Laparoscopic cholecystectomy in the treatment of acute cholecystitis: comparison of outcomes and costs between early and delayed cholecystectomy

V. MINUTOLO, A. LICCIARDELLO, M. ARENA, A. NICOSIA[1], B. DI STEFANO,
G. CALÌ[3], G. ARENA[2]

Department of Surgical Sciences, Organ Transplantation and Advances Technologies, University of Catania, Catania, Italy
[1]Division of General Surgery, Civil Hospital of Ragusa, Ragusa, Italy
[2]Department of Surgery, McGill University, Montreal, QC, Canada
[3]Department of Clinical and Molecular Biomedicine, University of Catania, Catania, Italy

Abstract. – BACKGROUND: Several trials showed that early laparoscopic cholecystectomy is superior to delayed laparoscopic cholecystectomy for the treatment of acute cholecystitis. However actual practice does not conform to current evidence. The aim of this study is to compare outcomes and total hospital costs between early and delayed laparoscopic cholecystectomy for acute cholecystitis.

PATIENTS AND METHODS: A retrospective analysis of patients with acute cholecystitis that underwent a laparoscopic cholecystectomy at our institutions was performed. Patients were divided into 2 groups on the basis of the treatment received and statistical analysis was performed.

RESULTS: The study included 91 patients, 52 female and 39 male, with a mean age of 55. Early surgery was performed in 32 cases and delayed surgery in 59 cases. The two groups were comparable for demographics data and severity of disease on admission. There was a no significant difference (*p* = 0.174) in the mean operative time between early (54.8 min) and delayed group (47.8 min). Conversion rate was higher in the early group (34.3% vs. 20.3%), but difference was not statistically significant (*p* = 0.223). The overall complications rate was comparable (18.7% early vs. 16.9% delayed, *p* = 0.941). Length of postoperative stay (4.3 vs. 3.8 days) was similar (*p* = 0.437), but total hospital stay was significantly 4 days shorter in the early group (*p* < 0.0001). The mean total cost was higher for the delayed group (4171 vs. 6041), with a significant difference of 1870 Euro (*p* < 0.0001).

CONCLUSIONS: Early laparoscopic cholecystectomy has an outcome comparable to the delayed procedure, with a shorter total hospital stay and lower total costs, and it should be considered as the preferred approach in treatment of acute cholecystitis.

Key Words:
    Acute cholecystitis, Early laparoscopic cholecystectomy, Delayed laparoscopic cholecystectomy, Costs.

Introduction

Cholelithiasis affected approximately 10% of the general population[1]. About 20-40% of patients with asymptomatic cholelithiasis have a risk for developing symptoms during their lifetime, and 1-3% of patients annually presented severe symptoms or complications. The most frequent complication is acute cholecystitis, accounting for 15%-26% of all complications in patients with symptomatic cholelithiasis[2].

There is still a considerable debate over the timing of laparoscopic cholecystectomy (LC) in acute cholecystitis. In the pre-laparoscopic era, prospective randomized studies demonstrated that early cholecystectomy within 7 days of the onset of symptoms was the preferred strategy to manage the acutely inflamed gallbladder, because of shorter hospital stay and reduced potential risk of late complications such as gangrenous or emphysematous cholecystitis, without an increase of postoperative morbidity and mortality[3,4]. In the first decade of laparoscopic era, acute cholecystitis was considered a contraindication for minimally invasive approach for increased postoperative morbidity, longer operative time, and higher conversion rate[5-7]. Surgeons preferred to treat patients with LC after conservative medical treatment on the assumptions that inflammatory tissue is more vulnerable to surgical interventions and leads to an increased risk of surgical complications. In the last 15 years, several randomized trials[8-11] showed that if one hand early LC is comparable to delayed LC in terms of conversion rate, postoperative morbidity, and mortality, on the other hand it is superior in terms of hospital stay which is shorter in early LC.

Corresponding Author: Manuel Arena, M.D.; e-mail: manuelarena@live.it

Despite this evidence, a delayed LC performed at least six-eight week after the symptoms onset is still frequently preferred to early LC in clinical practice[12-14].

In our institutions, there is no consensus on the standard surgical treatment of acute cholecystitis and the two approaches are chosen according to the surgeon's preference. The aim of this study is to compare outcomes in term of operative time, intraoperative and postoperative complications, length of postoperative stay, total hospital stay, and the total hospital costs between early LC and delayed LC for treatment of acute cholecystitis.

