

Operative Timing of Laparoscopic Cholecystectomy for Acute Cholecystitis in a Japanese Institute

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ABSTRACT

Background and Objectives: In patients with acute cholecystitis who cannot undergo early laparoscopic cholecystectomy (within 72 hours), 6 weeks to 12 weeks after onset is widely considered the optimal timing for delayed laparoscopic cholecystectomy. However, there has been no clear consensus about it. We aimed to determine optimal timing for delayed laparoscopic cholecystectomy for acute cholecystitis.

Methods: Medical records of 100 patients who underwent standard laparoscopic cholecystectomy were reviewed retrospectively. Patients were divided into group 1, patients undergoing laparoscopic cholecystectomy within 72 hours of onset; group 2, between 4 days to 14 days; group 3, between 3 weeks to 6 weeks; group 4, >6 weeks.

Results: No significant differences existed between groups in conversion rate to open surgery, operation time, blood loss, or postoperative morbidity, and hospital stay. However, total hospital stay in groups 1 and 2 was significantly shorter than that in groups 3 and 4 ($P<.01$). In addition, the total hospital stay in group 3 was also significantly shorter than that in group 4 ($P<.01$).

Conclusions: Best timing of laparoscopic cholecystectomy for acute cholecystitis may be within 72 hours, and the delayed timing of laparoscopic cholecystectomy in patients who cannot undergo early laparoscopic cholecystectomy is probably as soon as possible after they can tolerate laparoscopic cholecystectomy.

Key Words: Acute cholecystitis, Laparoscopic cholecystectomy, Operation timing.

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INTRODUCTION

Cholecystectomy is the definitive treatment for patients with acute cholecystitis. Until the 1980s, urgent open cholecystectomy had proved to be beneficial for the management of acute cholecystitis in terms of reducing the morbidity rate and shortening the hospital stay in comparison with conventional conservative treatment with subsequent interval open cholecystectomy.^{1,2} However, early urgent cholecystectomy was often difficult to implement due to logistical reasons related to patient comorbidities and emergent availability of equipment and an operating room. In the early days of laparoscopic cholecystectomy (LC), acute cholecystitis was a contraindication of LC, and many surgeons have believed that it was a matter of skill and training until now. Thereafter, LC for acute cholecystitis started with the increases in laparoscopic experience and has been generally performed.³ In the case of LC after the acute phase, the accepted timing has generally been considered to be 6 weeks to 8 weeks after the onset of symptoms to allow resolution of the acute inflammation of the gallbladder.⁴ Recent metaanalyses have demonstrated that compared with delayed-interval LC (performed 6 to 12 weeks later), early urgent LC (performed within 24 to 72 hours of onset) provides benefit in terms of total hospital stay but not in terms of conversion rates and postoperative complications.⁵⁻⁷

In Japan, the Tokyo Guidelines were announced by the Japanese Society of Hepato-Biliary-Pancreatic Surgery about 5 years ago. These guidelines were determined at an International Consensus Meeting⁸ and show diagnostic criteria and therapeutic strategies for acute cholangitis and cholecystitis including the clinical flowcharts.⁹ They also recommend early LC after admission but do not define delayed-interval LC.¹⁰ Many Japanese surgeons consider elective or delayed timing of LC to mean all timings after the acute phase (>72 to 96 hours), not just 6 weeks to 12 weeks after onset.¹¹ Indeed, many Japanese reports show that elective or delayed LC was almost always performed within 6 weeks.^{12,13} However, the elective timing of LC has not been a problem in the clinical management of acute cholecystitis in Japan.¹²

Recently, Low et al¹⁴ compared delayed urgent LC (72 hours to 2 weeks) with early urgent LC (within 72 hours)

in patients with acute cholecystitis. The results of delayed urgent LC were comparable to those of early LC in terms of conversion rates, operative morbidities, and postoperative hospital stay. They recommend early-interval LC within 2 weeks of onset in patients who cannot undergo early urgent LC. Thus, there has been no clear consensus on the timing of delayed-interval LC for acute cholecystitis. In this study, we retrospectively analyzed data on LC in 100 patients with acute cholecystitis and determined how timing of LC influenced the results.

