with acute cholecystitis who underwent emergent laparoscopic cholecystectomy from August 2007 to January 2015 at a single center. All patients were diagnosed with acute cholecystitis and underwent surgery within 24 hours of hospital presentation.

The primary outcome was operation length. We also assessed the amount of intraoperative blood loss and the rate of conversion to open surgery. We then analyzed factors associated with a longer operation time, defined as $\geq$120 minutes; substantial blood loss, defined as $\geq$100 mL; and conversion to open surgery.

Clinical characteristics included age, sex, body mass index (BMI), comorbidities, and the results of blood tests and computed tomography (CT) scans. Clinically relevant thresholds were used as cutoff values for continuous variables. The cutoff value for BMI was set at 25 kg/m^2, which is the value generally used in Japan to demarcate a patient as obese. The cutoff values for white blood cell (WBC) count, C-reactive protein (CRP), and gallbladder wall thickness were determined by referring to other reports.[7,8]

The protocol for this study was approved by our hospital's institutional review board; informed consent was waived because of the historical cohort nature of the study.

Diagnosis

Following the Tokyo guidelines, the diagnosis of acute cholecystitis was established by the following: (1) local signs of inflammation (mass, pain, or tenderness of the right upper abdomen or Murphy's sign); (2) systemic signs of inflammation: fever, elevated WBC count or CRP; and (3) imaging findings (abdominal ultrasound or CT scan) characteristic of acute cholecystitis.[9,10] The diagnosis was confirmed by 2 or more hepato-biliary surgeons and radiologists within 24 hours of presentation at the hospital. Calculus cholecystitis was diagnosed by preoperative abdominal ultrasound or CT scan or by postoperative examination of the specimen. Presence or absence of the dirty fat sign, *i.e.*, high density of the fat around the gallbladder on CT scan indicating the spread of inflammation, was assessed

Table 1 Patient characteristics

Variables	Mean ± SD, median [range], or no. (%)
Age (y)	65.5 ± 15.9
Sex	
Male	52 (71.2)
Female	21 (28.8)
BMI (kg/m^2)	23.9 ± 3.2
Diabetes mellitus	9 (12.3)
Antiplatelet or anticoagulation therapy	15 (20.5)
Symptom duration (d)	1 [1–3]
Body temperature	
>38.0°C	14 (19.2)
≤38.0°C	59 (80.8)
WBC (/μL)	12,068 ± 4725
CRP (mg/dL)	7.2 ± 8.0
Gallbladder wall thickness (mm)	3.5 ± 2.2
Dirty fat sign	17 (23.3)
Calculi	36 (49.3)
Length of operation (min)	128.4 ± 58.7
Intraoperative blood loss (mL)	170.7 ± 629.7
Conversion to open surgery	16 (21.9)
Complication	
Common bile duct injury	1 (1.4)
Biliary fistula	1 (1.4)
Postoperative hospital stay (days)	5 [1–134]

by 2 or more hepato-biliary surgeons and radiologists.

Operative methods

All surgeries were performed laparoscopically by 2 or 3 experienced hepato-biliary surgeons. Procedures were performed using 3 or 4 ports, a hook-shaped electric scalpel, and, if necessary, laparoscopic coagulating shears (LCS). Metallic clips or linear staplers were used to ligate the cystic artery and cystic duct.

Statistical analyses

Continuous variables are presented as mean ± SD or median [interquartile range], and categorical variables are expressed as number and percentage. We used the χ^2 test and logistic regression models to assess associations between clinical characteristics and outcomes. Variables with significant associations in the univariate analyses were included in the multivariate logistic regression model. To ensure robustness, we added variables considered to be clinically relevant (BMI > 25 kg/m^2, symptom duration > 24 hours, WBC > 10,000/μL). Factor effects are depicted by odds ratios (OR) and their 95% confidence intervals (CIs). All statistical analyses were conducted by a physician (TY) under the supervision of the chief statistician (TM) using JMP10 (SAS Institute Inc, Cary, North Carolina), and all reported P values are 2 sided. $P < 0.05$ was considered statistically significant.

Table 2 Relationship between patient characteristics and operation length

Variables	Operation length, no. (%) >120 minutes (n = 39)	Operation length, no. (%) ≤120 minutes (n = 34).	P value
Age > 75 years	8 (20.5)	9 (26.5)	0.548
Male	31 (79.5)	21 (61.8)	0.095
BMI > 25 kg/m^2	15 (38.5)	8 (23.5)	0.400
Diabetes mellitus	6 (15.4)	3 (8.8)	0.395
Antiplatelet or anticoagulant therapy	5 (12.8)	10 (29.4)	0.080
Symptom duration > 24 hours	21 (53.8)	11 (32.4)	0.065
Body temperature > 38.0°C	9 (23.1)	5 (14.7)	0.365
WBC >10,000/μL	26 (66.7)	17 (50.0)	0.149
CRP > 5 mg/dL	25 (64.1)	11 (32.4)	0.006*
Gallbladder wall thickness > 4 mm	10 (25.6)	8 (23.5)	0.759
Dirty fat sign	14 (35.9)	3 (8.8)	0.004*
Calculi	17 (43.6)	19 (55.9)	0.295

*$P < 0.05$.

