

A Comparative Study of Early Versus Delayed Laparoscopic Cholecystectomy in Acute Cholecystitis and its Associated Complication

Ravi Kumar¹, Saikalyan Guptha Achuta², S Arjun³, DV Chalapathi⁴, Jay Prakash⁵, Gogineni Tarun Chowdary⁶

¹Associate Professor ²Assistant Professor ³Senior Resident ⁴Professor, Department of Surgery, ⁵Assistant Professor, Department of Anaesthesiology and Critical Care Medicine, ⁶Junior Resident, Department of Oncosurgery, Vydehi institute of Medical Science & Research Centre, Bengaluru, Karnataka 560066, India.

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Abstract

Context: Acute cholecystitis is a common surgical problem and was usually treated with conservative management followed by a delayed laparoscopic cholecystectomy after an interval of 6 to 8 weeks. Our aim was. *Aims:* To compare the efficacy of Early laparoscopic Cholecystectomy (ELC) with delayed laparoscopic cholecystectomy (DLC) in patients of acute cholecystitis, and also to assess the complications between the two. *Settings and Design:* This study was a prospective randomized controlled trial in Vydehi Institute of Medical Sciences and Research Centre from January 2015 to June 2016 that was conducted on 50 consecutive patients diagnosed to have acute cholecystitis. *Methods and Material:* 25 patients underwent immediate laparoscopic cholecystectomy within 24-72 hours of admission and 25 patients underwent a delayed laparoscopic cholecystectomy after 6-8 weeks of the initial episode. Parameters related to surgery, complications and postoperative period were observed, tabulated and analysed. *Statistical analysis used:* The demographic variables were represented in percentage and continuous variables were represented using Mean and Standard Deviation. Possible associations were found out using chi-square test / Fisher exact test. *Results:* In the early surgery group, intraoperative complications noted

were adhesions (16%), bleeding (16%), GB perforation (8%) and bile duct injury (4%). In late surgery group, complications that were noted were adhesions (68%), bleeding (40%), and GB perforation (12%), bile duct (12%) injury. Postoperatively, complications seen in early surgery were bile leak (4%), bile leak (4%) and postoperative jaundice (4%) which included SSI for 2 patients. In late surgery, postoperative complications seen were bile leak (16%) and jaundice (12%), again not statistically significant. Duration of surgery in ELC patients was statistically higher at 76.16 ± 23.38 minutes than that in LLC group which was 116.48 ± 23.14 minutes. Mean hospital stay was more in LLC when compared with ELC (6.48 days vs 3.84 days). *Conclusions:* Early laparoscopic surgery had similar intraoperative and postoperative complications compared to delayed surgery in acute cholecystitis, but was associated with a shorter surgery and lesser stay in the hospital.

Keywords: Early laparoscopic cholecystectomy; Delayed laparoscopic cholecystectomy; Late laparoscopic cholecystectomy; Acute cholecystitis.

Introduction

Acute cholecystitis is a common general surgical emergency scene in various setting from the district hospital to specialized tertiary level institutions [1]. Acute cholecystitis is due to gallstones in up to 90% of patients the reported prevalence of gallstones is up to 10% in the adult eastern population and upto 15% in the adult Western population. It is estimated that 20 to 40% of individuals with gallstones will develop associated symptoms and 12% will develop after cholecystitis [2]. It was first performed in 1985

Corresponding Author: Saikalyan Guptha Achuta, Assistant Professor, Department of Surgery, Vydehi institute of Medical Science & Research Centre, Bengaluru, Karnataka 560066, India.

E-mail: drsaikalyanguptha@gmail.com

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by Dr. Erich Muhe. Laparoscopic cholecystectomy has now replaced open cholecystectomy as the first choice of treatment for gallstones and inflammation of the gallbladder unless contraindications are found with the laparoscopic approach. With the development of laparoscopic skills and equipment, laparoscopic cholecystectomy has been reported to have significantly lower complication rates than open cholecystectomy [3].

