

A 72-Hour Boundary for Laparoscopic Cholecystectomy in Acute Cholecystitis Is Not Necessary: A Prospective Trial

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Abstract

Background: Laparoscopic cholecystectomy (LC) in acute cholecystitis (AC) is currently considered safe, especially in settings where skilled and experienced surgeons are available, and if performed within the first 72 hours from the onset of inflammatory symptoms. Patients with symptoms persisting beyond 72 hours are often treated with antibiotics and undergo surgery by 6-8 weeks later.

Objective: To compare clinical outcomes between patients who underwent early LC within 24 to 72 hours and those who underwent late LC beyond 72 hours, from the onset of inflammatory symptoms of AC.

Methodology: A prospective data collection of consecutive AC patients undergoing LC during the study period at Saraburi Hospital.

Result: Data was collected during 1 January 2014 and 31 July 2015. There were 71 patients, of whom 35 received early LC (49%) and 36 underwent late LC (51%). According to TG13-severity grading, we found more patients with moderate severity (TG13, grade II) in the early LC group than in the late LC group. There was a higher number of gangrenous gallbladders and mucosal necrosis in the early LC group, while in the late LC group there was a higher incidence of thickened gallbladder wall (> 5 millimeters) and uncertain anatomy of cystic duct-common bile duct (CBD) junctions. There were no differences regarding operating time, incidence of complications, especially as a result from bile duct injury, conversion to open surgery, length of hospital stay and hospital deaths, between the two groups.

Conclusion: LC for AC beyond 72 hours is feasible and safe in the setting where skilled and experienced laparoscopic surgeons are available.

Keywords: Acute cholecystitis, laparoscopic cholecystectomy, cystic duct injury, conversion of laparoscopic cholecystectomy to open surgery

INTRODUCTION

Laparoscopic cholecystectomy (LC) is the gold standard for the treatment of patients with symptomatic gallstones. With increasing experience in laparoscopic surgery, a number of centers have reported on the use of early LC for acute cholecystitis (AC), recommending elective LC within 24 to 72 hours after symptoms of gall

bladder inflammation, with advantages in terms of hospital stay, cost of treatment, and low risk of complication and death²⁻⁷. Therefore, the early LC has become a standard treatment for AC.

It has been advisable to perform early LC for AC within 72 hours of onset of symptoms because in the early phase, the stages of hyperemia and edema

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predominate. Beyond that period LC becomes more difficult, because of mucosal necrosis, fibrosis formation, and high vascularity, with a consequent higher risk of bile duct injury. Recently updated Tokyo guidelines in 2013¹ suggested scheduling early LC in mild to moderately severe AC, in the setting where skilled and experienced surgeons are available, and to perform LC later after 6 to 8 weeks (delayed LC) in moderate to severe AC, following administration of antibiotics or gallbladder drainage.

There are few reports of LC in AC beyond the 72 hours boundary, evaluating safety and conversion rates. Thus, we began to prospectively collect the data comparing early LC, within 24 to 72 hours of symptoms, to late LC beyond 72 hours, in patients with AC, looking at clinical findings, type of surgical intervention, operating time, intraoperative complications, conversion to open cholecystectomy, post-operative complications, hospital stay, and hospital mortality.

MATERIALS AND METHOD

This was a prospectively designed study. Data of patients were collected at Saraburi Hospital from 1 January 2014 to 31 July 2015. The diagnosis of AC was made according to the 2013 Tokyo guidelines, which uses 3 criteria: 1) local symptoms or signs of pain or tenderness at the right upper quadrant, or a mass in right upper quadrant with positive Murphy's sign; 2) systemic signs of inflammation i.e. fever, leukocytosis, increased C-reactive protein; and 3) a confirmatory radiologic diagnosis of AC. Patients who received antibiotic treatment prior to surgery and without clinical

symptom or sign of AC, or who presented with ascending cholangitis, acute pancreatitis, Mirizzi syndrome and choledocholithiasis, or who had a previous upper abdominal surgery, were excluded from the study.

