

Emergency Vs. Delayed Cholecystectomy in Acute Cholecystitis- Hospital based Prospective Randomized comparative study

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Abstract-

Background: Acute cholecystitis is a very common gastrosurgical emergency. The timing of laparoscopic cholecystectomy (LC) in cases of acute cholecystitis is still a matter of debate. In general, delayed LC is preferred because of higher morbidity and conversion rate when LC is performed in acute cholecystitis.

Aim and objective: To compare the various parameters and outcomes between early and delayed laparoscopic cholecystectomies with safety and feasibility evaluation.

Materials and methods: A prospective, randomized controlled, interventional study was conducted from October 2021 to December 2022. Patients with a diagnosis of acute cholecystitis post-randomization were assigned into the early group ($n = 50$; LC within 72 hours of admission) and the delayed group ($n = 50$; initial conservative treatment followed by delayed LC 6–12 weeks later). The primary outcome measures were intraoperative and postoperative complications (bile duct injuries, bile leak, and wound infection), morbidity, mortality conversion, and length of hospital stay. The secondary outcome measures were the mean duration of surgery, the mean blood loss, other complications (subhepatic collection, postoperative pneumonia), and unsuccessful nonoperative management.

Results: In our study, the conversion rate in early laparoscopic cholecystectomy (ELC) group was 5 (10%) and delayed laparoscopic cholecystectomy (DLC) group was 7 (14%), respectively. The mean operative time was 77.30 ± 20.078 vs 66.94 ± 29.501 minutes; $p < 0.001$ in ELC and DLC groups, respectively; the mean blood loss was 82.60 ± 59.67 vs 65.40 ± 74.21 ; $p < 0.007$ in ELC and DLC groups, respectively.

Conclusion: Early cholecystectomy is safe and feasible in patients with acute cholecystitis.

Keywords: Acute cholecystitis, Cholecystectomy, Early cholecystectomy, Laparoscopic.

INTRODUCTION

For symptomatic cholelithiasis, laparoscopic cholecystectomy (LC) is a gold standard treatment. The timing of LC in acute calculus cholecystitis is still a matter of considerable debate and related controversies. Before the laparoscopic era, randomized studies revealed that the strategy of early open cholecystectomy within 7 days of the onset of symptoms was preferred as it provided shorter hospital stay and reduced potential risk of complications, such as pancreatitis, gangrenous, or emphysematous cholecystitis, without an increase of postoperative morbidity and mortality.^{1,2}

Till 1990, acute cholecystitis was considered as a contraindication for LC due to increased postoperative morbidity, longer operative time, and higher conversion rate.^{3,4} Consequently, delayed LC (DLC) was preferred after conservative medical treatment on the assumption that inflamed tissue is more vulnerable to laparoscopic intervention and may increase the risk of complications. In the last 15–20 years, as the surgeons excelled in laparoscopic surgeries, with improvement in laparoscopic devices and instruments, even acute cases were considered for LC. Randomized trials and meta-analysis have demonstrated that there was no difference in early LC (ELC) and DLC groups in terms of conversion rate, bile duct injuries, postoperative morbidity, and mortality. Moreover, the ELC group has reported the significantly shortened hospital stay and incurred low cost.⁵

Despite the evidence, DLC is still preferred in clinical practices due to controversial timings for LC in cases of acute cholecystitis.^{6,7} The aim of this study was to compare various parameters and outcomes between ELC and DLC with safety and feasibility evaluation. Outcomes were compared in terms of operative time, intraoperative and postoperative complications, length of postoperative, and total hospital stay between ELC and DLC groups.

MATERIAL AND METHODS

Patients and Methods

This study was a prospective randomized interventional study conducted in the Department of Surgery, at a Medical college hospital, India from October 2021 to December 2022 after approval from the institutional ethical committee. Written and informed consent was obtained from each patient for inclusion in the study, LC, and conversion to open.