Now a day, laparoscopic cholecystectomy for acute cholecystitis is mainly performed after the acute episode occurs while conservative therapy, usually antibiotics, and delayed laparoscopic cholecystectomy are still common in many centres [3].

Laparoscopic cholecystectomy is currently the gold standard treatment [4]. Many 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 [5].

However, the timing of laparoscopic cholecystectomy still remains controversial regarding the inflammation, edema, and adhesions during the acute course of the disease [3].

Hence, the proposed study to compare benefits and complications in cases of early vs. delayed laparoscopic cholecystectomy in acute cholecystitis has been carried out in our institution.

Materials and Methods

All patients between the ages 25 to 60 years, presenting with acute cholecystitis to Vydehi Institute of Medical Sciences and Research Centre between January 2015 and June 2016 were chosen for the study that presented with features of acute cholecystitis and was then diagnosed with acute cholecystitis based on clinical and relevant investigations. Inclusion criteria were acute upper abdominal pain with tenderness under the right costal margin; fever more than 37.5°C, leucocytosis, ultrasonographic evidence (thickened gallbladder wall, oedematous wall, and presence of gallstones, pericholecystic fluid collection and ultrasonographic Murphy's sign. Adults diagnosed with acute pancreatitis, cholangitis and Cholelithiasis were excluded from the study.

This was a randomized control study and the

randomization was done by an odd-even method. The sample size of the study was 50 patients. Patients fulfilling the selection criteria were invited to participate in the study and informed consent was taken. Patients were clinically examined and following investigations are done: CBC, renal function test (RFT), liver function test (LFT), random blood sugar, serum electrolytes, serology, urine routine and microscopy, USG abdomen, Chest X-Ray and ERCP (optional). All selected patients were randomized into two groups - one group underwent early laparoscopic cholecystectomy (ELC) and the second group underwent delayed or late laparoscopic cholecystectomy (DLC).

The early operation group was operated on within 24-72 hours of admission (25 patients), whereas the late operation group were started on conservative treatment and were discharged after a complete relief of symptoms and were called for laparoscopic cholecystectomy after 6 or 8 weeks, when the acute episode had subsided (25 patients). All patients were followed up till postoperative discharge of the patient. Outcomes of both the groups were assessed based on the following parameters: Operative time, conversion to open cholecystectomy, adhesions, biliary duct injury, wound infection and hospital stay in days. All collected data was documented, tabulated and analysed.

Statistical analysis: Descriptive statistical analysis was performed using SPSS-16. The demographic variables were represented in percentage and continuous variables were represented using Mean and Standard Deviation. Possible associations were found out using chi-square test/Fisher exact test. The benefits and complications were compared using independent t-test.

Results

Laparoscopic cholecystectomy was performed on 50 patients confirmed as acute cholecystitis from January 2015 to June 2016. The mean age of patients was 40.16 ± 10.15 and 36.92 ± 8.50 in ELC and DLC respectively. In all 48% of patients were female and 52% were male as shown in table 1. They were followed up till postoperative discharge of the patient.

As shown in Table 1, there was no statistically significant difference between mean age and gender in both groups. Table 2 shows the distribution of subjects according to clinical feature, there was no statistically significant difference between clinical features.

Out of 50 laparoscopic cholecystectomies, Pericystic fluid collection seen in 12 patients in ELC whereas in DLC it was seen in 17 patients, gallbladder thickening was similar in both groups. 5 out of 50 cases of laparoscopic cholecystectomy needed to be converted to open cholecystectomy in ELC group while 8 cases were converted to open cholecystectomy in DLC group. Conversion to open cholecystectomy of all these 5 patients was done while performing delayed laparoscopic cholecystectomy i.e. after 72 hours of presentation. Adhesion, bleeding, and perforation were also more in DLC group. Bile duct injury, postoperative wound infection,

bile leak, and postoperative jaundice were less in ELC group. Overall, the majority of these complications were found in delayed cases. Patients having bile leak managed endoscopically, patients who had wound infection managed with antibiotics and dressing. The mean duration of surgery was 76.16 ± 23.39 min in ELC whereas in DLC group it was 116.48 ± 23.14 min. The mean duration of postoperative stay in the early group was 3.84 ± 2.27 days as compared to 6.48 ± 5.77 days in the delayed group. The difference was statistically significant (p value: 0.039). The overall comparison of the patients in the early and delayed groups is shown in Table 3.