Patients with AC were divided into two groups according to the time from onset of symptoms to the time of operation. The early LC group (ELC) referred to patients operated on within 72 hours of symptom onset; and the late LC group (LLC) referred to those operated beyond 72 hours to 14 days of symptom onset.

Data collected included gender, age, BMI, report laboratory test, comorbidity, severity according to TG13 severity grading, surgical procedure, duration of surgical procedure, occurrence of bile duct injury, laparoscopic to open surgery conversion, intraoperative complications, length of hospital stay, and hospital death.

Data were summarized as counts, percentage, mean $\pm$ standard deviation (SD) or median. Statistical tests included Student's t-test for continuous data, and Pearson's chi square test for discrete data. *P*-values of 0.05 or less were considered statistically significant.

RESULTS

There were 71 patients with AC who underwent LC during the study period. Of the 71 patients, 35 received ELC (49%) and 36 underwent LLC (51%). In the ELC group the median time from symptom onset to operation was 2 days (48 hours) with a range of 1 to 3 days (72 hours), and in the LLC group the median time from symptom onset to surgery was 6 days with a

Table 1 Characteristics of patients with AC in ELC and LLC groups

Characteristic	ELC (n=35)	LLC (n=36)	<i>P</i> value
Age, years: mean $\pm$ SD	57.2 $\pm$ 16.5	48.8 $\pm$ 14.7	0.028
Male (%)	17	13	0.533
BMI, kg/m ² : mean $\pm$ SD	24.0 $\pm$ 3.1	26.0 $\pm$ 5.5	0.063
Diabetes mellitus (%)	17	8	0.265
Duration of clinical symptoms, days: median (range)	2 (1 to 3)	6 (4 to 14)	
WBC count, cell/ μ L: mean $\pm$ SD	13,995 $\pm$ 5,337	11,945 $\pm$ 5877	0.129
TG13 severity grading (%)			
- Grade I (mild)	34	66	0.004
- Grade II (moderate)	69	31	
- Grade III (severe)	0	0	

Table 2 Operative findings and outcomes in the ELC and LLC groups

Findings & outcomes	ELC (n=35)	LLC (n=36)	p value
Operative time, minutes: mean $\pm$ SD	84.37 $\pm$ 30.88	89.25 $\pm$ 30.92	0.508
Operative finding (%)			
- Omental wall off and adhesion	29	44	0.165
- Perforation of gall bladder	3	3	0.984
- Gangrenous gall bladder	34	6	0.002
- Mucosal necrosis	51	14	0.001
- GB wall thickness > 5 mm	57	81	0.033
- Uncertain anatomy of cystic duct-CBD junction	6	22	0.046
- Stone impaction at Hartmann's pouch	26	17	0.350
- Pus in gall bladder	20	8	0.067
- Large and short cystic duct	0	6	0.081
Intraoperative complication (n)			
- Bile duct injury	1	0	-
- Perforation of gall bladder	0	0	-
- Stone left in abdominal cavity	0	0	-
- Raw surface bleeding	1	0	-
- Vascular injury	0	1	-
- Liver injury	0	0	-
- Bowel injury	0	0	-

range of 4 to 14 days. The mean of age of patients undergoing ELC was 57.2 ± 16.5 years, and in the LLC group, 48.8 ± 14.7 years ($p=0.129$). The AC clinical severity grading according to the 2013 Tokyo guidelines (TG13-severity grading) for the ELC vs LLC groups revealed: TG13-grade I, 34% vs 69%; TG13-grade II, 54% vs 31%, respectively ($p=0.004$) (Table 1).