Inclusion Criteria

Acute cholecystitis patients admitted to the Department of Surgery of age from 18 to 60 years of either sex, with the American Society of Anesthesiologists (ASA) grade I and II, were included. Right upper abdominal pain, temperature more than 98.6°C , total leukocytes counts (TLC) more than 10,000/dL, or both, and presence of gallstones, thickened and edematous gallbladder (GB) wall

with pericholecystic fluid were considered as diagnostic criteria. Finally, intraoperative findings were reckoned as diagnostic for acute cholecystitis.

Exclusion Criteria

Exclusion criteria included patients with simple biliary colic, obstructive jaundice, choledocholithiasis, gallstone-induced acute pancreatitis, post-endoscopic retrograde cholangiopancreatography, previous biliary tract surgery, previous abdominal surgery, biliary peritonitis, decompensated liver cirrhosis, intra-abdominal abscess, GB polyp, or malignancy, ASA grade III and IV, refusal of surgery, acute cholecystitis in pregnancy, and other contraindication to surgery.

Sample Size Calculation

Sample size calculation was done on the basis of the study of Gutt et al.⁸ in which the overall complications were 14.1 and 40.4% in early group and delayed group, respectively. Considering the 80% power and 5% level of significance, the minimum number of patients required was 40 in each group. The sample size was increased by 10% on the basis of the assumption of nonparametric statistics and dropout, and finally we consider 50 patients in each group.

Randomization

Block randomization with a sealed envelope system was used. We prepared randomly generated ten opaque sealed envelopes assigning A and B in five blocks each: A represented the ELC group and B represented the DLC group. Patients who underwent LC within 72 hours of symptoms were included in the ELC group, whereas LC done after 6–12 weeks were included in the DLC group. These patients were initially managed conservatively (broad-spectrum intravenous antibiotics and intravenous fluid resuscitation) and discharged when asymptomatic.

Data Collection

Data were collected from the index admission of patients, which included age, sex, associated comorbidities, BMI, past history of biliary disease, history of previous abdominal surgeries, duration of symptoms, and clinical examination. Other data included were laboratory, radiological, intraoperative, and postoperative parameters.

LC was performed by conventional four ports operative technique. Certain modifications were done as and when required, like GB decompression, use of laparoscopic specimen retrieval bag, epigastric port enlargement, suction/irrigation, and subhepatic closed suction drain placement.

Conversion to open cholecystectomy was done through right subcostal incision during difficulty in dissection, excessive bleeding, and adhesion of Calot's triangle. The drain was removed after 24–72 hours postoperatively. Surgical procedures were performed by surgeons having more than 5 years of experience of LC in a single surgical unit. All patients were allowed to eat and drink 6–8 hours postsurgery, in the absence of nausea or vomiting. Intramuscular diclofenac injection was advised for pain relief. Antibiotics were prescribed as per hospital protocol.

Primary outcome measures were conversion to open surgery, mean duration of hospital stay, complications (bile leak, bile duct injuries, and postoperative wound infection), and mortality. The secondary outcome measures were the mean duration of surgery, intraoperative blood loss, other complications (subhepatic collection, postoperative pneumonia), and unsuccessful nonoperative management.

Statistical Analysis

The data were entered in an Excel spreadsheet and analyzed by the Statistical Package for Social Sciences (SPSS) version 21.0. Categorical variables were presented in number and percentage (%). Continuous variables were presented as mean \pm standard deviation (SD) and median. Normality of data was tested by the Kolmogorov–Smirnov test. Quantitative variables were compared using the unpaired t-test/Mann–Whitney test while qualitative variables were compared using the Chi-square test/Fisher's exact test. A p value of <0.05 was considered statistically significant.

