Timing of laparoscopic cholecystectomy for acute calculous cholecystitis after a clear clinical picture is established: is it important?

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ABSTARCT

Objectives: To compare the outcome of laparoscopic cholecystectomy performed within and after three days of admission in patients with acute calculous cholecystitis after establishment of the clear clinical picture.

Methods: Between November 2015 and March 2018, our prospective study was conducted among 197 patients presenting with acute calculous cholecystitis. They were aged 31-66, of both genders, and scheduled for laparoscopic cholecystectomy at Prince Rashid Military Hospital (Irbid) and King Talal Military Hospital (Mafraq), Jordan. Acute calculous cholecystitis was divided into 3 grades (I-III) according to TG13 (the Tokyo guidelines 2013). Patients were divided into two groups: those in Group I (GI, n = 98) undergoing laparoscopic cholecystectomy within 3 days of the establishment of the clear clinical picture. Patients in Group II (GII, n = 99) undergoing laparoscopic cholecystectomy between 4 days and 14 days after the onset of the symptoms. Data were recorded regarding the preoperative period and complications after surgery.

Results: We found no significant differences in term of body mass index, sex, age, white blood cell count, or ultrasound results. Direct bilirubin and blood urea nitrogen were markedly increased in GII in comparison with GI ($P < 0.05$). Postoperative haemorrhage, bile leak, and respiratory infections were less common in GI than GII ($P < 0.05$). In addition, operation duration, conversion rate to open surgery, and total hospital stay were reduced in GI ($P < 0.05$).

Conclusion: The best time for laparoscopic cholecystectomy for acute calculous cholecystitis is early, within 3 days of admission after the establishment of the clear clinical picture. It can be performed safely in most patients and will decrease the complication rate.

Keywords: acute alculous cholecystitis, laparoscopic cholecystectomy, postoperative complication, operation timing.

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Introduction

Acute cholecystitisis major complication of gallstones, it is a common operative condition, for which cholecystectomy is the definitive treatment. The optimal timing for laparoscopic cholecystectomy was controversial. [1,7,14] Gallstone disease prevalence is 10-15%, and 35% of patients have common clinical features.[2] In a fifth of cholelithiasis cases, acute calculous cholecystitis has increased incidence and different intensities. [3] Approximately a fifth to a quarter of patients may not respond to medical management or may have difficulties during first admission requiring cholecystectomy . [5]

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At the acute inflammatory phase (>72 to 96 hours), laparoscopic cholecystectomy becomes more difficult and challenging because of oedema, fibrotic adhesions in Calot's triangle structures, friability of tissues, unclear ductal anatomy, gallbladder distension, hypervascularity, congestion, and the spread of infection. All these factors can cause suboptimal results leading to high conversion rates to open surgery . [6,12,19]

Traditional medical management of acute cholecystitis followed by late cholecystectomy (4 days to 6 weeks) was correlated with a negative postoperative outcome. [4,10] Delayed cholecystectomy actually increases the possibility of gallstone-related complications during the waiting period and thus involves more hospital admission. About 15–30% of patients discharged without surgery following acute calculous cholecystitis were readmitted with recurrent clinical features and had an unscheduled urgent cholecystectomy with gallstone-induced insults such as biliary colic in 65%, biliary tract obstruction in 25%, and biliary pancreatitis in 7% of cases. [5] Further, these unscheduled procedures were associated with increased complication rates, prolonged operation time, and increased conversion to open surgery rates. [13,16]

Previously, early laparoscopic cholecystectomy for acute cholecystitis was avoided in patients diagnosed with acute cholecystitis because of the risk of increased operative complication and high rates of conversion to open surgery that were considered to be disadvantages of laparoscopic surgery. [7,15,19] Admittedly, the bile duct injury rate of 4.7% during laparoscopic cholecystectomy for acute cholecystitis was a major issue. [6,8] However, several new studies have shown that urgent early laparoscopic cholecystectomy (within 3 days) for acute cholecystitis, when performed by experienced hands, is safe and feasible and must be the first line treatment for acute cholecystitis in fit patients. [14,18] The increased surgical difficulty of late acute cholecystitis demands it is performed electively after 6–8 weeks. [8,19]

