



## Early Versus Delayed Laparoscopic Cholecystectomy for the Management of Acute Cholecystitis; A Retrospective Review in Bangkok Metropolitan Administration General Hospital

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**Background:** Laparoscopic cholecystectomy (LC) is the gold standard for the management of acute cholecystitis. But timing for surgery is controversy depending on the severity of the disease and familiarity of the surgeon to the operation. According to Tokyo Guideline 2018, suggest early laparoscopic cholecystectomy (early LC) in mild form of acute cholecystitis, but decision to perform early LC in moderate form of acute cholecystitis is depended on the expertized of surgeon and clinical status of patients. In Thailand, there is limited data of the outcomes of these 2 choices of operation.

**Objective:** This study aimed to compare complication rates (bile duct injury, surgical site infection, and intraabdominal collection) and conversion rate of early versus delayed laparoscopic cholecystectomy (delayed LC) for the management of acute cholecystitis.

**Methods:** We retrospectively reviewed 170 patients with the diagnosis of acute cholecystitis in mild and moderate severity (76 patients in early LC group and 94 patients in delayed LC group) that admit to department of surgery, Bangkok Metropolitan Administration General Hospital between January 2015 to November 2019.

**Results:** There is no significant difference between early LC and delayed LC in term of bile duct injury (1.3% vs 1.1%,  $p = 0.88$ ), surgical site infection (3.9% vs 1.1%,  $p = 0.326$ ), intra-abdominal collection (2.6% vs 0%,  $p = 0.198$ ), operative time (92 minutes vs 86 minutes,  $p = 0.318$ ), and conversion rate (14.5% vs 5.3%,  $p = 0.63$ ). Mean post-operative length of hospital stay was shorter in delayed LC group (6 days vs 3 days,  $p = 0.001$ ). And there is 1 re-admission in delayed LC group.



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**Conclusion:** Early laparoscopic cholecystectomy is safe modality for the management of acute cholecystitis in mild and moderate severity with not increase in complication rate.

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## Introduction

Gallstones represent a common health problem with the incidence of 6.5-15% in the Western population<sup>1</sup>, 10-15% of adult population in the developed country may harbor gallstones<sup>2</sup>. Most patients with gallstones remain asymptomatic for many years and may never develop symptoms. Approximately 1-4% of these patients develop complications (mainly acute cholecystitis) related to the gallstone every year<sup>2</sup>.

Acute cholecystitis occurs when the cystic duct becomes obstructed, mostly by a gallstone, leading to gallbladder distention, serosal edema, mucosal sloughing, venous and lymphatic congestion, and ischemia<sup>3</sup>. Mortality and complication rates of acute cholecystitis ranging from 0.6-6% and 7-26% respectively<sup>4</sup>.

In the past, patients with acute cholecystitis were treated by open cholecystectomy through an abdominal incision. With the improvement in laparoscopic technique, the surgeon started to perform laparoscopic cholecystectomy (LC) for the treatment of symptomatic gallstone. Nowadays, LC has become the gold standard for treatment of symptomatic gallstone<sup>5,6</sup>. The major advantages of LC include less postoperative pain, less time required for hospitalization and recovery, and better cosmetic result<sup>2</sup>.

However, LC was contraindicated in the treatment of acute cholecystitis in the early days<sup>6</sup>. The patients with acute cholecystitis were treated conservatively with intravenous antibiotics, bowel rest, analgesia, and intravenous hydration then discharged and re-admission for elective LC for definitive treatment after a period of 6-8 weeks<sup>6</sup>.

Randomized controlled trials and meta-analysis had shown the benefits of early surgery within 72 hours of admission period compared with delayed LC with respect to hospital stay and cost, with no significant difference in morbidity and mortality<sup>6-8</sup>. Delayed cholecystectomy has some disadvantage including the need for emergency surgery due to failure of medical treatment, re-hospitalization due to symptom recurrence, a difficult and unsafe interval cholecystectomy because of fibrosis, and possible of being lost to follow-up<sup>9</sup>.

