Outcomes of an Early Laparoscopic Cholecystectomy in Acute Cholecystitis, Grades I and II

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ABSTRACT

Objective: According to the accumulated benefits of laparoscopic cholecystectomy (LC) in acute cholecystitis (AC), early LC is becoming a standard management for selected patients. While patients with mild AC usually gain the advantages of this approach, removing a more inflamed gallbladder in patients with moderate AC has various results, depending on the institute where the procedure is performed. The aim of the study was to compare the outcomes between early LC in patients with grade I and II AC.

Materials and Methods: From June, 2015 to December, 2019, electronic medical records in the division of Acute Care Surgery at Siriraj Hospital in Bangkok were reviewed retrospectively. An early LC was performed consecutively in 105 cases of AC grades I and II. The overall results and the outcomes comparing grades I and II AC were evaluated.

Results: Forty-two patients were grade I (40%). Patients with grade I AC tended to be younger (56 +/- 17 years vs. 63 +/-15 years, $p = 0.03$). Among grade II patients, the late onset of more than 72 hours was the most common measure (62%). The estimated blood loss was significantly lower in grade I [30 (5-450) ml. vs. 100 (5-3,000) ml., $p = 0.018$]. The overall conversion rate was 21%, which was significantly higher in grade II AC (28.6% vs. 9.5%, $p = 0.026$). There were no differences in operating time (125 +/- 47 minutes vs. 117 +/- 44 minutes. $p = 0.365$), total lengths of stay [4 (2-7) days vs. 5 (3-28) days, $p = 0.163$], and post-operative complications (19% vs 25%, $p = 0.448$). The minor bile duct injuries occurred in four patients (3.8%), 2 cases in each group. From the multivariate analysis, grade II AC did not statistically impact the conversion (adjusted OR 2.99, 95% CI 0.5-17.6, $p = 0.225$).

Conclusion: Our study shows that the overall and evolving outcomes of early LC for grade I and II AC were safe and feasible. While a higher conversion rate and estimated blood loss attributed to grade II AC, a pre-operative severity grading can guide surgeons to accommodate their ability so as to maximize the benefits of early LC.

Keywords: Early LC; acute cholecystitis grade I; acute cholecystitis grade II (Siriraj Med J 2022; 74: 495-501)

INTRODUCTION

In 1993, Wittgen et al.[1] reported the beneficial results of laparoscopic cholecystectomy (LC) in patients who required cholecystectomy comprising acute cholecystitis (AC). At that time, most patients with AC underwent open cholecystectomy (OC). After reaching the minimally invasive age, LC became a successor of standard OC in almost all situations, including AC. The safety and feasibility of laparoscopically removal of acutely inflamed gallbladder (early LC) became more evident.[2] The accumulating evidence-based advantages of urgent cholecystectomy[3] and insignificant difference of complications compared

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with delayed LC[4] had been strongly recommended. Not only were there advantages in terms of the LOS and the cost of treatment, but early cholecystectomy also eliminated the 6-23% risk of emergency operations for non-subsided AC during the wait prior to the delayed LC.[5]

After 2007, the Tokyo guidelines[6,7] became standardized surgical management of patients with AC, according to the severity of their condition. The early LC had been suitably applied for patients with grade I and II AC whose a Charlson comorbidity index (CCI) was < 5 and an American Society of Anesthesiologists physical-status classification (ASA-PS) was < 2. These days, the outcomes of early LC are regularly published.[8,9] For mild-disease, grade I AC patients obtain the benefits of a minimally invasive cholecystectomy, without increasing the peri-operative risks. Thus, in cases of grade I AC, early LC has been recommended. As the clinical criteria of grade II AC consist of more extensive inflammation, so early LC may encounter more challenges in the operating field and end up with open conversion to OC (LOC) or some unfavorable outcomes. Consequently, a subsided gallbladder can be resected after four to six weeks in those institutions that are unfamiliar with the early LC, so as to maximize the advantages of the minimally invasive approach.

Although, there was a study comparing the outcomes of emergency LC in mild (grade I) and moderate (grade II) AC which did not differ in term of the complications (7% vs 9%, $p = 0.517$) and conversions (6% vs 6%, $p = 0.985$). The conclusion was a retrospective design from a single institution.[10] In this author's institute, which is a teaching hospital, early LC has become one of the most common urgent laparoscopic procedures. This study assessed the outcomes of early LC and compared the operative results between two grades, according to Tokyo guideline 2018 (TG18).[6] The present study also provided intra-operative details and evolvement of conversion within the institute.