The goal of our study was to evaluate the outcome of early urgent laparoscopic cholecystectomy (within 3 days) and to compare the results with delayed urgent laparoscopic cholecystectomy (after 4 days to 2 weeks), paying attention to clinical outcome to determine the optimal timing of laparoscopic cholecystectomy for patients with acute calculous cholecystitis, and assessing the benefits in terms of costs and hospital stay. [4,14,17]

Methods

This prospective study was undertaken at Prince Rashid Military Hospital (Irbid) and King Talal Military Hospital (Mafraq), Jordan, between November 2015 and March 2018 included 197 patients diagnosed with acute calculous cholecystitis. They were aged 31-66 years, of both genders, and scheduled for laparoscopic cholecystectomy. Written informed consent was obtained from all patients, as was approval from the ethical and research board review committee of the Royal Medical Services. Patients with incomplete data, no gallstones, previous abdominal surgery, GB tumours, or comorbid diseases were excluded. All our patients were selected depends on first presentation of acute onset of clinical picture of acute calculous cholecystitis and were admitted as emergency cases via the Emergency/Out Patients Department.

Patients were divided into two groups after admission. Patients in GI (GI, n = 98) underwent laparoscopic cholecystectomy within 3 days of the establishment of the clear clinical picture. Patients in GII (GII, n = 99) underwent laparoscopic cholecystectomy more than 3 days after the establishment of the clear clinical picture. Laparoscopic cholecystectomy in both groups was performed by senior

general surgery specialists. Data regarding the period between the establishment of the clear clinical picture and surgery, rate of conversion from laparoscopic cholecystectomy to open surgery, and complication after surgery (haemorrhage, bile leak and chest infection) were recorded. Follow-up was undertaken every week after discharge until patients were fully recovered.

Acute cholecystitis was diagnosed when patients had at least two of the following: an acute right subcostal abdominal pain and positive Murphy's sign, fever (>37.5 °C), white blood cell (WBC) count >10 × 10^9/L, and ultrasound findings of acute cholecystitis (presence of gallstones, thick gallbladder wall (>0.4 cm), pericholecystic fluid and positive probe Murphy's sign). Acute calculous cholecystitis was divided into 3 grades (I-III) according to TG13 (Tokyo guidelines 2013) as follows: Grade I (mild): acute cholecystitis with mild gallbladder inflammation without organ disturbance in a healthy patient; Grade II (moderate): acute cholecystitis with one of the following: WBC count >18×10^9/L, tender mass in the right hypochondrium, positive clinical picture established for more than 3 days, biliary peritonitis, pericholecystic abscess, liver abscess, gangrenous gallbladder, or emphysematous gallbladder; and Grade III (severe): acute cholecystitis with complications presenting one of the following : reduced level of consciousness, hypotension requiring vasopressors, creatinine more than 2.0 mg/dl, oliguria, and PaO2/FiO2 ratio of 1.5 . [7,8]

For patients with high bilirubin levels (>2 mg/ml), Magnetic Resonance Cholangiopancreatography (MRCP) was performed before surgery to rule out common bile duct (CBD) stones. Endoscopic retrograde cholangiopancreatography (ERCP) was performed before surgery because of CBD stone and/or dilatation as shown by MRCP. In both Groups, laparoscopic cholecystectomy was performed 24-48 h after ERCP.

All our patients received third generation cephalosporin intravenously on admission, which continued at least for one day after surgery.

Statistics

Data was evaluated statistically using Wilcoxon's test for unrelated data and χ^2 test for numerical data. P values less than 0.05 were considered statistically significant.

Results

There was no discrepancy in terms of age, sex and BMI between the two groups. Median body temperature and the occurrence of positive Murphy's sign were markedly increased in GI compared with GII (P >0.05), Overall, before surgery direct bilirubin and BUN were significantly higher in GII patients than in GI patients (P<0.05). ERCP was performed before surgery in 7 patients (7.1%) in GI and in 19 patients (19.2%) in GII (P<0.05). The duration of surgery and total hospital stay in GII was significantly longer compared with GI (P<0.05), (Table I).