RESULTS

A total of 145 concordant patients were assessed for the study, out of which 45 patients were excluded as per criteria. The comparison group had 50 patients each with post-randomization at the final analysis. As shown in [Table 1](#), both groups were comparable and equally distributed in respect of age, sex, body mass index, laboratory reports, radiological parameters, and comorbidities. There was no failure of conservative treatment in the delayed group which required urgent surgery. Various parameters were observed and evaluated pre-, intra-, and postoperatively.

Table 1: Clinical data and laboratory results of patients

Variables	ELC group (N = 50)	DLC group (N = 50)
Age (mean), years	41.0 \pm 12.29	38.04 \pm 11.38
Sex: Male	8 (16)	10 (20)
Female	42 (84)	40 (80)
BMI (kg/m ²)	23.38 \pm 2.72	22.93 \pm 2.78
ASA	I/II	I/II

Table 1: Clinical data and laboratory results of patients

Variables	ELC group (N = 50)	DLC group (N = 50)
Clinical feature		
Pain duration, mean (hours)	25.0 ± 9.539	23.24 ± 7.305
Frist attack	34 (68)	36 (72)
Previous biliary symptoms	16 (32)	18 (36)
Previous antibiotics administration	5 (10)	49 (98)
Temperature (°F), mean	99.8 ± 0.1	99.9 ± 0.2
Nausea/vomiting	49 (98)	49 (98)
RHC pain	50 (100)	50 (100)
Murphy's sign	45 (90)	40 (80)
Laboratory finding		
Hemoglobin gm/dL	12.886 ± 1.15	12.45 ± 1.17
White blood cells(N*10 ³)	13.04 ± 2.59	12.20 ± 2.49
Serum bilirubin(mg/dL)	0.867 ± 0.22	0.740 ± 0.14
SGOT (IU/L)	46.66 ± 18.28	36.96 ± 11.41
SGPT (IU/L)	47.92 ± 19.97	38.16 ± 14.14
ALP (IU/L)	215.38 ± 90.07	179 ± 52.98
Serum amylase (IU/L)	55.16 ± 22.12	36.58 ± 8.79
Comorbidities		
Diabetes mellitus	3 (6)	3 (6)
Hypertension	5 (10)	6 (12)
COPD	1 (2)	1 (2)
Hypothyroidism	1 (2)	2 (4)

RHC, right hypochondrium; Figure in parentheses denotes percentage

The physical examination findings were similar in comparison groups. The pain duration, first symptoms, and previous biliary symptoms were comparable in both the groups. The use of antibiotics was significantly more common in the DLC group (49; 98%) as compared to the ELC group 5 (10%); $p < 0.001$. All patients had pain in right hypochondrium. Murphy's sign was positive in 45 (90%) and 40 (80%) of ELC and DLC groups, respectively. Laboratory findings, viz TLC, Kidney function test (KFT), and liver function test (LFT), were comparable in both the groups ([Table 1](#)). The ultrasound findings were also comparable in both the groups ([Table 2](#)).

Table 2: USG findings for the patients

Characteristics/parameters	ELC group (n = 50)	DLC group (n = 50)
Gallstones: Single	7 (14)	5 (10)
Multiple	43 (86)	45 (90)
Thickened GB	48 (96)	42 (84)
Distended GB	46 (92)	47 (94)
Pericholecystic fluid	22 (44)	20 (40)
Murphy's sign	45 (90)	46 (92)

The mean intraoperative time and the mean intraoperative blood loss were significantly higher in the ELC group. The mean operative time was 77.30 ± 20.078 vs 66.94 ± 29.501 minutes; ($p < 0.001$) and the mean blood loss 82.60 ± 59.67 vs 65.40 ± 74.21 mL; ($p < 0.007$) in ELC and DLC groups, respectively. No patients in the comparison groups required blood transfusion. Conversion to open cholecystectomy and achievement of critical view of safety were comparable in both the groups. The adhesion in Calot's triangle, adhesion with the inferior surface of the liver, tensely distended GB, and mucocele/pyocele were more common in the ELC group ($p < 0.010$) ([Table 3](#)).