MATERIALS AND METHODS

The electronic medical records of patients who were older than 15 years and in the division of Acute Care Surgery were reviewed retrospectively. Consecutive cases of grade I or II AC who were admitted for urgent LC between June, 2015 and December, 2019 were examined. The patients with suitable clinical parameters, with definite diagnostic criteria of AC in accord with the TG18, and whose pathological reports revealed acute inflammations, were enrolled in the study. Those with incomplete pre-operative data or any other pathology were excluded. The demographic details, medical history, pre-operative physiologic data, laboratory measurements, and diagnostic ultrasonography or computed tomography were collected. The research project was reviewed and approved by an Institutional Review Board, Faculty of Medicine Siriraj Hospital (Si 425/2019, 305/2021).

The patients who have any one of the following conditions: the duration of symptom of more than 72 hours, a palpable, tender mass in the right upper quadrant, white blood cell (WBC) count of more than 18,000/mm^3, marked local inflammations detected by pre-operative imaging were categorized into grade II AC. The other patients who did not consist of these criteria were in grade I. The operations were performed by acute care, colorectal, HPB, and MIS surgeons, each performed more than fifty cases of LC for gallstone diseases per year. Nevertheless, the surgeon individually decided whether to operate the AC patients. The chronological data regarding onset, peri-operation times and lengths of stay were recorded. Associated intra-operative parameters - for example, the estimated blood loss, adverse events, decisions for conversion, and additional procedure - were analyzed. Information concerning complications at follow-up clinics and emergent visits within 30 days were obtained. The overall results of early LC and the outcomes comparing grades I and II AC were evaluated.

Statistical analysis

The quantitative data were described as mean and standard deviations. The categorical variables were shown as numbers and percentage. The output of the sample size was calculated from the study of Lee W.[11] of which conversion rates of an early LC in grade I and II AC were 20% and 44%. For the evaluations between two independent proportions (two-tailed test); the proportion in group 1 = 0.200 and group 2 = 0.440. The calculated sample size was 59 in each group. Independent student t-tests were used to compare the continuous data. Chi-squared test or Fisher's exact test was used to compare categorical variables. Multivariate logistic regression was performed to identify independent clinical risk factors associated with unfavorable outcomes such as conversions or complications which were reported as odd ratio (OR) and 95% confident interval (CI) and adjusted OR and 95% CI. All p-values of less than 0.05 were considered as statistically significant. Data were recorded and analyzed using PASW statistic version 18.0 (SPSS Inc. Chicago, IL, USA).

TABLE 1. Demographic data and preoperative parameters between grade I and II AC.

	Grade I (n = 42)	Grade II (n = 63)	*P*-value
Female	24 (57.1%)	34 (53.9%)	0.749
Age (years)	56.2 ± 17.3	63.1 ± 15.2	0.030
Body temperature (Celsius)	37.5 ± 0.8	37.8 ± 0.9	0.292
Charlson comorbidity index <5	42 (100%)	61 (96.8%)	0.515
ASA classification 1 and 2	33 (78.6%)	49 (77.8%)	0.923
Body mass index (kg/m^2)	25.5 ± 3.7	25.5 ± 4.5	0.718
Positive Murphy's sign	34 (81%)	39 (61.9%)	0.038
Tenderness	42 (100%)	61 (96.8%)	0.244
Guarding	7 (16.7%)	13 (20.6%)	0.615
Mass	0 (0%)	8 (12.7%)	0.020
WBC count (cells/mcL)	13,659 ± 2,759	16,600 ± 7,586	0.001
WBC count >18,000 cells/mcL	0 (0%)	28 (44.4%)	<0.001
Total bilirubin (mg/dL)	0.7 (0.13 - 3.24)	1 (0.23 - 9.5)	0.39
Wall thickening ≥ 4 mm.	29 (69.0%)	53 (84.1%)	0.067
Positive sonographic Murphy sign	23 (54.8%)	28 (44.4%)	0.300
Positive pericholecystic fluid	19 (45.2%)	35 (55.6%)	0.300
Preoperative time (hours)	24 (3-336)	72 (5-216)	<0.001
Onset to OR >72 h	0 (0%)	39 (61.9%)	<0.001

Data were presented in n (%), mean +/- SD, or median (range).