In the late 1980s early surgery for acute cholecystitis had gained popularity<sup>6</sup>. With the increasing experience in laparoscopic surgery, a number of surgeons start to perform LC for acute cholecystitis. The updated Tokyo Guideline announced in 2013 by the Japanese Society of Hepato-Biliary-Pancreatic Surgery suggested that early LC performing within



72 hours after onset of symptom, is the first-line treatment in patients with mild acute cholecystitis, whereas in patients with moderate acute cholecystitis, delayed LC after initial medical treatment with antimicrobial agents is the first-line treatment<sup>10</sup>.

With the increased experience in laparoscopy, surgeons started to attempt early LC for acute cholecystitis<sup>6,11</sup>. But early LC is still performed by only a minority of surgeons<sup>6,12</sup>. According to Tokyo Guideline 2018, suggest early laparoscopic cholecystectomy (early LC) in mild form of acute cholecystitis, but decision to perform early LC in moderate form of acute cholecystitis is depended on the expertized of surgeon and clinical status of patients<sup>13</sup>. However, in Thailand there is limited data of the outcomes of these 2 choices of operation. According to the study of Sert et al., found no different in early LC performed within 72 hours and within 7 days of onset<sup>9</sup>. So, this study was conducted with aims to compare the complication rates of early LC (performed within 7 days of onset) versus delayed LC (performed after 6 weeks of onset) for the management of mild and moderate form of acute cholecystitis.

## Material and Methods

This study was a retrospective cohort study. We collected data from the medical charts of patients with the diagnosis of acute cholecystitis in mild and moderate severity according to Tokyo Guideline for the diagnosis of acute cholecystitis 2013<sup>4</sup>, who underwent laparoscopic cholecystectomy between January 2015 to November 2019 in Bangkok Metropolitan Administration General Hospital, Bangkok, Thailand.

The primary outcome of this study was the complication rate, such as bile duct injury, surgical site infection, and intra-abdominal infection. The secondary outcomes were operative time, total length of stay, and post-operative length of stay. For the total length of stay was defined as the summation of the admission days for the conservative management and the second admission to perform delayed LC.

A total of 170 patients that met the inclusion criteria were enrolled. There were 76 patients for the early LC group (within 7 days of onset) and 94 patients for the delayed LC group (after 6 weeks of onset). Patient demographic data (age, gender, comorbidities such as diabetes mellitus, hypertension, dyslipidemia, chronic liver disease, etc.), time to operation, ASA score, operative time, rate of conversion, postoperative complication (bile duct injury, surgical site infection, and intraabdominal infection), postoperative length of stay, and total length of stay were collected.



This study had been approved by Bangkok Metropolitan Administration Ethic Committee (R003h/63\_EXP). Patient informed consent was not obtained due to retrospective nature of the study. Patients with concomitant CBD stone that required ERCP to remove stone was excluded from this study.

Diagnosis of acute cholecystitis was based on patients local examination (Murphy's sign positive, pain, tenderness or mass in right upper quadrant of abdomen), systemic sign (fever, leukocytosis), and imaging finding compatible with acute cholecystitis according to the Tokyo Guideline 2013 (presence of gallstone, thickening wall of gallbladder > 4 mm, pericholecystic fluid collection, and sonographic Murphy's sign positive). Patients were classified into mild and moderate acute cholecystitis.

All patients received intravenous antibiotic treatment on admission. Laparoscopic cholecystectomy was performed with 3 or 4 trocar operative technique. Early LC was performed within 7 days of the onset of symptoms and delayed LC was performed after 6 weeks when clinical of acute cholecystitis had subsided. In case of distended gallbladder, it was decompressed by using needle aspiration. Open cholecystectomy was performed with right subcostal incision. All operations were performed by experience surgeons. Decision to convert to open cholecystectomy was based on surgeon preference.

### Statistical Analysis

All statistical analysis was performed with the Statistical Package for the Social Science for Windows, software program (SPSS Inc.; Chicago, IL, USA). Continuous variables were presented as means  $\pm$  SD and compared using Student-t test. Categorical variables were presented as frequency and percentage and compared using Chi-square or fisher exact test. P-value of < 0.05 was considered statistically significant.