Table 3: Intraoperative findings, modification, and complications

	ELC group (n = 50)	DLC group (n = 50)
Intraoperative finding		
Mean operative time (minute)	77.30 ± 20.078	66.94 ± 29.501
Mean blood loss (mL)	82.60 ± 59.67	65.40 ± 74.21
Conversion to open Cholecystectomy	5 (10)	7 (14)
Critical view of safety achieved		
Yes	45 (90)	43 (86)
No	5 (10)	7 (14)
Adhesion in Calot's triangle	39 (78)	24 (48)
Adhesion with inferior surface of liver	24 (48)	7 (14)
Tensely distended gallbladder (GB)	36 (72)	14 (28)
Contracted GB	0 (0)	6 (12)
Turbid bile	8 (16)	3 (3)
Perforated GB	2 (4)	0 (00)
GB gangrene	3 (6)	0 (00)
Mucocele/pyocele	32 (64)	10 (20)
Operative modifications		
GB decompression	40 (80)	20 (40)

Table 3: Intraoperative findings, modification, and complications

	ELC group (n = 50)	DLC group (n = 50)
Endo-bag retrieval of GB	19 (38)	9 (18)
Epigastric port enlargement	10 (20)	11 (22)
Suction/irrigation	44 (88)	23 (46)
Subhepatic drain	40 (80)	21 (42)
Intraoperative complications		
Spillage of bile/stone	4 (8)	3 (6)
GB perforation	3 (6)	2 (4)
Cystic artery bleeding	3 (6)	6 (12)
Liver bed bleeding	00	1 (2)
Accessory bile duct leak	00	1 (2)
Bowel injury	00	1 (2)

More operative modifications were required in the ELC group, viz GB decompression, laparoscopic bag retrieval of a specimen, suction/irrigation, and subhepatic drain placement. No significant difference was noted in both the groups with intraoperative complications, like bile/stone spillage, GB perforation, and cystic artery bleed. No bile duct injury occurred in both the groups. One patient in the DLC group had an accessory bile duct leak, which was identified by magnetic resonance cholangiopancreatography and managed conservatively ([Table 3](#)).

Multiple causes were found in both the groups for conversion as shown in [Table 4](#), which were comparable and statistically not significant. Cholecysto-colonic fistula and Mirizzi syndrome were found in one patient of the DLC group.

Table 4: Causes of conversion to open cholecystectomy

Cause	ELC group (n = 5)	DLC Group (n = 7)
Dense adhesion	5 (10)	6 (12)
Difficulty in identifying Calot's	4 (8)	6 (12)
Bleeding	5 (10)	6 (12)
Technical difficulty	4 (8)	6 (12)
Cysto-colonic fistula	0	1 (2)
Mirizzi syndrome	0	1 (2)

Total hospital stay was 4.46 ± 1.32 vs 6.0 ± 2.83 days in ELC and DLC groups, respectively. The difference was statistically significant $p < 0.002$. Statistically no difference was found in subhepatic drain duration and postoperative hospital stay. The requirement of postoperative analgesia and use of antibiotics were comparable in both the groups. The postoperative complications in terms of pulmonary, wound infections, intra-abdominal infections, and bile leak were similar in both the groups ([Table 5](#)). Feature of acute cholecystitis on histopathological examination was more prevalent in the ELC group ($p < 0.001$) ([Table 6](#)).