Table 1: Demographic characteristics of patients

Characteristics	Early laparoscopic cholecystectomy (N=25)	Delayed laparoscopic cholecystectomy (N =25)	p-value
Mean age in years (\pm SD)	40.16 \pm 10.15	36.92 \pm 8.50	0.227
Gender (%)			
Male	12	12	1.00
Female	13	13	

Table 2: Distribution of subjects according to clinical feature

Fever	Surgery		Total	p-value
	ELC	DLC		
No	13	12	25	0.77
Yes	12	13	25	
Pain abdomen	25	25	50	
Vomiting				0.260
No	13	18	31	
Yes	12	7	19	
Jaundice				0.552
No	23	24	47	
Yes	2	1	3	
Temperature				0.777
Afebrile	13	12	25	
Febrile	12	13	25	
Guarding				1.000
No	23	23	46	
Yes	2	2	4	

Table 3: Clinical outcome

Gallbladder calculi	Surgery		Total	p-value
	ELC	DLC		
Multiple	22	21	43	0.684
Single	3	4	7	
Pericystic fluid collection				0.176
No	13	8	21	
Yes	12	17	29	
Gall bladder wall thickening				1.00
Increased	6	6	12	
Normal	19	19	38	
Conversion to open				0.333
No	20	17	37	
Yes	5	8	13	
Adhesion				

No	22	16	38	0.046
Yes	3	9	12	
Bleeding				
No	22	15	37	0.024
Yes	3	10	13	
Gall bladder perforation				
No	23	22	45	0.637
Yes	2	3	5	
Bile duct injury				
No	24	22	46	
Yes	1	3	4	
Postoperative wound infection				
No	23	20	43	0.221
Yes	2	5	7	
Bile leak				
No	24	21	45	0.157
Yes	1	4	5	
Postoperative jaundice				
No	24	22	46	0.297
Yes	1	3	4	
Duration of surgery (min)	76.16±23.39	116.48±23.14		<0.001
Hospital stay (days)	3.84±2.27	6.48±5.77		0.039

Discussion

Acute cholecystitis develops in up to 10% of patients with symptomatic gallstone disease. In 90-95% of cases, acute cholecystitis is related to gallstone disease and is caused by complete obstruction of the cystic duct. At the time of introduction of laparoscopic cholecystectomy, acute cholecystitis was a relative contraindication, but with increased experience, laparoscopic cholecystectomy has become the gold standard method to treat the condition. A patient with acute cholecystitis would be treated non-operatively and advised an interval cholecystectomy which was usually planned after 6 to 8 weeks. Over years, many randomized controlled trials have demonstrated no difference in morbidity among patients undergoing early versus delayed surgery. In fact, early cholecystectomy reduced overall hospital stay and costs. Early cholecystectomy also decreases the risks of failed conservative management and recurrent bouts of acute cholecystitis in the waiting period.

In our study, 50 patients diagnosed with acute cholecystitis who reported to General Surgery OPD or Emergency Department in Vydehi Institute of Medical Sciences and Research Centre, Bangalore were studied over a period of one year. These patients were divided into 2 groups Group A being patients who underwent early laparoscopic cholecystectomy (less than 72 hours) and group B being patients who underwent late laparoscopic cholecystectomy (more than 6-8 weeks) and the results noted. In our study, the mean age of patients

undergoing early laparoscopic cholecystectomy was 40.16 yrs ± 10.14 yrs and the mean age in late laparoscopic cholecystectomy group was a statistically comparable 36.92 yrs ± 8.49 yrs. 13 female and 12 male patients underwent early cholecystectomy and 13 female and 12 male patients underwent late laparoscopic cholecystectomy respectively. Totally, 48% of subjects were male and 52% of them were female.