Patients and Methods

A retrospective analysis of all patients affected by acute cholecystitis and admitted in the Unit of Laparoscopic Surgery at the Gaspare Rodolico Hospital of the A.O.U. "Policlinico - Vittorio Emanuele" of Catania, and in the Division of General Surgery of the Civil Hospital of Ragusa, Italy, from January 2011 to October 2013, was performed. The acute cholecystitis was defined clinically by the presence of fever ($> 38°C$), painful upper abdomen, and radiological signs of inflammation (US, TC). Patients with diagnosis of acute pancreatitis, cholangitis, and common bile duct lithiasis were excluded. Early cholecystectomy was defined as an operation performed within 72 hours from admission to the hospital or within 7 days after the onset of the symptoms. Delayed cholecystectomy was defined as surgery performed during a second hospitalization, after at least 6 week from the onset of symptoms. All patients were treated with broad-spectrum intravenous antibiotics therapy on emergency admission. The decision to perform an early LC for acute cholecystitis or a delayed LC after conservative treatment was left to the surgeon who had been in charge of the patient. Patients discharged after conservative treatment who had a recurrence of symptoms and were readmitted underwent an emergency LC, were included in the delayed group for the analysis. The laparoscopic procedures were performed by surgeons skilled in laparoscopy. All operations were done using a 4-ports standardized technique, with the surgeon placed between the patient's legs. Minimum diathermic coagulation was used to dissect the triangle of Calot and obtain the critical view of safety (CVS). The choice of the method of dissection of the gallbladder off the liver bed, with the use of hook coagulation or scissors, was left to the surgeon's preference.

Patients were divided into two cohorts: group A "early LC" and group B "delayed LC". Demographic and clinical data as gender, age, comorbidities, American Society of Anesthesiologists (ASA) risk score, white blood cell (WBC) count and C-reactive protein (CRP) on first admission, and outcomes data as operative time, rate of conversion to open cholecystectomy, reason of conversion, rate of major and minor complications, length of postoperative hospitalizations, total length of hospital stay, were collected and compared between the two groups. The total length of hospital stay of patients that underwent a delayed LC was calculated by adding the duration of the first to the duration of the second hospitalization. The total hospital costs were calculated as a mean for each group and then compared. The cost was evaluated taking into account the operative time, the cost of the material utilized during surgery and the cost of the total hospital stay for each patient.

Statistical Analysis

The results were analyzed using the *t* Student test for comparison of data measured as quantitative variables. Categorical data were compared using the Chi-square test with Yates correction and the Fisher exact test, as appropriate. A *p*-value < 0.05 was considered significant. Statistical analysis was performed with SPSS computer software (SPSS 21 for MacOS, SPSS Inc., Chicago, IL, USA).

Results

Patients

A total of 91 patients underwent laparoscopic cholecystectomy for acute cholecystitis from January 2011 to October 2013. The mean age was 54.9 ± 13.2 (28-88) years. Male patients were 39 and female patients were 52. An early LC was performed in 32 patients (35.2%), and a delayed-interval LC in 59 patients (64.8%). The two groups were comparables for demographics data (age, gender), comorbidities (ASA score), severity of disease on first admission (WBC count, PCR), and rate of previous abdominal interventions (Table I). In the delayed LC group, 15 patients over 59 (25.4%) experienced recurrence of symptoms during the interval period. Five patients (8.4%) required re-admission and emergency LC.

Table I. Demographic data and laboratoristic values on first admission of patients.

	Early LC group (n = 32)	Interval-delayed LC group (n = 59)	p value
Gender			
Males	15 (46.9%)	24 (40.7%)	0.727
Females	17 (53.1%)	35 (59.3%)	
Age: years (range)	57.9 (37- 88)	53.2 (28- 77)	0.102
ASA risk score			
2	18 (56.3%)	41 (69.5%)	
3	14 (43.7%)	18 (30.5%)	0.301
Previous abdominal surgery	8 (25.0%)	14 (23.7%)	0.903
WBC value: n × 1000/mL (range)	17.2 (14.0-25.0)	15.8 (13.6-22.5)	0.056
PCR: mg/L (range)	50.4 (10- 121)	41.5 (9-112)	0.214

Operative Time

The mean operative time for LC in the early group was 54.8 ± 19.9 (range 35-90) min. In the delayed LC group was 47.8 ± 25.0 (range 25-120) min. There was a difference of 7 min between the two groups, that it was not statistically significant ($p = 0.174$; 95% confidence interval (CI): -3.1-17.2) (Table II).

Conversion

The overall conversion rate was 25.2% (23 on 91 patients). A conversion from laparoscopic to open cholecystectomy was required in 11 patients in the early LC group, and in 12 patients in the delayed-interval LC group, with a rate of conversion of 34.3% and 20.3% respectively. However, this difference was not statistically significant ($p = 0.223$). (Table II) In the early LC group the reasons for conversion were the presence of acute inflammatory changes (gangrene, phlegmon or empyema) that made it difficult to identify the structures of the Calot's triangle (ten patients), and the presence of extensive intra-abdominal adhesion secondary to previous abdominal opera-

tion (one patient). In the delayed LC group the reasons for conversion were acute inflammatory changes (two patients), the inability to define the anatomy of the Calot's triangle due to fibrosis (six patients), intra-abdominal adhesion (two patients), detection of gallbladder cancer, not identified preoperatively (one patient), and common bile duct injury (one patient) (Table III).