RESULTS

Patient characteristics

One hundred and five cases were recruited for this study. The mean age was 60 (21 to 89) years. Fifty-five percent of the patients were female. Most patients had less than 5 CCI. Thirty-two (30.4%), fifty (47.6%), and twenty-three (21.9%) patients were in the ASA-PS class I, II, and III, respectively. The average onset of symptoms was at 30 hours (ranging from three hours to one week). The mean body temperature was 37.7 degrees Celsius. On physical examination, Murphy's sign was 70% positive, 23% equivocal, and 5% negative. The average white blood cell count was 15,612 (3,870-50,900) cells per cubic-millimeter. A thicker-than-4-mm. wall was revealed in 77.4% of the patients, while the rest had less than 4 mm. The sonographic Murphy's sign was positive in 61%, negative in 13%, and equivocal in 5% of the patients. For 21% of the patients, this examination was not available via CT scan or was not mentioned in the ultrasonography (US) reports. The median pre-operative time interval was 48 (3 to 336) hours. Thirty-nine patients (37.1%) received a cholecystectomy after 72 hours of onset.

Operative findings

The mean operation time was 120 minutes. The estimated blood loss was 174 ml. per case. An LC was successfully performed in 83 patients (79%), with five cases of subtotal cholecystectomy (LsC). The rate of LOC was 21% (22 cases), which included a subtotal cholecystectomy (LsOC) in two patients. The reasons for conversion involved adhesion in 14 cases (63.6%); inflammation in 11 cases (50%); contamination in 8 cases (36.3%); and bleeding in 5 cases (22.7%). Overall extra-steps were added to the standard cholecystectomy in 56 cases (53.3%), and a Jackson-Pratt drain was the most commonly implemented (39 cases). Eighteen patients (21.7%) needed either a 10 mm. clip or loop ligatures to secure their gallbladder stump. Six patients required laparoscopic suturing. In the LOC group, nine of 22 patients (41%) had an additional procedure; three had cystic duct suturing; two had a closing of their gallbladder remnant; and there was one patient requiring each of the following: IOC; cystic artery ligation; suturing a vein; and ceasing the bleeding of the liver bed.

Post-operative outcomes

The total rate of post-operative complications was 22.9% (24 cases). The most common complication was superficial surgical site infections (7 cases, 6.7%) followed by bile duct injuries and Gram-negative sepsis (4 cases, 3.8%). All four cases of bile duct injuries were minor, two patients experienced post-operative bile leakage were successfully treated by a watchful-waiting strategy. One required re-admission for hydration. Two LsC patients had retained CBD stones which were detected and treated endoscopically during follow-ups at one and six months, respectively. One of these individuals had concurrent cholecystitis and then proceeded through a completed LC uneventfully. The pathological findings revealed acute on-top chronic inflammation in 37 patients (35.2%) and there were complicated inflammations, such as gangrene, necrosis, or perforation in 33 patients (31.4%). The total LOS was 4 (2 to 28) days. In addition, there was no intra-abdominal collection, 30-day mortality, or re-operation in this study.

Comparative data between two grades

Forty-two patients were categorized in severity grade I (40%). There was no difference in the CCI and ASA-PS classification. Patients with grade I AC tended to be younger (56 years vs. 63 years, $p = 0.03$). Among the grade II patients, a late onset of more than 72 hours was the most common measure, followed by findings of suspected gallbladder perforation e.g. irregular or less-enhanced wall of gallbladder, fluid collections, marked leukocytosis, and palpable mass. The WBC counts were lower in grade I (mean difference = 2,941 cells/cubic-millimeter, $p = 0.001$). Positives in Murphy's sign was documented more in grade I ($p = 0.028$). The conversion rate was significantly higher in grade II AC (28.6% vs. 9.5%, $p = 0.026$). The EBL was slightly higher in the grade II AC. The situations that needed an extra-instrument or an add-on procedure occurred insignificantly difference between two groups. The post-operative complications were comparable between two groups including two cases of bile duct injuries in each group. In grade I, a small laceration of the right-posterior intra-hepatic duct and the duct of Luschkar were identified and then repaired laparoscopically. On the other hand, both cases of grade II were postoperative bile leakage after LOC. The median of total LOS were not considerably longer in grade II AC (5 versus four days, $p = 0.163$). As for pathology, complicated cholecystitis was more reported in grade II (36.5% vs. 23.8%, $p = 0.17$).