Results

We enrolled 73 patients; their characteristics are presented in Table 1. The mean age at surgery was 66 ± 16 years, and 52 patients (71%) were male. Fifteen patients had received antiplatelet or anticoagulation drugs, and 9 patients had diabetes mellitus. The median hospital stay length was 5 days (range, 1–134 days). Regarding postoperative complications (≥IIIa according to the Clavien-Dindo classification),[11] biliary fistula was seen in 1 patient, which was treated conservatively. One partial injury of the common bile duct occurred intraoperatively and was repaired immediately with no adverse effects. No reoperations were necessary. There was no postoperative mortality during hospitalization.

The mean operation length was 128 ± 59 minutes. Table 2 presents the factors associated with operation length. In univariate analysis, CRP ≥5 mg/dL and dirty fat sign were significantly associated with increased operation length. As shown in Table 3, in multivariate analysis, we added BMI >25 kg/m^2, symptom duration >24 hours, and WBC >10,000/μL along with these 2 factors (because

Table 3 Multivariate analysis of the relationship between patient characteristics and operation length

Variables	OR	95% CI	*P* value
CRP > 5 mg/dL	3.338	0.640–20.572	0.154
Dirty fat sign	5.329	1.049–34.167	0.043*
BMI > 25 kg/m^2	3.554	1.409–30.932	0.014*
Symptom duration > 24 hours	2.523	0.589–11.597	0.212
WBC > 10,000/μL	4.817	0.861–38.149	0.075

*$P < 0.05$.

these factors are generally considered to affect operation length in acute cholecystitis), and BMI ≥25 kg/m^2 (OR: 3.6; 95% CI: 1.4–30.9) and dirty fat sign (OR: 5.3; 95% CI: 1.0–34.2) were significantly associated with operation length.

The mean amount of blood loss was 171 ± 630 mL. Conversion to open surgery occurred in 16 patients (21.9%). Table 4 presents the factors associated with blood loss and conversion to open surgery. Age ≥75 years, diabetes mellitus, body temperature ≥38.0°C, and dirty fat sign were significantly associated with substantial blood loss. Male sex, symptom duration ≥24 hours, body temperature ≥38.0°C, WBC ≥10,000/μL, CRP ≥5 mg/dl, and dirty fat sign were all significantly associated with higher conversion rates.

Discussion

Laparoscopic cholecystectomy has become the gold standard treatment not only for symptomatic cholecystolithiasis but also for acute cholecystitis. The optimal timing of laparoscopic cholecystectomy for acute cholecystitis has long been discussed in a number of reports, and many reports have shown the benefit of early laparoscopic cholecystectomy rather than delayed laparoscopic cholecystectomy after conservative management.[1–6] For example, in a systematic review of approximately 488 patients with acute cholecystitis, Gurusamy *et al*[3] showed that, although there was no significant difference between the early and delayed groups in terms of operation length or complication rate, the total hospital stay was approximately 4 days shorter in the early group compared with the delayed group. In these reports, however, early laparoscopic cholecystectomy was generally defined as laparoscopic cholecystectomy performed within 7 days of presentation. Recently, the superiority of even earlier surgery, *i.e.*, ILC performed within 24 hours of presentation, has been proven by several reports.[1,12,13] In a randomized multicenter trial, Gutt *et al*[1] compared results achieved by ILC (performed within 24 hours of hospital admission) and delayed laparoscopic cholecystectomy (performed on days 7–45) and found that ILC was significantly associated with a lower morbidity rate, shorter hospital stay, and lower total hospital costs.

Karakayali *et al*[14] analyzed patients who had experienced symptoms of acute cholecystitis for >72 hours at hospital presentation and found that, in this patient population, emergent laparoscopic cholecystectomy was associated with a higher conversion rate, longer hospital stay, higher complication rate, and increased blood loss. In our study, patients with acute cholecystitis symptoms for ≤72 hours at hospital presentation underwent emergency laparo-

Table 4 Relationship between patient characteristics and the amount of blood loss/conversion rates