MATERIALS AND METHODS

Patients

Between October 1999 and November 2009, 426 consecutive Japanese patients underwent cholecystectomy in our surgical department at Oita University Hospital, and 103 of them were diagnosed as having acute cholecystitis. Three of these 103 patients underwent open cholecystectomy because of concomitant diseases: pulmonary and heart failure, pulmonary thrombosis due to vascular Behçet's disease, and a huge incisional hernia intended to be repaired at the same time. The remaining 100 patients comprising 37 women and 63 men, ranging from 20 to 99 years of age (mean age 64 ± 15 years, mean \pm standard deviation) underwent LC. Seven of the patients had undergone previous surgery in the upper abdomen (6 gastrectomies and 1 colectomy). Thirty-seven patients (37%) were classified as having an American Society of Anesthesiology (ASA) score of 3 or 4 at the onset of cholecystitis, and 63 patients (63%) had comorbidities possibly hindering emergency operation, including cerebral and cardiac diseases, diabetes mellitus, chronic renal failure, and other disease. In addition, 20 of the patients were on anticoagulation therapy at the onset of cholecystitis. Seventy-three of the patients (73%) had received conservative treatment including percutaneous transhepatic gallbladder drainage (PTGBD) in other hospitals or another department of our hospital and were then referred to our department. PTGBD was performed preoperatively in 40 of the patients (40%).

Diagnosis and assessment of the severity of acute cholecystitis were performed according to the Tokyo Guidelines.¹⁵ Briefly, acute cholecystitis was diagnosed not only by clinical manifestation (Murphy's sign, upper abdominal pain, and fever) and laboratory data (elevated C-reactive protein and white blood cell counts) but also by imaging findings of ultrasonography and computed tomography (enlarged gallbladder and thickened gallbladder wall of

>4 mm). Severity was classified into 3 grades: grade I, mild acute cholecystitis without marked local inflammation of the gallbladder and organ dysfunction; grade II, moderate acute cholecystitis with marked local inflammation of the gallbladder (pericholecystic abscess, hepatic abscess, gangrenous cholecystitis, and biliary peritonitis); and grade III, severe acute cholecystitis with organ dysfunction (cardiovascular, neurological, renal, or hematological dysfunction). Severity in the 100 patients was classified as grade I in 66 patients (66%), grade II in 33 patients (33%), and grade III in 1 patient (1%).

The mean duration from the onset of acute cholecystitis to the LC operation was 25 ± 20 days. The patients were divided into 4 groups according to the timing of LC from the onset of acute cholecystitis: group 1, patients undergoing LC within 72 hours; group 2, patients undergoing LC between 4 days and 14 days of onset; group 3, patients undergoing LC between 3 weeks and 6 weeks of onset; and group 4, patients undergoing LC more than 6 weeks after onset. Clinical features of the patients and perioperative outcomes including conversion rate to open surgery, operation time, blood loss, postoperative morbidity, and lengths of postoperative hospital stay (until patients returned home) and total hospital stay were compared in each group.

Operative Technique

The LC surgical procedure used a standard 4-port technique and followed the technique previously reported.^{16,17} Briefly, carbon dioxide (CO₂) was used for peritoneal insufflations, and abdominal pressure was maintained between 8mm Hg and 10mm Hg. A Hasson-type trocar was inserted at the subumbilical region for the laparoscope. Operator access ports of 10mm and 5mm in diameter were inserted into the epigastrium and the right hypochondrium, respectively. The fundus of the gallbladder was grasped with the forceps inserted via a 5-mm port placed at the right iliac fossa. If it were difficult to grasp the gallbladder due to inflammation and the thickness of the wall, gallbladder decompression would be performed using an aspiration needle. On the occasion of severe inflammation and adhesion, blunt dissection with a suction device was very useful to keep a clear field and dissect tissues safely. The cystic artery and cystic duct were freed from the surrounding tissue at Calot's triangle, and the critical view of safety established by Strasberg was attempted to be created in each case.¹⁸ Intraoperative cholangiography was performed when the critical view of safety was not created. A drain was routinely inserted to the foramen of Winslow to assess intraperitoneal bleeding and bile leakage postop-

eratively, and removed on postoperative day 1. The pathological diagnosis was routinely performed to confirm acute cholecystitis.

Statistical Analyses

Data are expressed as mean±standard deviation. Statistical analyses were performed with one-way analysis of variance with Bonferroni correction, chi-square test, and Fisher’s exact test. A value of P<.05 was considered statistically significant. All calculations were performed with SPSS II (SPSS, Chicago, IL, USA).