DISCUSSION

From the start, the results from the early and delayed LC[5] had a comparable rate of conversion (20.3% versus 23.6%) and complications. Still, 17.5% of the patients in the delayed group could not avoid emergency LC, and that procedure had a 45% conversion rate. Subsequently, early LC had widely accepted, albeit various diagnostic criteria and forms of management, and there were increased reports of better outcomes afterward. In 2013, Lee et al.[11] defined early LC as an operation performed within three days of the symptoms' onset. Their report showed that 24.5-44.2% of early LC cases had an open conversion and that 14.4-19.5% of cases had complications. The most common cause of conversion and complication was bleeding. The researchers concluded that delayed LC in AC with mild symptoms (according to the Tokyo guidelines of 2007) had the lowest rate of conversion, at 7.7%, with no different complications. Inoue K. et al.[12] reported the outcomes of early LC (classified by the Tokyo guidelines of 2013) as follows: the conversion rate of early LC in grade II AC was only 13%, with 9.8% of patients having complications and 4% having bile leakage. In 2020, Yu-Ning L. et al.[13] published the satisfactory outcomes of early LC, in accord with the TG18. Their results showed 0% and 8% conversion rate in grade I and II AC, respectively, without complications. In our cohort, a conversion rate of 9.5% and 28.5% in grade I and II, respectively. Our results were slightly higher than from the TG18, which ranged from 2.4 to 7% for grade I and 1.7 to 25.6% for grade II. A high conversion rate seems to be a significant disadvantage of an early LC from the start particularly in grade II. If we decide to commence an early LC, improvements in will occur. We hope an early LC will outrank the delayed LC eventually and become the operation of choice for operable patients with grade I and II AC.

The samples in the study were recruited from the emerging usage of the early LC epoch in the author's institute. Some conversions should be omitted later as a result of the competency of surgeons who are gaining familiarity with the inflammation. As expected, there were some changes in the particulars of conversion which appeared over time. We found that extra maneuvers were needed in only five-fifteenth of the LOC cases in the first three years of the study, whereas all four cases that were converted to OC in the last two years were associated with additional procedures. The purpose of conversions such as suturing the gallbladder stump or stopping a profuse hemorrhage have been documented, instead of simply

giving vague reasons, such as "severe inflammation" or "severe adhesion." In cases of non-converting LC, a sentinel drain was increasingly placed in the last two years of our cohort. This indicates that there were more events related to infection, bleeding, or stump-securing that were managed without an open conversion. Some conversions were omitted by laparoscopic skills such as suturing the gallbladder stump, particularly in grade II AC. However, operating surgeons should not hesitate when they encounter situations in which the advantages of the open approach will be significantly achieved. Meanwhile, the physicians should realize that severe inflammation or adhesion of the AC can be overcome by personnel with longer learning curve. In addition, early LC may be conducted in patients with grade II AC when the indications for conversions are clearer, regarding the surgeons' own abilities.

While there are no specific criteria determining the difficulty in the operating fields, the individual conversion rate of each institute is used to weigh the benefits of early LC. An early operation is quite decisive for simple AC with a low likelihood for conversion, due to the fewer inflammations in such cases. When encountering clinical parameters of marked local inflammation that is classified as grade II AC, surgeons should anticipate a more difficult cholecystectomy. In the past, surgeons would decide to convert freely when encounter the unfamiliar situations such as a markedly-inflamed or distended, gangrenous, or perforated gallbladder. The recent data tend to show that both grades could be managed comparably.[9] In our multivariate analysis for risk of conversion likewise found that grade II AC was not a factor for conversion (adjust OR 2.99, 95% CI = 0.51-17.56, $p = 0.225$). Similarly, none of the determinant was the independent risk of conversion. In addition, additional procedures might reduce the conversion, yet were not statistically significant (adjust OR 0.53, 95% CI = 0.19-1.48, $p = 0.224$). Given the controversial evidence of those clinical parameters which may predict intra-operative difficulties, Inoue K. et al. proposed a predictive criteria of difficult LC by focusing on 122 patients with grade II AC. An early LC was difficult when performed after 96 hours of onset (OR 6.32, 95% CI = 2.126-20.15, $p = 0.0009$), with a 47.1% conversion rate ($p < 0.0001$). Unfortunately, there were only two cases in our study in which early LC was started after 96 hours. However, both patients underwent successful laparoscopic procedures and had uneventful post-operative courses. As mentioned, a substantial quantity of LOC was in patients with grade II AC. While searching for more accurate predictors of open conversion, the severity grading of the TG18 can help surgeons enhance their options, in these cases, the conversion rate or the sequelae of a subtotal cholecystectomy must be discussed.