Table I. Patients' clinical characteristics.

	GI	GII	P-value
	Surgery within first 3 days	**Surgery(3 days-2wks)**	
Number of patients (%)	98 (49.7)	99 (50.3)	
Age: median (range)	44.2 (31-59)	46.6 (38-66)	
Gender (%) M	46 (46.9)	54 (54.5)	
F	52 (53.1)	45 (45.5)	
BMI(kg/m^2): median(range)	32.4 (29-37)	33.6 (30-36)	
Clinical picture:			
Fever median(range)	39.1(38.4-39.4)	38.5(37.3-38.8)	>0.05
Palpable tender mass, n (%)	17(17.3)	37(37.4)	<0.05
Positive Murphy sign, n (%)	94(95.9)	85(85.9)	>0.05
Ultrasound results			
Gallstones, n (%)	98(100)	99(100)	-
Thick wall gallbladder, n (%)	84(85.7)	86(86.9)	<0.05
Pericholecystic fluid, n (%)	70(71.4)	59(59.6)	>0.05
CBD dilatation, n (%)	7(7.1)	19(9.2)	<0.05
ERCP, n (%)	7(7.1)	19(9.2)	<0.05
Laboratory: median(range)			
WBCs(10^9/L)	17.4 (13.5-22.4)	16.8 (12.3-21.5)	>0.05
Total bilirubin(mg/L)	1.6 (1-3.7)	1.7 (1-4.6)	<0.05
Direct bilirubin(mg/L)	1.2 (0.1-3.3)	1.6 (0.4-4.2)	<0.05
BUN(mg/L)	18.1 (11-33)	20.8 (14-32)	<0.05
Operation duration (min)median (range)	79.3 (65-110)	125.1 (86-145)	<0.05
Total hospital stay (days)	4.7 (+,- 2.2)	8.2 (+,- 5.6)	<0.05

In GI, 52.04% of surgeries were performed during the first day after establishment of the clear clinical picture, while 31.63% and 16.33% of surgeries were performed on the second and third days, respectively. In GII, 54.5% of surgeries were performed between the fourth and seventh days after the establishment of the clear clinical picture and 45.5% were performed between the eighth and fourteenth days (Table II).

Table II. Time (in days) between establishment of clinical picture and surgery.

Time in days since start of clinical picture and surgery	**GI (n = 98)**			**GII (n = 99)**	
	1	2	3	4-7	8-14
n (%)	51 (52%)	31 (31.6%)	16 (16.3%)	54 (54.5%)	45 (45.5%)

Regarding the Tokyo Severity Grading (TG13) of acute calculous cholecystitis, the gallbladder was mildly inflamed (Grade I) in 87.8% of patients in GI and in 50.5% of patients in GII. In 12.2% of GI and 40.4% of GII, the gallbladder was moderately inflamed (Grade II). In addition, 0% of GI and 9.1% of GII had intense (Grade III) acute calculous cholecystitis (P<0.05), (Table III).

Table III. Participants in terms of Tokyo intensity grading (TG13) for acute cholecystitis

	GI (n = 98)	GII (n = 99)	P-value
Grade I (mild) n (%)	86 (87.8%)	50 (50.5%)	<0.05
Grade II (moderate) n (%)	12 (12.2%)	40 (40.4%)	<0.05
Grade III (intense) n (%)	0	9 (9.1%)	<0.05

There was a discrepancy between the two groups in terms of complications of surgery and conversion rate. (Table IV). In our investigation, overall peri- and postoperative complications were more common in GII compared with GI (23 vs. 9, respectively). Five patients in GI and eleven patients in GII experienced haemorrhage (via the abdominal drain) during the first four days postoperatively and they were treated conservatively. Two patients in GII had a biliary leak via the drain during the first six days postoperatively, on the seventh day postoperatively, bile leakage ceased completely. Hospital-acquired respiratory tract infection was found in four GI patients and ten GII patients. Conversion rate to open surgery was markedly low in GI in comparison with GII (3 vs. 7, respectively). (P<0.05), (Table IV).

Table IV. Peri- and postoperative complications.