In a study by Ann Y. Lee et al. [6], the mean age of patients in the ELC age group were 44 ± 16 yrs while in LLC group was 42 ± 14 yrs and was found to be statistically insignificant as well.

Among the selected patients, mean duration of symptoms in patients undergoing surgery in <72 hrs was 25.86 ± 15.37 hrs while those operated after 72 hrs was 79.18 ± 20.49 hrs. On comparing the symptoms, it was seen that both groups had complaints of pain abdomen in all patients. However, fever was noted in 48%, vomiting in 12% and jaundice in 2% in those who underwent early surgery while 52% patients had a fever, vomiting in 7% and jaundice in only 3% in the other group. Although not statistically significant the number of patients operated after 72 hrs had increased incidence of fever, which may be because of longer duration of symptoms.

A study by Ozkerdes AB et al. [7] showed that both groups revealed similar physical examination findings: all patients had tenderness and defence in the abdominal area (this term means tensing the muscles in the abdominal area, a clinical finding that may present when the internal organs are

inflamed in some manner) and 90% had Murphy sign, and 13.3% in the early and 26.7% in the late laparoscopic cholecystectomy groups had rebound tenderness. Blood count and liver function results were not different between groups.

On comparing the ultrasound findings between the 2 groups in our study, it was noted that gallbladder calculi were observed in all the patients included in the study, pericholecystic fluid collection was noted in 12 patients in group A and 12 patients in group B and gallbladder wall thickening was noted in 6 of group A and 6 of Group B. Thus, there was signifying no statistical difference between the 2 groups.

Ozkerdes AB et al. [7] too had similar observations on ultrasonography - calculi in the gallbladder were detected in all of the patients, and thickness of the anterior gallbladder wall was increased in 23 and 21 patients in the early and delayed laparoscopic cholecystectomy groups, respectively. Other ultrasonography findings were pericholecystic fluid (5 patients each from the early and delayed laparoscopic cholecystectomy groups). In ELC, 16.7% (3 patients) underwent laparoscopy converted to open cholecystectomy due to dense adhesions and excessive intraoperative bleeding; while in LLC 41.2% (7 patients) were converted to open cholecystectomy. Although a higher number of patients required conversion in LLC, the results were not significant. Similar findings were documented by other authors. A study conducted by Menahen B et al. [8] found that the rate of conversion was not significantly different after ELC than after DLC (86/617, 13.9% versus 84/603, 13.9%; RR, 0.97; 95% CI, 0.74–1.28; $p = 0.84$).

Another study conducted by Al-Mulhim AA [9] showed that there were 2 conversions (2.4%) in ELC and 8 in LLC (7%) ($p=0.3$). Obscure anatomy at Calot's triangle was the sole reason for conversion in group 1. The reasons for conversion in group 2 were obscure anatomy at Calot's triangle in 4 patients and difficulty to expose the gallbladder due to severe omental adhesions, inability to grasp the friable gallbladder, liver bleeding, and common bile duct injury in one case each.

In the ELC group, intraoperative complications noted were adhesions (16%), bleeding (16%), GB perforation (8%) and bile duct injury (4%). In LLC, complications that were noted were adhesions (68%), bleeding (40%), and GB perforation (12%), bile duct (12%) injury. Although the percentage of complications was high in the delayed surgery group patients, no statistical significance could be derived between the two groups. A most common

complication in both groups was adhesions followed by bleeding from GB fossa or cystic artery.