RESULTS

LC was completed in all but 2 patients who were converted to open surgery due to severe inflammation. The mean LC operation time was 148±57 minutes, and estimated blood loss was 72±113mL. Nine of the patients (9%) undergoing LC experienced postoperative complications: wound infection in 4 patients, bile leakage in 2, abscess formation at the liver bed in 2, and postoperative hemorrhage in one. A patient who was classified as grade III had the abscess formation postoperatively. Four of 66 patients in grade I (6%) and 4 of 33 in grade II (12%) experienced the complications, but there were no significant differences between the 2

groups. PTGBD was not related to the incidences of overall postoperative complications and infectious complications (wound infection and abscess formation), respectively (PTGBD (+) vs. (-): 10% vs. 8%; 8% vs. 5%). One of the 2 patients with postoperative bile leakage and the 2 patients with abscess formation were treated by endoscopic or ultrasonographic and fluoroscopic interventions, and the postoperative hemorrhage was stopped by laparoscopic reoperation. The other complications were cured conservatively. The mean postoperative hospital stay was 9.1±5.8 days, and the mean total hospital stay was 29±16 days.

The clinical features of the 100 patients by group according to the timing of LC from the onset of acute cholecystitis are shown in **Table 1**. Group 1 comprised 11 patients; group 2, 20 patients; group 3, 52 patients; and group 4, 17 patients. The patients in group 1 were statistically significantly younger than those of the other 3 groups. There were significant differences in the number of patients with an ASA score of 3 or 4 between groups 1 and 3 and between groups 1 and 4. There were also significant differences in comorbidities between groups 1 and 4. Significant differences in the number of referrals from another hospital or another department within our hospital were recognized between the 4 groups except be-

Table 1. Clinical Features of the Patients According to Timings from the Onset of Acute Cholecystitis to Laparoscopic Cholecystectomy

	Groups			
	1	2	3	4
	(Timing from onset to laparoscopic cholecystectomy)			
	(≤72 hours)	(4-14 days)	(3-6 weeks)	(>6 weeks)
Number of patients	11	20	52	17
Age (years)	48 ± 15	64 ± 13 ^a	66 ± 13 ^b	70 ± 16 ^b
Sex (female/male)	5/6	9/11	17/35	6/11
ASA score 3 or 4 (%)	0 (0)	6 (30)	21 (40) ^a	10 (59) ^b
Comorbidities (%)	5 (45)	11 (55)	32 (62)	15 (88) ^a
Other hospital/department referrals (%)	0 (0)	8 (40) ^a	49 (94) ^{b,c}	16 (94) ^{b,c}
Preoperative PTGBD ^d (%)	0 (0)	9 (45) ^a	23 (44) ^b	8 (47) ^b
Severity of cholecystitis, grade II or III (%)	4 (36)	6 (20)	15 (29)	9 (53)

^aP<.05 vs. group 1.

^bP<.01 vs. group 1.

^cP<.01 vs. group 2.

^dPTGBD=percutaneous transhepatic gallbladder drainage.

tween groups 3 and 4. PTGBD was performed relatively frequently in patients in groups 2 to 4, whereas it was not performed at all in the patients in group 1. There were no significant differences in the severity of acute cholecystitis between the 4 groups.

There were no significant differences between the 4 groups in perioperative outcomes of conversion rate to open surgery, operation time, blood loss, postoperative morbidity, interventional treatments including operation for postoperative complications, and postoperative hospital stay (Table 2). However, total hospital stay in groups 1 and 2 was significantly shorter than that in groups 3 and 4 and was also significantly shorter in group 3 than in group 4, indicating that the patients in group 4 experienced the longest total hospital stay of any of the patients in the present study.

DISCUSSION

This study demonstrates that the duration between the onset of acute cholecystitis and the performance of LC did not statistically significantly influence almost any perioperative outcome except for that of the total hospital stay. However, our data do not deny benefit to patients with acute cholecystitis treated by early urgent LC (≤72 hours after onset). Although we could find no statistically significant differences between early LC and the other timings of LC, early LC for acute cholecystitis in the patients

treated in our institution also showed excellent results including no conversions to open surgery, shorter operation times, no complications, and shorter postoperative hospital stays. The patients in this study frequently possessed comorbidities and could not undergo early urgent LC. However, only 37% of the patients were classified as having an ASA score of 3 or 4, and 63% had comorbidities. If Japanese physicians in other referring hospitals and in other departments within our own hospital had more knowledge of benefits of early LC performed within 72 hours of onset, we estimate about half of the patients might possibly receive it. Therefore, we believe that the evidence for optimal timing for LC in patients with acute cholecystitis should be announced more widely through guidelines such as the Tokyo Guidelines in Japan.