Table 5: Postoperative variables and complications

Variables	ELC group	DLC group
Postop hospital stay (days)	1.96 ± 1.24	2.46 ± 2.54
Total hospital stay (days)	4.46 ± 1.32	6.0 ± 2.83
VAS		
Day 1	3.60 ± 0.67	3.74 ± 0.52
Day 2	1.32 ± 0.86	1.40 ± 0.96
Postoperative analgesia		
12 hours	42 (84)	46 (92)
24 hours	15 (30)	19 (38)
Duration of antibiotics (days)	2.98 ± 2.93	2.90 ± 3.3
Complications N (%)		
Pulmonary complications	1 (2)	3 (6)
Bile duct injuries	00	00
Wound infections	2 (4)	3 (6)
Intra-abdominal infections	1 (2)	00
Bile leak	00	1 (2)

DISCUSSION

On ultrasound screening, gallstones are found in 5 to 20% of the adult population.⁹ The gallstone-related complications, such as acute cholecystitis, develop in 1 to 4% of patients.¹⁰ Acute cholecystitis is the most frequent cause for hospitalization among all gastrointestinal diseases.¹¹ For symptomatic cholelithiasis, LC is “the gold standard” for definite treatment. LC in acute cholecystitis is still considered a challenging procedure due to anticipated anatomical difficulties. Traditionally, elective cholecystectomy is preferred after weeks of strict medical therapy, called “cool down”. In the interval period, more than 20% of these patients do not respond to medical treatment or develop recurrent cholecystitis. This leads to multiple readmission and emergency surgery in more than 50% of patients.¹²

For good outcomes, “the timing of surgery” is of great significance. Preferably, the surgery should be performed promptly after the presentation at hospital. The norm of early surgery within golden 72 hours of symptoms in acute cholecystitis has been advocated, which has been proven safe and feasible.^{13,14}

Merely, such early surgery in clinical practice is not always possible due to logistic difficulties and the availability of experienced surgeons in an emergency. The timing for surgery in the early group varies from 72 hours to 7 days, whereas it may vary from 6 to 12 weeks in the delayed group. We performed LC in the ELC group within 72 hours of symptoms whereas in the DLC group, 6–12 weeks after the symptoms. The bile duct injury remains the most important entity for comparison of the outcome, safety, and feasibility of the study.

The rates of minor bile duct injury and major bile duct injury after laparoscopic surgeries are 0.1–1.7% and 0.1–0.9%, respectively.¹⁵ Well-known risk factors for bile duct injuries are obesity, local inflammation, and perioperative bleeding.¹⁵ No patient in our study had bile duct injury.

Similar findings were reported by Kolla et al.,¹⁶ Gul et al.,¹⁷ Sánchez-Carrasco et al.¹⁸ The meta-analysis by Menahem et al. suggested that the rate of major bile duct injury was insignificant in both ELC and DLC groups [2/247, 0.8% vs 2/223, 0.9%; relative risk (RR), 0.96; 95% confidence interval (CI), 0.25–3.73; $p = 0.950$].¹⁵ Similarly, Skouras et al.¹⁹ found no significant difference in the incidence of postoperative complications and the bile duct injury ratio (0.5% for the ELC group vs 1.4% for the DLC group; $p = 0.54$).¹⁹

In our study, the mean blood loss was significantly more in ELC than DLC group, because of inflammatory reactions leading to neovascularity, adhesions around GB, and Calot's triangle in the acute phase of acute cholecystitis (82.60 ± 59.67 vs 65.40 ± 74.21

mL; $p < 0.007$). However, no patient required blood transfusion. Similarly, recent studies reported more blood loss in the ELC group.^{17,18}

The higher conversion rate obviates the advantage of ELC. However, various meta-analysis of randomized studies showed that conversion to open surgery in ELC and DLC groups ranged from 12.7 to 20.7% and from 13.9 to 23.6%, respectively.^{15,20}

There were different reasons for conversions in the comparison groups:

ELC group: The edematous, friable, and distended GB perforated when grasped and bleeding.

DLC group: Contracted GB, dense adhesions, and difficult exposure obscured the Calot's triangle due to chronic inflammation. Our study found the conversion rate 5 (10%) and 7 (14%) in ELC and DLC groups, respectively.