	Blood loss, no. (%)			Conversion, no. (%)		
Variable	>100 mL (n = 19)	≤100 mL (n = 54)	*P* value	Yes (n = 16)	No (n = 57)	*P* value
Age > 75 years	8 (42.1)	9 (16.7)	0.024*	6 (37.5)	11 (19.3)	0.143
Male	15 (78.9)	37 (68.5)	0.388	15 (93.8)	37 (64.9)	0.024*
BMI > 25 kg/m^2	5 (26.3)	18 (33.3)	0.494	3 (18.8)	20 (35.1)	0.133
Diabetes mellitus	5 (26.3)	4 (7.4)	0.031*	2 (12.5)	7 (12.3)	0.981
Antiplatelet or anticoagulant	4 (21.1)	11 (20.4)	0.950	3 (18.8)	12 (21.2)	0.839
Symptom duration > 24 hours	11 (57.9)	21 (38.9)	0.151	12 (75.0)	20 (35.1)	0.004*
Body temperature > 38.0°C	7 (36.8)	7 (13.0)	0.023*	6 (37.5)	8 (14.0)	0.035*
WBC > 10,000/μL	14 (73.7)	29 (66.7)	0.128	14 (87.5)	29 (50.9)	0.009*
CRP > 5 mg/dL	13 (68.4)	23 (42.6)	0.053	14 (87.5)	22 (38.6)	<0.001*
Gallbladder wall thickness > 4 mm	5 (26.3)	13 (24.1)	0.628	6 (37.5)	12 (21.1)	0.195
Dirty fat sign	12 (63.2)	5 (9.3)	0.045*	10 (62.5)	7 (12.3)	<0.001*
Calculi	11 (57.9)	25 (46.3)	0.465	7 (43.8)	29 (50.9)	0.614

*$P < 0.05$.

scopic cholecystectomy within 24 hours of presentation. However, even in patients symptomatic for ≤72 hours and undergoing immediate surgery, severe inflammatory changes in the tissues around the gallbladder make laparoscopic surgery difficult (even for experienced surgeons). In the present study, we selected only patients with acute cholecystitis who underwent emergency laparoscopic cholecystectomy within 24 hours of presentation, and we analyzed the preoperative factors that influenced the length of their operations.

In the present study, BMI ≥25 kg/m^2 and dirty fat sign on preoperative CT scan were independent significant risk factors for increased operation length. Male sex, symptom duration ≥24 hours, body temperature ≥38.0°C, WBC ≥10,000/μL, CRP ≥5 mg/dL, and dirty fat sign were potential risk factors for conversion to open surgery. In previous reports looking at all gallbladder diseases, a number of risk factors for increased operation length and conversion rates have been established: male sex, previous history of acute cholecystitis, CRP elevation, gallbladder wall thickness, calculi, diabetes mellitus, obesity, and others.[7,15–18] In previous studies involving only acute cholecystitis cases, Teckchandani *et al*[8] indicated that elevated WBC count, CRP, Alkaline phosphate, and amylase, as well as male sex, were risk factors for conversion, and Asai *et al*[19] identified longer presurgical symptom duration and elevated CRP as risk factors for conversion. Gallbladder thickness has been shown to be a significant predictor of laparoscopic cholecystectomy difficulty in several prior reports.[7,18,20] However, it was not a significant factor in the present study. The previous reports that found gallbladder thickness to be a risk factor for surgical difficulty analyzed all laparoscopic cholecystectomy cases, including acute and chronic cholecystitis and cholecystolithiasis. In cholecystolithiasis, gallbladder thickening is often caused by chronic inflammation around the gallbladder, and this fibrotic tissue reaction can make dissection extremely difficult. In contrast, in immediate cholecystectomy for acute cholecystitis, gallbladder wall thickening is due to tissue edema, which makes dissection easier rather than more difficult in many cases.

The overall conversion rate of laparoscopic cholecystectomy is reported to be 2.7–11.6%.[7,16–18,20] However, the conversion rate is reported to be higher in acute cholecystitis, at 13–28%.[8,19,21–24] This is similar to the conversion rate of 21.9% identified in our study (16 of 73 cases).

Age ≥75 years, diabetes mellitus, body temperature ≥38.0°C, and dirty fat sign were identified as significant risk factors for increased blood loss in our study. The data do not delineate the pathophysiology of this relationship, but one could theorize that, in elderly patients and those with diabetes mellitus, increased vessel vulnerability may have translated to increased blood loss; in patients with a high fever, hyperdynamic blood flow may have caused increased blood loss. In acute cholecystitis with severe inflammation that causes a dirty fat sign on CT scan, tissue dissection readily creates bleeding. In our study, antiplatelet and anticoagulation therapy did not significantly influence blood loss, which is in accordance with many other reports. Joseph *et al*[25] and Noda *et al*[26] indicated that emergency laparoscopic cholecystectomy could be safely performed in patients with acute cholecystitis who were receiving antiplatelet and anticoagulation therapy. In these analyses, antiplatelet and anticoagulation therapy did not significantly influence operative blood loss or the rate of postoperative bleeding-related complications.

This study had several limitations. First, each laparoscopic cholecystectomy was performed by different operators, and the reasons for increases in operation length and for conversion to open surgery were inconsistent, *e.g.*, adhesions secondary to inflammation, bleeding, and common bile duct injury. Additionally, this study was conducted at a single center and the number of patients was small. A large-scale multicenter study should be planned to confirm our findings.

Conclusions

Laparoscopic cholecystectomy for acute cholecystitis should be performed more carefully in patients with these risk factors when performed within 24 hours of hospital presentation.

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