The operative time in the ELC and LLC groups were 84 ± 31 and 89 ± 31 minutes, respectively ($p=0.508$). Operative findings included omental wall off and adhesions in 29% vs 44% ($p=0.165$), perforation of gallbladder (GB) 3% vs 3% ($p=0.984$), gangrenous GB 34% vs 6% ($p=0.002$), mucosal necrosis 51% vs 14% ($p=0.001$), thickened gallbladder wall (>5 millimeters) 57% vs 81% ($p=0.033$), uncertain anatomy of cystic duct-CBD junction 6% vs 22% ($p=0.046$), stone impacted at Hartmann's pouch 26% vs 17% ($p=0.350$), pus in GB 20% vs 6% ($p=0.067$), and large and short cystic duct 0 vs 8% ($p=0.081$) in the ELC and LLC groups, respectively. Difficulties in controlling the cystic duct stump were seen in 3 and 9 patients in the ELC and LLC groups, respectively ($p=0.065$). These patients required the use of knot pushers and subtotal cholecystectomy with suture closure at Hartman's

pouch. No difference was found in the conversion rate in both groups. There was only one case of bile duct injury, and other intraoperative complications were similar in both groups (Table 2).

There were no differences in post-operative complications between the two groups. The mean of hospital stay was 9.9 ± 6.4 and 7.9 ± 4.3 days in the ELC and LLC groups, respectively ($p=0.129$). There were no hospital deaths in both two groups (Table 3).

Table 3 Postoperative complications & outcomes of ELC and LLC

Postoperative Outcomes	ELC (n=35)	LLC (n=36)	P value
Postoperative complication (n)			
- Port-site infection	0	0	
- Collection	0	0	
- Fistula	0	0	
- Bowel ileus	0	0	
- Pneumonia	1	0	
Hospital stay, days: mean $\pm$ SD	9.9 $\pm$ 6.4	7.9 $\pm$ 4.3	0.129
Death (n)	0	0	

DISCUSSION

Laparoscopic cholecystectomy (LC) is the gold standard for the treatment of patients with symptomatic gallstones and acute cholecystitis. There have been a number of studies in the literature showing no significant difference between ELC and LLC for patients with AC in terms of operative time, conversion to opened cholecystectomy, operative complications, and mortality²⁻¹². ELC has become a preferred surgical intervention for AC because of shorter hospital stay and lower risk of recurrent acute cholecystitis prior to the planned operation.

According to the updated 2013 Tokyo guidelines (TG13)¹, treatment of AC should depend on its clinical severity. TG13 suggests ELC for AC with mild or grade I severity, and delayed LC for moderately severe to most severe or grades II-III AC, in the setting where skilled and experienced surgeons are available, and GB drainage in patients non-responsive to antibiotics. ELC for AC should be done within 72 hours from onset of symptoms because in the early phase, the stages of hyperemia and edema predominate, and this may even facilitate laparoscopic surgery. After 72 hours chronic inflammation predominates with adhesions, fibrosis, hyper-vascularity and necrosis, possibly leading a difficult LC because identification of critical structures at Calot's triangle may not be easy.

Nonetheless, a number of studies on clinical outcomes of LLC for AC beyond the 72-hour boundary reported of safety of LC regardless of timing¹³⁻¹⁴. There are also studies on the impact of duration from the

onset of symptoms or signs of AC till surgery, on clinical severity and clinical pathology of AC, and on clinical outcomes of both ELC and LLC. In these studies, clinical pathology was not related to duration of onset of AC¹⁵. LLC was found to be safe in settings where expertise in laparoscopic surgery is available.

In the present prospective trial, LC was performed by experienced laparoscopic surgeons using a 3-port technique, with the insertion of a 10 mm trocar at the umbilicus as the laparoscope port, a 5 mm port for surgeon's left hand instruments at the right mid-clavicular line just below the liver edge, and a 5 mm port for surgeon's right hand instruments at the high epigastric region just to the right of the Falciform's ligament. Decompression of distended gallbladders was done when necessary, and a retrieval bag for specimen removal from the abdominal cavity was used routinely.

There were almost no differences in demographics between the ELC and LLC groups, except that patients in LLC group were younger on average. The severity of AC was higher in the ELC group. There were also more gangrenous GB and mucosal necrosis in the ELC group, while in the LLC group a higher number of thickened GB wall and uncertain cystic duct-common bile duct (CBD) junction anatomy was seen. The latter finding may possibly be related to prolonged inflammation, and a higher proportion of grade II AC (67%), in the LLC group. No patients in the present study had grade III AC, since all these patients underwent open cholecystectomy.

