Original paper

Determination of optimal operation time for the management of acute cholecystitis: a clinical trial

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Abstract

Introduction: Although all studies have reported that laparoscopic cholecystectomy (LC) is a safe and effective treatment for acute cholecystitis, the optimal timing for the procedure is still the subject of some debate.

Aim: This retrospective analysis of a prospective database was aimed at comparing early with delayed LC for acute cholecystitis.

Material and methods: The LC was performed in 165 patients, of whom 83 were operated within 72 h of admission (group 1) and 82 patients after 72 h (group 2) with acute cholecystitis between January 2012 and August 2013. All data were collected prospectively and both groups compared in terms of age, sex, fever, white blood count count, ultrasound findings, operation time, conversion to open surgery, complications and mean hospital stay.

Results: The study included 165 patients, 53 men and 112 women, who had median age 54 (20–85) years. The overall conversion rate was 27.9%. There was no significant difference in conversion rates (21% vs. 34%) between groups ($p = 0.08$). The operation time (116 min vs. 102 min, $p = 0.02$) was significantly increased in group 1. The complication rates (9% vs. 18%, $p = 0.03$) and total hospital stay (3.8 days vs. 7.9 days, $p = 0.001$) were significantly reduced in group 1.

Conclusions: Early LC within 72 h of admission reduces complications and hospital stay and is the preferred approach for acute cholecystitis.

Introduction

Cholelithiasis has prevalence between 10% and 15%, and approximately 35% of patients develop complications or recurrent symptoms in their lifetime [1, 2]. Although more than 70% of acute cholecystitis responds to medical treatment in the first 24–48 h, laparoscopic cholecystectomy (LC) is the definitive treatment of symptomatic gallstone disease and its complications. Initially, LC was contraindicated in patients with acute cholecystitis because of the fear of increased morbidity and high rates (60%) of conversion to open surgery [3]. Most surgeons were previously in agreement that conservative treatment with antibiotics followed by interval elective operation several weeks after the acute inflammation subsides could result in a safer operation with a lower conversion rate [4]. The potential hazard of severe complications and the high conversion rate of LC in the phase of acute inflammation is a major concern [4]. Later, as a result of increasing experience and confidence in LC and technical support, the indications of early LC were extended to include patients with acute cholecystitis. Initial medical treatment for acute cholecystitis followed by delayed LC is associated with several shortcomings [5]. First, 20% to 26% of patients fail to respond to conservative treatment or develop early complications during the first admission and require an urgent and technically demanding cholecystectomy. Secondly, another 15% to 30% of patients are readmitted with recurrent symptoms and undergo an unplanned emergency cholecystectomy while waiting for their scheduled elective procedure. Thirdly, a small proportion (2.2%) of patients are lost during the interval period. Finally, at the times of operation, scarred gallbladder and dense fibrotic adhesions at Calot's triangle make interval LC extremely difficult and unsafe [5]. The feasibility and safety of early LC for acute cholecystitis have been reported in several randomised and non-randomised studies [6–8].

Aim

In the current study, we reviewed our experience with LC for patients with acute cholecystitis and compared the results of early versus delayed surgery.

Material and methods

The study was conducted at the general surgery and gastroenterology surgery department of Izmir Bozyaka Research and Training Hospital between January 2012 and August 2013. All acute cholecystitis patients admitted to the emergency unit were hospitalised. This retrospective analysis of a prospective database was designed to compare early with delayed LC for acute cholecystitis. The patients were divided into two groups depending on the timing of LC after admission within 72 h (group 1) and after 72 h (group 2), as in previous studies.

Patient's data sheets containing demographic data and preoperative, operative and postoperative information were generated. The data were prospectively entered into a standardised form. Demographic data such as age, sex, race, comorbid disease (such as hypertension, coronary diseases etc.) and duration of symptoms to surgery were recorded. Laboratory tests such as haemoglobin level, white blood cell count, glucose, urea, total bilirubin, amylase, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were also collected. Postoperative notes of interest were recorded regarding rate and reasons for conversion, postoperative complications and length of stay. The collected information was entered into a database as categorical variables for statistical analysis.