Postoperatively, complications seen in early surgery were bile leak (4%), bile leak (4%), and postoperative jaundice (4%) which included SSI for 2 patients. In late surgery, post-operative complications seen were bile leak (16%) and jaundice (12%). A study by Skouras C¹⁰ showed no significant difference was demonstrated in the morbidity, but the DLC group had a larger number of complications (13% in the ELC group versus 29% in the DLC group, $P_{1/4} 0.07$). One of the DLC patients that underwent an urgent interval procedure suffered a common bile duct injury, which was managed with a hepaticojejunostomy. Furthermore, two DLC patients developed post-operative bile leak which was treated conservatively and subsided spontaneously within 7 days.

Duration of surgery in ELC patients was 76.16 ± 23.38 minutes while that in LLC group was 116.48 ± 23.14 minutes. There was a statistical difference between the duration of surgery.

A study by MenahenB et al. [8] showed that the mean total length of hospital stay was significantly lower in patients who underwent ELC than in patients who underwent DLC (5.4 days versus 9.1 days; $p < 0.001$). Ozkerdes AB et al. [7] found that the total hospital stay was longer (5.2 ± 1.40 versus 7.8 ± 1.65 days; $p=0.04$) in the delayed laparoscopic cholecystectomy group than in the early laparoscopic cholecystectomy group. In our study, too, mean hospital stay was more in LLC when compared with ELC (6.48 days vs 3.84 days) and there was a statistically significant difference found.

Guruswamy K [11] performed a meta-analysis of 5 randomized controlled trials; 223 patients were allocated to the ELC group and 228 to the DLC group. The patients of the ELC group were operated upon within a week after the onset of symptoms and the ones of the DLC group 6-12 weeks after their symptoms had settled. No significant difference was shown in the incidence of postoperative complications and in the bile duct injury ratio (0.5% for the ELC group versus 1.4% for the DLC group; $P_{1/4} 0.54$). The conversion rate was not significantly different (20.3% for the ELC group versus 23.6% for the DLC group; $P_{1/4} 0.47$). There was, however, a trend of the ELC group towards a greater incidence of postoperative bile leak requiring ERCP, but it did not reach statistical significance ($P_{1/4} 0.05$). The median overall hospital stay was shorter in the ELC group by 4 days ($p<0.001$), but the mean operating time was longer by 15.1 min ($P_{1/4} 0.02$). On the other

hand, the DLC group presented a considerable risk (17.5%) of subsequent emergency surgery during the interval period, for non-resolved or recurrent symptoms with a high rate of conversion to open cholecystectomy (45%).

A study conducted by Zhu B et al. [12] showed that patients undergoing ELC experienced a significantly shorter operating time (44.1 ± 5.32 vs. 66.4 ± 3.05 min, $p < 0.01$). There was no significant difference regarding wound infection rates [1/34 (2.94%) vs. 2/99 (2.02%), $p > 0.05$] or postoperative hospital stay (6.50 ± 1.31 vs. 6.67 ± 0.73 , $p > 0.05$) between groups.

There were no conversions to open cholecystectomy, no biliary tract injury or biliary leak. ELC was less costly than LLC ($6,692 \pm 794$ vs. $8,378 \pm 802$ RMB, $p < 0.05$) and concluded that both ELC and LLC are safe for treating AC, but the operative difficulty of LLC is greater. ELC is superior to LLC as it tends to shorten the total LOS and is less expensive.

A retrospective analysis by Minutolo V et al. [13] 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 demographic 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 the 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 ($p < 0.0001$) and thus concluded by 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.

The meta-analysis of Siddiqui T et al. [14] preceded the one from Guruswamy K [11] and included a combined total of 375 patients. The definitions of the two groups are identical. No significant differences were recorded in the complication rates ($P^{1/4}$ 0.813) or conversion rates ($P^{1/4}$ 0.718) between the two groups. The DLC

group had a significantly shorter operating time ($P^{1/4}$ 0.02) and a shorter postoperative hospital stay ($P^{1/4}$ 0.004), but the ELC group had a significantly shorter overall hospital stay ($P^{1/4}$ 0.0005). There were no significant differences in the bile duct injury rate ($P^{1/4}$ 0.644) or the bile leak rate ($P^{1/4}$ 0.137).