	GI (n = 98)	GII (n = 99)	P-value
Conversion to open surgery, n (%)	3 (3.1%)	7 (7.1%)	<0.05
Hemorrhage (via abdominal drain), n (%)	5 (5.1%)	11 (11.1%)	<0.05
Bile leak, n (%)	0	2 (2%)	<0.05
Chest infection, n (%)	4 (4.1%)	10 (10.1%)	<0.05

Discussion

Previously, it was considered that the appropriate time for laparoscopic cholecystectomy for acute calculous cholecystitis was 6–8 weeks following clinical treatment of an acute episode. [11,15-19] However, recently a review of the literature has shown that early urgent (within 3 days) and delayed (6-8 weeks) laparoscopic cholecystectomies for acute cholecystitis are safe, providing the same reduced operation time, conversion rates, and overall complications. [4,14,18] However, early urgent laparoscopic cholecystectomy results in a significantly shorter hospital stay and prevents the risks of conservative treatment failing. [16] This development is making most surgeons consider early

laparoscopic cholecystectomy as the best treatment for acute cholecystitis, which is well-supported by a recent international consensus published as the Tokyo Guidelines. [7,9-13,18]

With improved skills, new instruments, and increased experience, the high rates of conversion to open cholecystectomy, CBD injury, increased morbidity, and prolonged surgery time of early urgent laparoscopic cholecystectomy for acute cholecystitis have been significantly reduced. [6,13-15] However, acute cholecystitis is still the most important risk factor for complications and conversion of laparoscopic cholecystectomy. Furthermore, the timing of the surgery remains a highly contested issue and a strong predictor of laparoscopic cholecystectomy success for acute cholecystitis disease. [16,18]

The debate over relating the timing of laparoscopic cholecystectomy for acute calculous cholecystitis to onset of symptoms or admission has been exaggerated. [17-20] In our view, each clinical decision must be individualized. However, we concur that patient-physician factors, such as patient variable delay in diagnosis of more than 48 hours, influence surgical decisions and timing of intervention. These tend to vary according to the population's attitude to illness and type of health care facility. [7,20]

According to international guidelines and our results, we suggest that early laparoscopic cholecystectomy within three days of admission with onset of clinical symptoms
for acute calculous cholecystitis is safer. We also note that laparoscopic cholecystectomy within this early period is technically less demanding because the oedema planes magnify the structures and make dissection easier. So for those patients diagnosed after 3 days of onset of acute calculous cholecystitis, it is recommended to postpone the surgery for 6-8 weeks to avoid above mentioned complications. [14,18-20]

Overall, laparoscopic cholecystectomy is cheaper than open surgery, mainly because the patient's stay in hospital is shorter. [18,19]

In our study early laparoscopic cholecystectomy was performed during the first 3 days for Grade I and II acute calculous cholecystitis. Urgent management of symptoms was concluded then late elective laparoscopic cholecystectomy was performed on patients with Grade III disorders. [7,8]
Decreasing operation duration and bleeding may enhance both safety and outcomes. In our investigation, surgical duration was significantly longer in GII compared with GI.

The conversion rate and number of complications in GII were higher than in GI. This emphasises further that laparoscopic cholecystectomy for acute calculous cholecystitis is safer than late procedures. In GI, there is an oedematous plane near the gallbladder, smoothing its dissection whereas in GII, there are firm adhesions with scarring and contraction cementing with adjacent structures and distortion of normal anatomy. These factors mean delayed laparoscopic cholecystectomy was associated with longer surgical duration, more bleeding, more biliary insult, and a higher conversion rate. [14,19]

Early laparoscopic cholecystectomy is the best management procedure for acute calculous cholecystitis . [20] The management of acute calculous cholecystitis should be limited to patients in good shape for urgent surgery. [7,18]

Conclusion

The best time to perform laparoscopic cholecystectomy for acute calculous cholecystitis is during the same admission, within three days of the establishment of a clear clinical picture. Early urgent laparoscopic cholecystectomy within three days is feasible, safe and is associated with a decreased conversion rate to open surgery, a lower complication rate, shorter operation time, and reduced total hospital stay.

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