Complications

Sixteen complications occurred in our series, one intraoperative and fifteen in the postoperative phase. The overall complication rate was 17.5%. The only intraoperative complication that occurred in the delayed LC group was a type D bile duct injury according to the Strasberg's classification. This injury was detected intraoperatively and repaired, after conversion to laparotomy, with a 5/0 absorbable monofilament suture. The postoperative course was uneventful. In the early LC group postoperative complications occurred in 6 patients. There were 4 wound infections, 1 urinary tract infection, and 1 case of prolonged fever. In the delayed LC group 9 postoperative

Table II. Comparison of outcomes and total hospital costs betweeen the two study groups.

	Early LC group (n = 32)	Interval-delayed LC group (n = 59)	p value
Operative time: min ± SD	54.8±19.9	47.8±25.0	0.174
Conversion rate (n)	34.3% (11)	20.3% (12)	0.223
Complications rate (n)	18.7% (6)	16.9% (10)	0.941
Postoperative stay: days (range)	4.3 (3- 11)	3.8 (2- 15)	0.437
Total hospital stay: days (range)	6.3 (3- 13)	10.5 (7- 23)	0.000
Total hospital costs: Euro	4171	6041	0.000

Table III. Reasons for conversion from laparoscopic to open cholecystectomy.

	Early LC group	Interval-delayed LC group
Flogosis	10 (90.9%)	2 (18.2%)
Adhesions	1 (9.1%)	1 (9.1%)
Fibrosis of triangle of Calot	–	6 (54.5%)
CBD injury	–	1 (9.1%)
Cancer	–	1 (9.1%)

complications occurred: two patients suffered from prolonged ileus, 6 patients had wound infections, and one patient had pneumonia. The complication rate was 18.7% in the early LC group and 16.9% in the delayed-interval LC group (Table II). There wasn't any statistically significant difference between the two group in terms of complication rate ($p = 0.941$), wound infection ($p = 0.763$), prolonged ileus ($p = 0.538$), urinary tract infection ($p = 0.351$), pulmonary infection (p value 1.000), prolonged fever (p value 0.351), and iatrogenic biliary lesion (p Value 1.000). Prolonged ileus was defined as a postoperative ileus lasting more than 5 days. No mortality and 30 days re-admissions were recorded (Table IV).

Hospital Stay

The mean postoperative stay for patients who underwent early LC was 4.3 (range 3-11) days, as opposed to the delayed LC group, which had a postoperative stay of 3.8 days (range 2-15). The difference of 0.5 days was not statistically significant ($p = 0.437$; 95% CI, -0.8-1.8 days). The mean total hospital stay was 6.3 (range 3-13) days and 10.5 (range 7-23) days for early LC and delayed LC group, respectively, with a statistically significant difference of -4.2 days ($p < 0.0001$; 95% CI, -5.7 to -2.5 days) (Table II).

Costs

Mean total cost was 4171 Euro for the early LC group and 6041 Euro for the delayed LC group, with a difference of -1870 Euro, that was statistically significant ($p < 0.0001$; 95% CI, -2689 Euro to -1051 Euro) (Table II).

Discussion

The benefits of early LC in treatment of acute cholecystitis reported by randomized prospective studies are clearly evident and confirmed by several meta-analyses[13,15,16]. The more recent meta-analysis of randomized trials published in 2013 by the Cochrane Collaboration[17] showed no significant difference between early LC and delayed-interval LC in terms of bile duct injuries, other serious complications, rate of conversion, and operative time, with a 4 days shorter hospital stay in the early group compared to the delayed group. On the basis of these data, early LC is supported by many expert groups[18,19], however the practice pattern differs significantly. A survey of Japanese surgeons[12] showed that 42% of patients with acute cholecystitis underwent an early LC. In the United Kingdom[13] 20% of the surgeons perform a LC during the acute attack and only 15% of patients with acute cholecystitis are operated on, during the same admission. In the United States[14], about 20% of patients with acute cholecystitis are treated with an early operation. Our data are consistent with those reported in literature. About 35% of patients with acute cholecystitis were treated with an early LC. There were a no significant difference between early LC group and delayed LC group in terms of operative time, conversion rate, major and minor complications, and postoperative stay, with a significant shorter total hospital stay by 4 days in

Table IV. Complications.

	Early LC group	Interval-delayed LC group	*p* value
Complications	6	10	0.941
Biliary duct injury	–	1	1.000
Wound infection	4	6	0.763
Prolonged ileus	–	2	0.538
Pulmonary infection	–	1	1.000
Urinary tract infection	1	–	0.351
Prolonged fever	1	–	0.351

favour of the early LC group. Along with the results of other studies[10,11,15,17], our analysis revealed that early LC is a better cost-effective procedure, with a significant lower cost of 1870,00 Euro.