The diagnosis of acute cholecystitis was based on the presence of at least two of the following criteria: acute upper abdominal pain and Murphy's sign, fever (> 37.5°C) and white blood cell count > 10 × 10^9/l and ultrasound findings of thick-walled (> 4 mm) gallbladder, ultrasound Murphy's sign and pericholecystic fluid, in the presence of gallstones. Exclusion criteria included patients who had no gallstones, those who had no complete data, those who had an open cholecystectomy to start with and co morbid diseases. The severity of acute cholecystitis was assessed according to Tokyo Guidelines [9]: Mild (grade I) acute cholecystitis can be defined as acute cholecystitis in a healthy patient with no organ dysfunction and only mild inflammatory changes in the gallbladder, making cholecystectomy a safe and low-risk operative procedure. Moderate (grade II) acute cholecystitis is accompanied by one of the following conditions: 1) elevated WBC count (> 18 000/mm^3), 2) palpable tender mass in the right upper abdominal quadrant, 3) duration of complaints > 72 h, 4) marked local inflammation (biliary peritonitis, pericholecystic abscess, hepatic abscess, gangrenous cholecystitis, emphysematous cholecystitis). Severe (grade III) acute cholecystitis is accompanied by dysfunctions in one of the following organs/systems: cardiovascular dysfunction (hypotension requiring treatment with dopamine 5 µg/kg per minute, or any dose of dobutamine); neurological dysfunction (decreased level of consciousness); respiratory dysfunction (PaO_2/FiO_2 ratio < 300); renal dysfunction (oliguria, creatinine > 2.0 mg/dl); hepatic dysfunction (PT-INR > 1.5); and haematological dysfunction (platelet count < 100 000/mm^3).

Once diagnosis was confirmed, all patients received intravenous antibiotic treatment on admission, which was continued for 24 h after surgery. Nasogastric suction catheters and urinary catheters were inserted when clinically indicated. Our surgical unit's practice on timing for cholecystectomy is somewhat variable and it tends to perform both early and interval LC for our patients. Early LC is generally performed when conservative management with intravenous antibiotics fails, when there is gallbladder perforation or gangrene on radiological investigation, or upon the patient's request.

Endoscopic retrograde cholangiopancreatography (ERCP) is indicated for patients with elevated liver enzymes or with choledocholithiasis evident on radiological investigation. The ERCP is performed under sedation by consultant endoscopists. All biliary stones are removed prior to surgery. Biliary stones are removed using a Dormia basket or a Fogarty balloon with or without lithotripsy. Cholecystectomy is performed 1 or 2 days after ERCP procedure in the early LC group and 6 weeks after in the interval LC group. Cholecystectomies were performed by experienced surgeons using the standard four-port technique, and who had performed at least 200 laparoscopic cholecystectomies before the study. The first port (10-mm cannula) is inserted in the subumbilical region. Three 5–10-mm ports are inserted along the subcostal margin under direct vision at midline, midclavicular and anterior axillary line. Dissection of the Calot's triangle and gallbladder from the liver bed is accomplished by using monopolar electrocautery. The gallbladder is retrieved in an endoscopic bag and extracted through the subumbilical port site. Conversions were performed by median or subcostal laparotomy according to each patient and the surgeon's decision.

Statistical analysis

Statistical analysis was performed using SPSS (SPSS 21.0 for Windows) software. For comparison of the two groups, χ^2 analysis or Fisher's exact test were used when appropriate for qualitative data, and Student's *t*-test for quantitative data. For statistical analysis, continuous variables were expressed as standard deviation and categorical variables as frequencies and percentages. Value of $p < 0.05$ was considered statistically significant.