### Result

The median age of the patients was 51 years in the early LC group and 50 years in the delayed LC group. There were 32 male patients (42.1%) in the early LC group and 36 (38.3%) male patients in the delayed LC group. Eighty-three patients had no comorbidity disease, 34 (44.7%) in the early LC group and 49 (52.1%) in the delayed LC group. Diabetes mellitus was found in 24(31.5%) patients in the early LC group and 13(13.9%) patients in the delayed LC group. Sixty-three patients with hypertension (33 (43.3%) and 30(31.9%)), 38 patients with dyslipidemia (17(22.3%) and 21(22.3%)) in the early LC and



delayed LC group respectively. There were 2 patients with liver disease in the early group (2.6%), none in delayed LC group, 2 patients with chronic kidney disease in the delayed LC group (2.2%), and none in the early LC group. The demographic data of the patients are shown in Table 1 and 2.

Early LC was performed at the mean interval of 2.4 days and delayed LC was performed at 53 days after the onset of symptoms.

For the primary outcome of this study, there were 2 patients with bile duct injury, 1 (1.3%) in the early LC group and 1 (1.1%) in the delayed LC group. Four patients with surgical site infection, 3 (3.9%) in the early LC group and 1 (1.1%) in the delayed LC group. Two patients with intraabdominal infection in the early LC group and none in the delayed LC group. The primary outcomes of this study are shown in Table 3.

The operative time was shorter in the delayed LC group ( $92 \pm 170$  min vs  $86 \pm 215$  min) but not statistically significant ( $p = 0.318$ ). The total length of stay was equal in both group (8 days). The postoperative length of stay was shorter significantly in delayed group ( $6 \pm 62$  days vs  $3 \pm 5$  days),  $p = 0.001$ . There was 1 re-admission in the delayed LC group. More conversion rate was found in the early LC group, 11 (14.5%) vs 5 (5.3%), but not significant ( $p=0.063$ ). In this study, no mortality was observed. The secondary outcomes are shown in Table 4.



Table 1: Demographic Data and Clinical Characteristics of Patients

	Operative Type				P-value
	Early		Delayed		
	Mean	SD	Mean	SD	
Age	51	16	50	15	0.709
Weight	70	15	66	15	0.04
Height	161	9	160	9	0.528

Table 2: Demographic Data and Clinical Characteristics of the Patients

		Operative Type				P-value
		Early		Delayed		
		Count	%	Count	%	
Sex	Male	32	42.10%	36	38.30%	0.639
	Female	44	57.90%	58	61.70%	
Comorbidity	None	34	44.70%	49	52.10%	0.087
	Diabetes mellitus	24	31.50%	13	13.90%	
	Hypertension	33	43.30%	30	31.90%	
	Liver diseases	2	2.60%	0	0%	
	Chronic kidney disease	0	0%	2	2.20%	
	Dyslipidemia	17	22.30%	21	22.30%	
	Others	10	13%	13	13.90%	
ASA	1	22	28.90%	40	42.60%	0.149
	2	39	51.30%	42	44.70%	
	3	15	19.70%	12	12.80%	



Table 3: Primary Outcome

		Operative Type				P-value
		Early		Delayed		
		Count	%	Count	%	
Bile duct injury	Yes	1	1.30%	1	1.10%	0.88
	No	75	98.70%	93	98.9	
Surgical site infection	Yes	3	3.90%	1	1.10%	0.326
	No	73	96.10%	93	98.90%	
Intraabdominal infection	Yes	2	2.60%	0	0%	0.198
	No	74	97.40%	94	100%	

Table 4: Secondary Outcome

	Operative Type				P-value
	Early		Delayed		
	Mean	Range	Mean	Range	
Operative time	92	170	86	215	0.318
Total LOS	8	65	8	16	0.893
Post-op LOS	6	62	3	5	0.001

Table 5: Readmission and Conversion Rate

		Operative Type				P-value
		Early		Delayed		
		Count	%	Count	%	
Readmission	Yes	0	0%	1	1.10%	
	No	76	100%	93	98.90%	
Conversion rate	Yes	11	14.50%	5	5.30%	0.063
	No	65	85.50%	89	94.70%	