In addition to the described benefits, early cholecystectomy is also favoured on the basis of the considerable risk for recurrent symptoms if cholecystectomy is delayed. In this study, about 25% of patients discharged after conservative treatment experienced a recurrence of symptoms during the interval period before cholecystectomy. Five patients (8.4%) required re-admission and emergency LC. In a meta-analysis published in 2006[15], failure of conservative treatment requiring emergency cholecystectomy occurred in 23% of patients in the delayed group. The recent study of Gurusamy et al.[13] showed that 17.5% of patients randomized to delayed LC suffered non-resolving or recurrent symptoms.

An important concern regarding LC for treatment of acute cholecystitis is the increased risk for bile duct injuries. Acute cholecystitis is considered a predisposing factor for iatrogenic bile duct lesion[18,19]. Some observational studies have suggested a greater number of injuries with early surgery[22,23]. However, a meta-analysis of randomized trials has not confirmed this finding. In our series, the only iatrogenic bile duct injury occurred in the delayed LC group. A recent large Canadian population-based study[24] showed that early LC was associated with a lower risk of major bile duct injury than delayed LC, with a risk ratio of 0.53. The authors concluded that the development of fibrosis in and around the Calot's triangle following resolution of the initial acute inflammatory changes due to cholecystitis, was a reasonable pathologic explanation supporting a casual association between delayed surgery and a higher risk of major bile duct injury. In order to minimize the risk of bile duct injury is mandatory to achieve the critical view of safety (CVS)[25]. A cephalic traction on the fundus of gallbladder, and lateral and caudal traction on Hartmann's pouch should be applied to place the cystic duct perpendicular to the common bile duct. Dissection should be started with an incision on the peritoneum of the infudibulum of the gallbladder. Then, dissection should be performed alternately on the lateral and the medial aspects of the gallbladder toward the cystic duct; to avoid thermal damage, monopolar elettrocautery should be used cautiously, and with short bursts. The triangle of Calot should be dissects carefully from the fat tissue, small vessels, and lymphatic. Visualization of the CVS is completed when only two tubular structures, the cystic duct and the artery, are identified joining the gallbladder and the liver can be seen through the space between these structures. The surgeon should proceed with ligation only when the cystic duct and artery are clearly identified and encircled. Subtotal cholecystectomy should be applied when the anatomic features of triangle of Calot are poorly indentified. During dissection of the gallbladder from the liver bed, the surgeon should carefully look for accessory ducts. Conversion should be considered when the surgeon does not obtain a clear view of the CVS.

Another issue of concern is the increased rate of conversion from laparoscopic to open cholecystectomy in acute cholecystitis. Acute cholecystitis is considered an independent risk factor for conversion[26,27]. Conversion results in longer operative time and hospital stay, and is associated with increased morbidity[28]. Conversion to open, however, should not be considered a failure or a complication of laparoscopic procedures, but rather a modification of the procedure required to avoid the occurrence of injuries or complications. In the first years of the laparoscopic era, conversion rates up to 35% were reported for early LC[11] and it was therefore argued that delayed surgery may be a better treatment option for acute cholecystitis. As previously mentioned, randomized trials and meta-analysis have not confirmed this hypothesis, showing no significant difference between the two approaches with regard to conversion rate. In the present study the conversion rate was higher in the early LC group (34.4%) than in the delayed LC group (20.3%), but the difference was not statistically significant. The reasons for conversion, however, were different. In the early LC group, the most frequent cause for conversion was the presence of acute inflammatory changes of the gallbladder that made difficult to obtain a clear CVS. In the delayed LC group the most frequent cause was the inability to define the anatomy of the triangle of Calot due to fibrosis. In this study the overall conversion rate was 25.2%. Although our conversion rate seems to be high, it reflects our concerns for safety when a laparoscopic approach is used for treatment of acute cholecystitis, and we think it will decline with increasing experience. The main limitation of this study is its retrospective nature. However, both

group analyzed are homogeneous with respect to demographic characteristics and severity of disease on first admission thus reducing the flaws of the statistical analysis.

Conclusions

Early laparoscopic cholecystectomy and delayed laparoscopic cholecystectomy can be regarded as safe procedures for the treatment of acute cholecystitis, with a comparable operative time, major and minor complication rate, and postoperative stay. Early laparoscopic cholecystectomy is associated with a shorter total hospital stay and is more cost-effective, and therefore should be considered as the preferred approach in treatment of acute cholecystitis.

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Conflict of Interest

Goffredo Arena is a surgical consultant for Covidien, Canada. All authors declare that there are no conflicts of interest.

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