Results

Overall findings

In total, 196 patients with acute cholecystitis were included in this study. Laparoscopic cholecystectomy was performed within 72 h of admission in 83 patients (group 1) and after 72 h in 82 patients (group 2). There were 112 (68%) female patients and 53 (32%) male patients. The median age was 54 (20–85) years. Conversion to open cholecystectomy was seen in 46 (27.9%) patients overall. The mean operation time, including conversions, was 109.3 ±23.7 min (range: 45–175). There were 21 (12.7%) complications in both groups. The mean postoperative stay was 2.2 ±1.6 days (range: 1–16), and the mean total hospital stay was 5.9 ±3.2 days (range: 2–18) for all patients. No mortalities occurred in this study.

Preoperative and operative procedures and operation time

Group 1 and 2 were compared in terms of age, sex, fever (> 37.5°C), Murphy's sign, laboratory tests – including white blood cell (WBC), ultrasound findings, severity of cholecystitis, complications, operation time, conversion to open cholecystectomy and hospital stay. The demographic characteristics and preoperative findings of the cases in this study are summarised in Table I. No statistically significant difference was found between groups in terms of age and sex ($p > 0.05$). Fever (> 37.5°C) was seen in 50 (62%) patients in group 1 and in 48 (58%) patients in group 2. Murphy's sign was found to be positive in 75 (93%) patients in group 1 and 76 (92%) patients in group 2. No statistically significant difference was found between groups in terms of fever (> 37.5°C), Murphy's sign and ultrasound findings ($p > 0.05$). The patients were classified according to Tokyo Guidelines in order to determine the severity of acute cholecystitis in both groups. In group 1, 49 (59%) patients were Tokyo grade I, 34 (41%) patients were Tokyo grade II , whereas in group 2, 61 (74%) patients were Tokyo grade I, 18 (22%) patients were Tokyo grade II and 3 (4%) patients were Tokyo grade III in ($p = 0.07$).

Preoperative ERCP was performed in 2 patients from group 1 and 6 from group 2, and common bile duct stones were detected and removed endoscopically in 1 and 4 patients, respectively. More modifications in operative technique including gallbladder decompression, close-suction drainage of sub-hepatic space, and use of endoscopic pouches to retrieve specimen were

Table I. Patient demographics and preoperative findings of LC for acute cholecystitis

Characteristics	Group 1 LC within 72 h (*n* = 83)	Group 2 LC after 72 h (*n* = 82)	Value of *p*
Age [years]	54 (24–82)	54.5 (20–85)	0.30
Sex (M : F)	23 : 57	28 : 54	0.58
Fever (> 37.5°C), *n* (%)	50 (62)	48 (58)	0.70
WBC [10 × 109/l], *n* (%)	56 (70)	60 (73)	0.76
Murphy's sign, *n* (%)	75 (93)	76 (92)	0.73
Ultrasound results, *n* (%):			
Gallstones	100	100	–
Thick-wall gallbladder	67 (84)	74 (90)	0.25
Pericholecystic fluid	15 (19)	19 (23)	0.45
Severity of cholecystitis, n (%):			
Tokyo grade I	49 (59)	61 (74)	0.07
Tokyo grade II	34 (41)	18 (22)	
Tokyo grade III	–	3 (4)	

applied in group 1. A statistically significant difference was found between groups in terms of gallbladder decompression ($p < 0.05$) (Table II).

The mean operation time was 116 ±19.7 min in group 1 and 102 ±25.4 min in group 2 , which was statistically significant ($p = 0.02$).