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## Discussion

In the past, acute cholecystitis was contraindicated for laparoscopic cholecystectomy. Patient was treated conservatively with antibiotics then delayed cholecystectomy was performed at 6-8 weeks after the onset of symptoms. Many multicenter randomized controlled trials demonstrated that early laparoscopic cholecystectomy yields similar mortality, morbidity and conversion rates as compared to delayed cholecystectomy<sup>11,14,15</sup>. Nowadays, early laparoscopic cholecystectomy is suggested as the first line management in mild form of acute cholecystitis. But in moderate severity of acute cholecystitis, the decision to perform early LC or delayed LC is depended in the expertized of the surgeon<sup>13</sup>.

The mortality rate in early LC was previously reported as 0.3-0.46%<sup>19,20</sup> but there is no mortality occur in our study. The rate of bile duct injury was reported as 0.2-3.5% in the literature<sup>10,16</sup>. In our study there were 2 cases of bile duct injury, 1 case (1.3%) in the early LC group and 1 case (1.1%) in the delayed LC group. For bile duct injury in the early LC group was found intraoperatively in patient with moderate severity of acute cholecystitis, the injury was occurred at common bile duct so the operation was converted to open cholecystectomy and repair bile duct injury with choledochojejunostomy. So, the operative time was prolonged to 175 min. This patient also developed intraabdominal collection postoperatively, due to anastomotic leakage of choledochojejunostomy, need for exploratory laparotomy for drainage and had prolonged length of hospital stay to 67 days. In the delayed LC group, bile duct injury was occurred in 1 patient at the side wall of common hepatic duct due to electrocauterization, no need for convert to open cholecystectomy, this bile duct injury was repaired by intracorporeal suture.

The rate of surgical site infection was 3 cases (3.9%) in the early LC group and 1 case (1.1%) in the delayed LC group, compared to the rate of 5 -20.7% in previous study<sup>9,10,16,17</sup>. All of these patients were treated by stitch-off, oral antibiotics drug, and local wound care.

There were 2 cases of intra-abdominal collection, they all were in the early LC group, 1 case were treated by exploratory laparotomy for drainage due to anastomotic leakage of choledochojejunostomy as described previously and the other case were treated by intravenous antibiotics only, no need for percutaneous drainage due to small site of collection.



The rate of conversion from LC to open cholecystectomy was reported as 9.9-31% in the previous study<sup>16-21</sup> and was higher in the early LC group<sup>7</sup>, but in our report was 11 cases (14.5%) for the early LC group and 5 cases (5.3%) for the delayed LC group, that was not statistical difference and comparable to the results of previous study<sup>21</sup>. The reason for conversion to open cholecystectomy in the early LC group was the friable tissue of gallbladder, ruptured gallbladder, bile duct injury, bleeding from cystic duct stump, and unclear anatomical structure at Calot's triangle. For the delayed LC group had severe adhesion of gallbladder to adjacent organ and unclear Calot's triangle.

In our study found no significant difference in the operative time between both groups, 92 minutes in the early LC group and 86 minutes in the delayed LC group, the result was comparable to the previous study<sup>7,21</sup>.

The result of previous study found shorter total length of stay in early LC group<sup>7</sup>. But in our study found equal total length of stay between both groups, because of the patients in the delayed LC groups were mostly transferred from the others hospital after complete course of conservative treatment, so the data of length of stay may be missed in some patients.

One patient in the early LC group had chest infection with respiratory failure postoperatively, he was treated with IV antibiotics, endotracheal intubation, and chest physiotherapy. Tracheostomy was done in this patient due to prolonged intubation. Provide prolonged length of hospital stay to 56 days.

## Conclusion

Early LC is safe to perform for the management of mild and moderate severity acute cholecystitis with not increase in the morbidity and mortality significantly when compared to delayed LC. There are similar rates of bile duct injury, surgical site infection, intra-abdominal infection, operative time, total length of stay. But post-operative length of stay is shorter in the delayed LC group.



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