The overall complication rates were 19% in grade I and 25.4% in grade II, when comparing the series in the TG18, which were 2.9 to 9.7% in grade I and 3.1 to 28% in grade II. There were no significant differences in the operative time or the complications rate between the two groups. The most common complication was associated with non-morbidity infections. The difference of median EBL was not clinically significant (30 ml. vs. 100 ml.). The most common added step was the insertion of a Jackson-Pratt drain, followed by the procedures for securing the gallbladder stump. So, equipment like the drain, the commercial loop ligation, and/or extra-large clips and trocars should be provided for early LC in both grades I and II. Nonetheless, the drain favorably enhanced post-operative recovery via removing the residual gas and fluid which caused peritoneum tension and pain.[14]

Both cases of LsC in this study had clinical manifestations of CBD stone exacerbations and needed further endoscopic and operative management, while the two cases of LOsC had uneventful post-operative complications during the follow-ups. In a systematic review of subtotal cholecystectomy in 2015[15], most patients who underwent LC in cases of severe cholecystitis revealed only 3.1% retained stones. The laparoscopic approach produced less risk of retained stones (OR 0.5; 95% CI = 0.3-0.9), compared with the open approach. Therefore, if not too difficult, the intra-operative cholangiography can be added to the subtotal cholecystectomy so as to detect a large portion of gallbladder remnant or retained stones. However, post-operative imaging or vigilant follow-ups are the best strategy for these patients.

The limitation of our study is that it has a retrospective design. Also, variations in the area of expertise and the experience of individual surgeons who participated in the pool emergency calls also substantially affected their intra-operative decisions. As a result of the multivariate analysis, none of peri-operative parameters significantly affected the conversion. The future research about surgeon factors, such as levels of competency or numbers of emergency cases performed annually, might precisely predict the conversion of the early LC.

CONCLUSION

After urgent laparoscopy had become more widely available, the authors studied the results of early LC in grade I and II AC, according to the TG18. The benefit of an early LC is that it yielded low morbidities but slightly higher conversion rates, compared to the guidelines.

Our data supports the leverage of early LC, particularly for patients with grade I AC. While the conversion rates were significantly higher in patients with grade II AC, the adverse events were not statistically different between the two grades.

TABLE 2. Operative results between grades I AC and grade II AC.

	Grade I (n = 42)	Grade II (n = 63)	*P*-value
Operations			0.039
LC	36 (85.7%)	42 (66.7%)	
LOC	3 (7.1%)	17 (27.0%)	
LsC	2 (4.8%)	3 (4.8%)	
LsOC	1 (2.4%)	1 (1.6%)	
Conversion	4 (9.5%)	18 (28.6%)	0.026
Added procedures to cholecystectomy	20 (50%)	36 (57.1%)	0.570
Estimated blood loss (ml.)	30 (5 - 450)	100 (5 - 3,000)	0.018
Operative time (min.)	125 ± 47	117 ± 44	0.365
Complications	8 (19%)	16 (25.4%)	0.448
Bile duct injury	2 (4.7%)	2 (3.2%)	1.000
Total length of stay (days)	4 (2 - 7)	5 (3 - 28)	0.163
Complicated cholecystitis on pathologic reports*	10 (23.8%)	23 (36.5%)	0.170

*Gangrene, necrosis, or perforation

Abbreviations: LC; laparoscopic cholecystectomy, LOC; laparoscopic converted to open cholecystectomy, LsC; laparoscopic subtotal cholecystectomy, LsOC; laparoscopic converted to open subtotal cholecystectomy

TABLE 3. Risk factors for conversion.

	Crude OR (95% CI)	*P* - value	Adjusted OR (95% CI)	*P*- value
Grade II acute cholecystitis	3.8 (1.18-12.2)	0.019	2.99 (0.51-17.56)	0.225
Onset to OR >72 h	2.49 (0.96-6.48)	0.057	1.41 (0.38-5.29)	0.612
Mass	1.28 (0.24-6.85)	0.672	0.9 (0.15-5.48)	0.91
WBC count >18,000 cells/mcL	1.8 (0.66-4.91)	0.247	1.4 (0.38-5.28)	0.606
Wall thickening > 4 mm.	0.94 (0.31-2.9)	0.916	0.7 (0.21-2.34)	0.557
Added procedures	0.67 (0.25-1.64)	0.35	0.53 (0.19-1.48)	0.224

TABLE 4. Additional procedures by timelines.

Procedure	Total	2015	2016	2017	2018	2019
LC with JPD	39	1	4	7	10	17
LC with loop ligature	12	2	1	1	2	6
LC with 10-mm clip	6	1	0	2	1	2
LC with suturing	6	0	1 (GB)	0	2 (GB, bowel)	3 (cystic duct, right intrahepatic duct, duct of Luschka)
LC with unplanned IOC	4	1	2	0	0	1
LOC with added procedures	9	0	2 (IOC, stop bleed at GB bed)	3 (suture GB x 2, suture cystic duct)	1 (ligate proximal cystic artery)	3 (suture cystic duct x 2, suture vein at GB bed)

Abbreviations: LC; Laparoscopic cholecystectomy, JPD; Jackson-Pratt drain, IOC; intra-operative cholangiogram, GB; gallbladder

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