Complications

Complications developed in 6 patients (9%) in group 1 and 15 (18%) in group 2 ($p = 0.03$). Causes of morbidities are summarised in Table III. Two patients in group 1 developed bile leakage after surgery. One of them was treated conservatively and the bile leakage subsided spontaneously within 10 days, and the other was managed by performing ERCP and nasobiliary stenting. One bile leakage developed in a patient from group 2, which probably led to cystic stump blowout and an increase in bile drainage through the drain. This was successfully managed by endoscopic retrograde cholangiopancreatography and stenting. In group 2, intra-abdominal fluid collection due to bile leakage from the cystic duct also developed in one patient and was treated conservatively by performing ERCP and ultrasound guided drainage. A bile duct injury including the right hepatic duct occurred in 1 patient from group 2. The injury was managed with conversion laparotomy. Primer suture and T drainage to the bile duct were performed. Bleeding from the surface of the gall bladder site of the liver was seen in both groups and was managed with conversion laparotomy and blood transfusion, respectively. All respiratory and wound infections were managed conservatively.

Conversion rates

Eighteen patients (21%) from group 1 and 28 (34%) from group 2 were converted to open surgery. No statistically significant difference was found between groups in terms of conversion ($p = 0.07$). The reasons for conversion were as follows: difficulty in dissection at Calot's triangle due to severe inflammation, difficulty in gallbladder exposure due to adhesions, liver bleeding and common bile duct injury. The causes and rates of conversion are summarised in Table IV.

Postoperative and total hospital stay

The mean postoperative stay was 2.0 ±1.8 days in group 1 and 2.4 ±1.3 days in group 2 (Table IV). No statistically significant difference was found between groups ($p = 0.6$). The mean total hospital stay in group 1 was 3.8 ±2.0 days and 7.9 ±2.8 days in group 2 ($p = 0.001$).

Table II. Preoperative and operative procedures in LC for acute cholecystitis

Variable	Group 1 LC within 72 h (n = 83)	Group 2 LC after 72 h (n = 82)	Value of p
ERCP procedure, n (%):	2 (2.4)	6 (7)	0.18
Stone extraction or sphincterotomy	1	5	
Stenting of common bile duct	1	1	
Gallbladder decompression, n (%)	42 (51)	19 (23)	< 0.01
Use of close suction drain, n (%)	68 (82)	65 (79)	0.6
Use of endoscopic pouches, n (%)	22 (27)	16 (20)	0.3

Table III. Cause of morbidity in LC for acute cholecystitis

Complications	Group 1 LC within 72 h (n = 83)	Group 2 LC after 72 h (n = 82)	Value of p
Wound infection, n (%)	2 (2.4)	8 (9.7)	
Respiratory infection, n (%)	1 (1.2)	3 (3.6)	
Biliary leakage, n (%)	2 (2.4)	1 (1.2)	
Bleeding, n (%)	1 (1.2)	1 (1.2)	
Bile duct injury, n (%)	–	1 (1.2)	
Intra-abdominal fluid collection, n (%)	–	1 (1.2)	
Total, n (%)	6 (7.2)	15 (18.2)	0.03

Table IV. Operative and postoperative findings of LC for acute cholecystitis

Variable	Group 1 LC within 72 h (*n* = 83)	Group 2 LC after 72 h (*n* = 82)	Value of *p*
Complications, *n* (%)	6 (7.2)	15 (18.2)	0.03
Operation time, mean ± SD [min]	116 ±19.7	102 ±25.4	0.02
Conversion, *n* (%):	18 (21)	28 (34)	0.07
Difficulty identifying anatomy	10 (56)	14 (50)	
Adhesions	7 (38)	11 (39)	
Haemorrhage	1 (6)	2 (7)	
Biliary tract injury	–	1 (4)	
Postoperative stay, mean ± SD [days]	2.1 ±1.8	2.4 ±1.3	0.60
Total hospital stay, mean ± SD [days]	3.8 ±2.0	7.9 ±2.8	0.001