The retrospective cohort study of Casillas R [15] included 173 patients, 71 of which underwent a laparoscopic cholecystectomy within 5 days from the onset of symptoms. The authors demonstrated an advantage of the ELC group on the mean length of hospital stay (2 days for the ELC group versus 5.4 days for the DLC group; $P^{1/4}$ 0.01). The conversion rates were comparable. There was one major bile duct injury in the DLC group which was managed with percutaneous drainage and ERCP with stenting. Interestingly, the authors emphasized on the potentially complex course of management of a ratio of patients of the DLC group that undergo a series of interventions before definitive management.

Uchiyama K et al. [16] carried out a retrospective analysis of 73 patients with acute cholelithiasis who were treated by either early laparoscopic cholecystectomy within 72 hours after initial onset or initial conservative treatment followed by delayed laparoscopic cholecystectomy 4 days later. There were 31 patients in the early group and 42 in the delayed group. There was no significant difference in the rate of conversion from laparoscopic to open surgery (6.4% vs. 20.0%), postoperative complications. However, the early group had significantly shorter operation time (103 vs. 135 min, $p < 0.01$) and shorter postoperative hospital stay (6.2 vs. 9.6 days, $p < 0.01$) and was concluded that, early laparoscopic cholecystectomy within 72 hours of onset of symptoms to decrease conversion rates from laparoscopic to open surgery. This decreased conversion rate results in decreasing the length of operation time and postoperative and total hospital stay.

Agarwal R et al. [17] studied in 50 patients with the diagnosis of acute cholecystitis were assigned randomly to early group, $n=25$ (LC within 24 hrs of admission), and delayed group, $n=25$ (initial conservative treatment followed by delayed LC, 6-8 weeks later). We found in our study that the conversion rate in ELC and DLC was 16% and 8%, respectively, Operation time for ELC was 69.4 min versus 66.4 min for DLC, postoperative complications for ELC were 24% versus 8% for DLC, and blood loss was 159.6 mL early group versus 146.8 mL for delayed group. However, ELC had significantly shorter hospital stay (4.1 days

versus 8.6 days). ELC for acute cholecystitis with cholelithiasis is safe and feasible, offering the additional benefit of shorter hospital stay. It should be offered to the patients with acute cholecystitis, provided that the surgery is performed within 96 hrs of acute symptoms by an experienced surgeon.

A retrospective cohort study carried out by Sánchez-Carrasco M et al. [18] included 1043 patients, with a group of 531 EC cases and a group of 512 DC patients. The following parameters were recorded: postoperative hospital morbidity, hospital mortality, days of hospital stay, readmissions, admission to the Intensive Care Unit (ICU), type of surgery, operating time, and reoperations.

In addition, direct cost savings of implementing an EC program were calculated. The overall morbidity of the EC (early cholecystectomy) group (29.9%) was significantly lower than the DC (delayed cholecystectomy) group (38.7%). EC demonstrated significantly better results than DC in days of hospital stay (8.9 versus 15.8 days), readmission percentage (6.8% versus 21.9%), and percentage of ICU admission (2.3% versus 7.8%), which can result in reducing the direct costs. EC is safe in patients with acute cholecystitis and could lead to a reduction in the direct costs of treatment. In our study limitation were small sample size and short duration of the study.

Conclusion

DLC is associated with a longer total hospital stay but equivalent morbidity as compared to ELC for patients presenting with acute cholecystitis. ELC would appear to be the treatment of choice for patients presenting with ELC.

By a study of the various above mentioned literature in the topic and by comparison of their documented findings, it is clear that our study has findings that are in accordance to most of them.

Key Messages

DLC is associated with a longer total hospital stay but equivalent morbidity as compared to ELC for patients presenting with acute cholecystitis. ELC would appear to be the treatment of choice for patients presenting with ELC.

Conflict of Interest: NIL

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