In patients with acute cholecystitis who cannot undergo early LC due to their general condition and/or comorbidities, 6 weeks to 12 weeks after the onset of acute cholecystitis has been widely considered to be the optimal timing for delayed-interval LC,⁵⁻⁷ because acute inflammation and reactive hyperemia of the gallbladder have been considered to be resolved after 6 weeks. However, Low et al¹⁴ showed efficacy of delayed urgent LC (72 hours to 2 weeks) for acute cholecystitis. Popkharitov¹⁹ performed a study of the timing of surgery for acute cholecystitis. Three groups were compared, acute (<72 hours), intermediate (4 to 7 days), and delayed (≥8 days), and no significant differ-

Table 2.
Perioperative Outcomes According to Timings from the Onset of Acute Cholecystitis to Laparoscopic Cholecystectomy

	Groups			
	1	2	3	4
	(Timing from onset to laparoscopic cholecystectomy)			
	(≤72 hours)	(4-14 days)	(3-6 weeks)	(>6 weeks)
Open conversion (%)	0 (0)	1 (5)	1 (2)	0 (0)
Operation time (min)	120 ± 50	151 ± 56	153 ± 59	150 ± 52
Blood loss (mL)	27 ± 59	59 ± 79	85 ± 120	79 ± 142
Postoperative complications (%)	0 (0)	2 (11)	5 (10)	2 (12)
Interventional treatment for complications (%)	0 (0)	1 (5)	1 (2)	2 (12)
Postoperative hospital stay (days)	6.4 ± 2.4	9.1 ± 4.4	9.3 ± 6.7	10.2 ± 5.4
Total hospital stay (days)	8.8 ± 2.0	18.5 ± 5.5	31.4 ± 11.5 ^{a,b}	49.1 ± 18.4 ^{a,b,c}

^aP<.01 vs. group 1.

^bP<.01 vs. group 2.

^cP<.01 vs. group 3.

ences could be found in conversion rates (11.4% to 14.3%), complication rates (6.1% to 11.4%), and postoperative hospital stay (2~3 days) between the 3 groups. Condilis et al²⁰ also investigated the best timing of LC for acute cholecystitis. They compared 3 groups as well: group I, <48 hours; group II, 48 hours to 4 weeks; and group III, 5 weeks to 8 weeks. They showed that in comparison with groups I and III, group II had the worst outcomes in regard to conversion rate (23.5% vs. 3.4%, 7.2%), complication rate (14.7% vs. 2.1%, 6%), and postoperative hospital stay (7.5 days vs. 2 days, 2.5 days), and their results followed the common sense of delayed-interval timing (6 weeks to 12 weeks after onset). However, Lee et al²¹ also performed a study of timing of surgery for cholecystitis, again comparing 3 groups: acute (<3 days), intermediate (4 days to 5 weeks), and delayed (>5 weeks). There were no significant differences in conversion rates (11% to 18%) and complication rates (7% to 16%) between the 3 groups. Therefore, they recommended that patients with acute cholecystitis should undergo LC during the same hospital admission. In our study, even if the delayed timing of LC is changed from >6 weeks to >5 weeks according to the Lee et al study,²¹ results of perioperative outcomes including conversion rate, operation time, blood loss, postoperative morbidity, and postoperative hospital stay do not change.

Although the postoperative hospital stay in this study (6.4 days to 10.2 days) was much longer than those described in the previous reports, because of differences in medical insurance systems and patient's habits, the conversion rate from LC to open surgery (0% to 5%) was lower and postoperative morbidity (0% to 12%) was comparable to those in the previous reports. We suspect that these good results might be a consequence of our surgical skill and experience, which may influence and reduce the differences between the 4 groups.

The Tokyo Guidelines show that PTGBD may be preferable for patients with moderate or severe acute cholecystitis who cannot undergo early LC.²² Actually, PTGBD has been widely performed before LC in Japan,²³ and its morbidity rate is quite low and the clinical relief is very frequent.²⁴ In addition, PTGBD may not increase postoperative infectious complications after LC, according to results of our study and published papers.^{25,26} It is still unclear whether PTGBD before LC improves surgical outcomes, although several reports have already been published to support its effectiveness.²⁶⁻²⁸

CONCLUSION

The best time to perform LC for acute cholecystitis may be within 72 hours of onset. In patients who cannot undergo early LC due to their general condition, comorbidities, or both, LC should probably be performed as soon as possible after the patients are well enough to undergo LC. The results of the present study could not affirm the conventional delayed timing of LC of 6 weeks to 12 weeks.

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