Discussion

In the early years of laparoscopic surgery, acute cholecystitis was considered a relative contraindication to LC. Recently, it has been shown that LC is feasible and safe for acute cholecystitis [10]. The LC for acute cholecystitis may still be associated with higher rate of morbidity and conversion to laparotomy. Although all studies have reported that LC is a safe and effective treatment for acute cholecystitis, the optimal timing for the procedure is still the cause of some debate. Both early and delayed LC appear to be effective and safe in the treatment of acute cholecystitis. Surgeons began to recognise that early cholecystectomy is the preferred strategy for managing acutely inflamed gallbladder four decades ago. In the early phase of acute inflammation, adhesions are easily separated, and there is usually an oedematous plane around the gallbladder. The oedematous plane facilitates dissection, and single-stage definitive treatment reduces both the total duration of morbidity and the potential for late complications, such as gangrenous or emphysematous cholecystitis [11]. After a period of conservative treatment, the inflammation and oedema are replaced by fibrotic adhesions between the gallbladder and surrounding structures, which occasionally render laparoscopic dissection extremely difficult [12]. Early LC may be more technically demanding and time consuming, and may be associated with a higher rate of wound infections; however, it also tends to shorten the total length of hospital stay and remove the risk of repeat cholecystitis [13]. A Japanese meta-analysis of ten prospective, randomised trials of open cholecystectomy and LC from around the world concluded that early cholecystectomy, within 24 h to 96 h, during the index admission results in shorter hospital stay and has similar complication and conversion rates compared with interval operations performed several weeks after the index admission [14]. Conversion rates tend to have a wide range (0 to 39%) in LC for acute cholecystitis [15–17]. The overall conversion rate to open cholecystectomy was 27.9% in our study and it has quite a high range. We believe these are attributed to differences in patient demographics, severity of inflammation and the surgeon's experience and discretion. The most common reason for conversion among our patients in both groups was unidentified anatomy at Calot's triangle due to inflammatory changes, as expected. In the literature, complication rates were reported between 4.5% and 10%, both early and delay LC [5, 16, 18–20]. Our complication rates were 9% and 18%, respectively, and a statistically significant difference was found between groups. Bile duct injury is one of the most feared complications during LC. Bile duct injury can sometimes even be fatal because of sepsis. The corrective surgery for bile duct injury also carries risk of mortality and morbidity [21]. The quality of life of these patients after corrective surgery can be poor even after three years of surgery [22]. In this study only one bile duct injury occurred in group 2, although no bile duct injury was seen in group 1. In this patient, a small injury occurred at the right hepatic duct-common bile duct junction while dissection of the inflamed Calot's triangle. This was detected during the laparoscopic procedure and the decision was made to convert to open surgery. The small injury was closed with a single interrupted suture of 5-0 polypropylene and a T tube was inserted into the common bile duct. This patient had an uneventful postoperative course and the T tube was taken away after 2 weeks. The technical difficulty of

LC is related to operative findings during early surgery. We believe that several technical key points, including decompression of the gallbladder and use of a fifth port and a retrieval bag, must be kept in mind when laparoscopic surgery is performed for acute cholecystitis, in our experience. In our study, decompression of the gallbladder was required for 51% and 23% of cases, and a sub-hepatic drain was required for 82% and 79% of the patients in group1 and 2, respectively.

One of the major advantages of LC over open surgery is a shorter hospital stay and the potential for patients to return to work early. Early LC combines the merits of early surgery with those of minimally invasive surgery and can provide maximal economic gain. Skouras *et al.* [23] concluded that there is strong evidence that early LC for acute cholecystitis offers an advantage in the length of hospital stay without increasing the morbidity or mortality. The operating time in early LC can be longer, however the incidence of serious complications (i.e. common bile duct injury) is comparable to the delay LC group. Similarly, we established longer operation time, shorter hospital stay and fewer complications in group 1 patients. The total hospital stay in the delayed group, which included the total time spent during two admissions, was significantly longer than in the early group.

Conclusions

The conversion rate and morbidity of LC for patients with acute cholecystitis are not reduced by a period of initial conservative treatment. Furthermore, early operation may be safer for surgeons with adequate experience and has definite economic benefits due to reduced total hospital stay. We concluded that early LC within 72 h of admission can reduce complications and hospital stay and therefore is the preferred approach for acute cholecystitis.

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