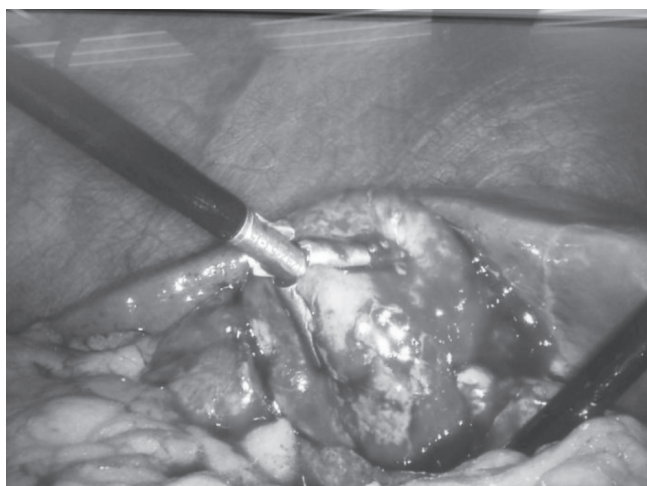


Figure 1 Intraoperative photograph of gangrenous acute cholecystitis

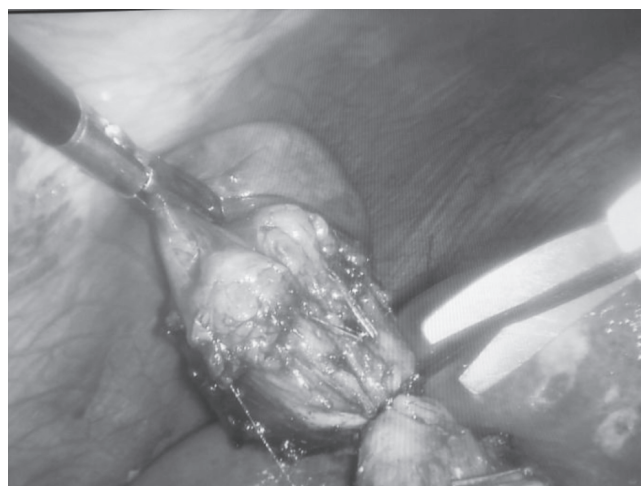


Figure 2 Laparoscopic cholecystectomy with knot pusher control at cystic duct in difficult cases



Figure 3 The use of a retrieval bag to remove gallbladder

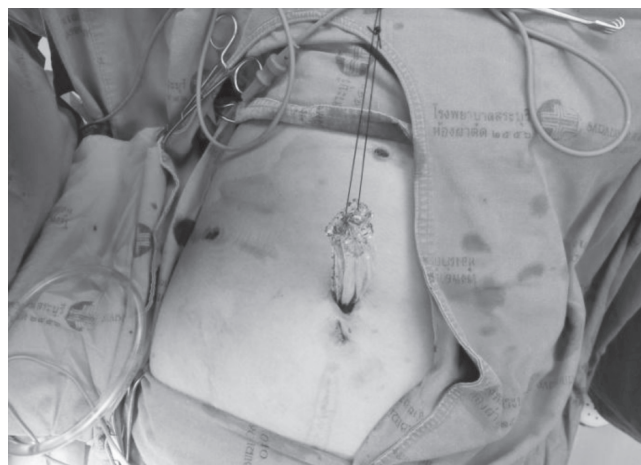


Figure 4 Removing the specimen through the umbilical port

There was no difference in operative time between both groups. There was only one bile duct injury in ELC group. This particular patient later underwent ERCP with CBD stent placement. There were three patients in ELC group and nine patients in LLC group in whom the cystic duct stump was difficult to control. In these patients we used a knot pusher to control the GB neck, or the Hartmann's pouch was sutured laparoscopically. One patient had conversion to opened cholecystectomy due to intraoperative vascular injury. There was neither port-site infection nor intra-abdominal collection in the present study, as a result of using a retrieval bag, good suctioning, and the insertion of a drainage tube when necessary. There was no difference in terms of hospital stay between the two groups, and there were no deaths in the present study. Limitations of the present study included a small sample size and a non-randomized design. However, the results of the present study were consistent with those of clinical studies done elsewhere, showing that LLC is safe, with comparable conversion rate to open cholecystectomy, infection rate, length of hospital stay, and complication rate, as ELC.