The increased duration of operation from 10 to 30 minutes for the ELC group as compared to the DLC group was demonstrated in studies.²¹ We found the duration of operation was 77.30 ± 20.07 and 66.94 ± 29.5 minutes in ELC and DLC groups, respectively ($p < 0.001$). The significant increased operative time in the ELC group was due to inflammation, edema, thickened and distended GB, adhesions, and bleeding, which required more operative modifications. The most common technical modifications included the following: (i) GB decompression to facilitate better grasping and exposure of Calot's triangle. (ii) The liberal use of suction and irrigation devices required for dissection and control of bleeding. (iii) The use of laparoscopic specimen retrieval bag for stone and GB extraction to avoid port-site infections.¹⁶ Reversely, Abdelkader and Ali, Kohga et al., and Chhaged et al. have demonstrated that the DLC group had more operative time. The increased operative time in the DLC group may be because of maturation of the surrounding inflammation leading to fibrosis, dense adhesions, and scarring and contracted GB, which makes dissection difficult.

The requirement of subhepatic drain was more common in the ELC group due to inflammation and exudates. The placement of postoperative drainage tube was significantly more frequent in ELC group than DLC group as demonstrated by Menahem et al.¹⁵ [77.8 vs 37.3%; odds ratio (OR), 6.18; 95% CI, 3.19–11.99; $p < 0.001$].¹⁵ In our study, the subhepatic drain required was 40 (80%) and 21 (42%) in ELC and DLC groups, respectively ($p < 0.001$).

The risk of postoperative wound infection varies in studies. The risk of postoperative infection was twice as high in the DLC group as in the ELC group, as reported by Sánchez-Carrasco et al.¹⁸ (OR = 1.98; 95% CI 1.78–2.17; $p < 0.05$),¹⁸ whereas Gurusamy et al.²¹ reported a higher proportion of infections in the ELC group. We found that the wound infection was comparable in both the groups ($p = 0.423$).

The overall complication rates were significantly less in the ELC group or comparable with the DLC group as in various studies. A meta-analysis suggests that overall morbidity was statistically insignificant in both groups.^{15,19}

Our study indicates that the DLC group had a higher rate of overall complications than the ELC group. However, these complications were minor and statistically insignificant ($p = 0.423$). The comparison groups had no mortality. The ELC group has a significantly lower mean total length of hospital stay as compared to the DLC group. Skouras et al. reported that the median total length of hospital stay was shorter in ELC group by 4 days ($p < 0.001$).¹⁹ Further, Menahem et al.¹⁵ found that the mean total length of hospital stay was 5.4 vs 9.1 days in ELC and DLC groups, respectively ($p < 0.001$).¹⁵ Repeated admission for recurrent symptoms and a higher rate of conversion have led to more hospital stays. Studies showed that the total hospital stay was more in DLC group, except in the studies of Kolla et al.¹⁶ and Roulin et al. We found that the mean total hospital stay was comparatively less in ELC group as compared to DLC group for acute cholecystitis ($p < 0.002$).

Studies showed that ELC was more economical and resulted in a better quality of life. This may be due to shorter hospitalization and devoid of conservative treatment in the ELC group. We are working in the government-funded hospital; the cost of treatment was therefore not assessed as it was free.

Moreover, meta-analysis of recent randomized studies points toward decreased incidence of postoperative wound infection, shorten total hospital stay, incurred low cost, increased mean duration of surgery, patient's satisfaction, quality of life, and decreased lost working days in the ELC group. Furthermore, no differences in bile leakage, bile duct injuries, morbidity, and conversion to open surgery were reported.^{22,23,24}

CONCLUSION

ELC in acute cholecystitis is safe and feasible in comparison to elective cholecystectomies. ELC avoids recurrent symptoms due to multiple episodes of acute cholecystitis and is a definite treatment for cholecystitis in failed conservative management. Moreover, ELC is more advantageous as it provides patients safety and lesser hospital stay. It has economic benefits due to lesser morbidity and mortality.

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