CONCLUSION

Laparoscopic surgery for acute cholecystitis beyond 72 hours is feasible and safe with low morbidity and low conversion rate, regardless of timing, in the settings where skilled and experienced laparoscopic surgeons are available.

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Conflict of Interest: None

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บทคัดย่อ การศึกษาไปข้างหน้า เรื่องการผ่าตัดถุงน้ำดีด้วยการส่องกล้องไม่จำกัดภายใน 72 ชั่วโมงหลังมีอาการในผู้ป่วยถุงน้ำดีอักเสบเฉียบพลัน

บัณฑิต เขียววรรณ

กลุ่มงานศัลยกรรม โรงพยาบาลสระบุรี

ภูมิหลัง: ปัจจุบันการผ่าตัดถุงน้ำดีด้วยการส่องกล้องในช่วงที่มีการอักเสบนั้นมีความปลอดภัยโดยเฉพาะในที่มีความชำนาญ โดยแนะนำให้ทำในช่วง 72 ชั่วโมงแรกหลังมีอาการถุงน้ำดีอักเสบ ในกลุ่มที่มีอาการเกิน 72 ชั่วโมงไปแล้วแนะนำให้ยาด้านจุลชีพแล้วทำการผ่าตัดภายหลัง 6 ถึง 8 สัปดาห์ แต่ข้อมูลการผ่าตัดถุงน้ำดีด้วยการส่องกล้องในช่วงที่มีการอักเสบหลัง 72 ชั่วโมงยังมีข้อจำกัด

วัตถุประสงค์: ศึกษาผลลัพธ์ของการผ่าตัดถุงน้ำดีอักเสบในช่วงแรก (24 ถึง 72 ชั่วโมง) เปรียบเทียบกับการผ่าตัดถุงน้ำดีอักเสบในช่วงหลัง (เกิน 72 ชั่วโมง) ในผู้ป่วยที่มีอาการของถุงน้ำดีอักเสบเฉียบพลัน

วิธีการศึกษา: เป็นการศึกษาไปข้างหน้าเพื่อเปรียบเทียบผลการผ่าตัดถุงน้ำดีอักเสบในช่วงแรกกับการผ่าตัดถุงน้ำดีอักเสบในช่วงหลัง

ผลการศึกษา: ข้อมูลตั้งแต่ 1 มกราคม 2557 ถึง 31 กรกฎาคม 2558 รวม 71 คน ได้รับการทำ early LC 35 คน (49.3%) และ late LC 36 คน (50.7%) ระดับความรุนแรงของโรคตาม TG13 grading พบ moderate severity (TG2) ในกลุ่ม early LC มากกว่า late LC ในกลุ่ม early LC จะพบ gangrene GB และ mucosal necrosis มากกว่าในขณะที่ในกลุ่ม late LC พบ GB wall > 5 mm. และ Uncertain anatomy of cystic duct-CBD junction มากกว่าอย่างมีนัยสำคัญทางสถิติ ไม่พบความแตกต่างในแง่ระยะเวลาการผ่าตัด ภาวะแทรกซ้อน โดยเฉพาะการบาดเจ็บของท่อน้ำดี อัตราการเปลี่ยนการผ่าตัดเป็นแบบเปิดหน้าท้อง ระยะเวลาอนโรพยาบาล และการเสียชีวิตของทั้งสองกลุ่ม

สรุป: การผ่าตัดถุงน้ำดีอักเสบเฉียบพลันด้วยการส่องกล้องหลัง 72 ชั่วโมงในผู้ป่วยที่มีภาวะถุงน้ำดีอักเสบเฉียบพลัน มีความปลอดภัยในสถานที่ที่มีความชำนาญ
