



TREATMENT OF ACUTE CHOLECYSTITIS EARLY VS DELAYED LAPAROSCOPIC CHOLECYSTECTOMY- A RANDOMIZED STUDY

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ABSTRACT

Background: Laparoscopic Cholecystectomy is the treatment for acute cholecystitis but timing (early and delayed) is controversial. The aim of our prospective, comparative study is to compare relative merits and demerits of early and delayed Laparoscopic Cholecystectomy which was designed in our institution.

Materials and Methods: The study was a prospective, comparative, randomised study and Subjects were selected from patients coming to the OPD and emergency of our department from Feb 2017 to March 2018 with total 100 sample size. Sampling Techniques by the help of computer generated random numbers by the process of randomization.

Results: Mean operative time for group I and group II were 51.4 ± 16.93 , 72.0 ± 25.25 respectively. This difference was again found to be statistically significant. Mean post-operative stay in group I was found to be 2.16 ± 1.78 , while in group II was 3.20 ± 2.96 . This difference was found to be statistically significant. In group I, 10/50 (20%) of patients suffered from shoulder pain, 4/50 (8%) had wound infection post surgery, 1/50 (2%) suffered from UTI, 2/50 (4%) experienced post-operative haemorrhage, post-operative bile leak noticed in 1/2 (2%) of cases. The incidence of above complications were 12/50 (24%), 2/50 (4%), 2/50 (4%), 1/50 (2%) respectively in the delayed group. These differences were found to be statistically not significant. 3/50 (6%) of patients in both groups were re admitted for management of complications.

Conclusion: Early Lap cholecystitis for acute cholecystitis is feasible and safe. Early cholecystectomy is superior to delayed surgery in terms of post operative and overall hospital stay with no increased requirement for readmission. Furthermore, a reduction of total hospital stay is a major economic benefit to the current health care system. We recommended that early Lap cholecystectomy should be the procedure of choice in treating acute cholecystitis.

KEYWORDS : Acute Cholecystitis, Early Laparoscopic Cholecystectomy, Delayed Laparoscopic Cholecystectomy

INTRODUCTION:

Laparoscopic cholecystectomy is the gold standard treatment of cholelithiasis¹. In acute cholecystitis the timing of laparoscopic cholecystectomy is debatable because of the fear of higher rate of morbidity and conversion from laparoscopic cholecystectomy to open cholecystectomy^{2,4}. During the period of acute cholecystitis successful laparoscopic cholecystectomy is associated with an early recovery and shorter hospital stay. In recent era many surgeons are perform early laparoscopic cholecystectomy in acute cholecystitis with safe outcome^{5,6}. The aim of this study was to compare relative merits and demerits of early and delayed (more than 72 hours of symptoms) laparoscopic cholecystectomy in acute cholecystitis with study on immediate and late complications and problems faced during the both forms of surgery. This study has been performed utilizing the facilities available in our hospital. This study aimed to establish a rational timing for laparoscopic cholecystectomy in the management of acute cholecystitis and to determine whether early laparoscopic cholecystectomy should be the procedure of choice in treating acute cholecystitis.

MATERIALS AND METHODS:

Study Design: The study was a prospective, comparative, randomised study and Subjects were selected from patients coming to the OPD and emergency of our department from Feb 2017 to March 2018 with total 100 sample size. Sampling

Techniques by the help of computer generated random numbers by the process of randomization.

Inclusion criteria-

All patients above the age of 12 years, both sexes admitted with acute cholecystitis either from OPD or from emergency of RKMSF in the department of surgery VIMS were considered eligible for the study.

Exclusion criteria-

- Generalized peritonitis or grade 3 acute cholecystitis requiring intervention immediately.
- Previous abdominal surgeries with scars.
- Known coagulation disorder.
- CBD stones with ductal dilatation /acute cholangitis /pancreatitis.
- Pregnancy

Diagnosis was based on the following criteria:

- Acute upper abdominal pain with tenderness under right costal margin.
- Fever $> 37^{\circ}\text{C}$ and/or leukocytosis $> 10 \times 10^9 / \text{l}$.
- USG evidence.

- Presence of gall stone in thickened oedematous gall bladder.

- Positive sonographic Murphy's sign.

Patients were then randomized into either early group or the Interval group according to a computer generated randomization list kept by a third party.

Group I - Early group: Lap cholecystectomy within 7 days of admission.

Group II - Delayed group: Conservatively managed for a period from 7 to 45 days followed by planned lap cholecystectomy.

Patients who failed conservative treatment with worsening clinical signs or those who developed a recurrent attack of acute cholecystitis before the scheduled delayed cholecystectomy were treated with emergency lap cholecystectomy

Statistical Methods

Categorical variables are expressed as Number of patients and percentage of patients and compared across the 2 groups using Pearson's Chi Square test for Independence of Attributes. Continuous variables are expressed as Mean \pm Standard Deviation and compared across the 2 groups using Mann-Whitney U test since the data does not follow normal distribution. The statistical software SPSS version 20 has been used for the analysis. An alpha level of 5% has been taken, i.e. if any p value is less than 0.05 it has been considered as significant.

RESULTS:

This Study included cases of acute cholecystitis admitted from OPD/ Emergency of Vivekananda institute of medical Sciences at Ramakrishna Mission Sevapratishthan from December 2013 to November 2015 meeting the previously mentioned inclusion criteria.

A total of 100 patients admitted with acute cholecystitis were included in this study. 50 of these underwent early laparoscopic cholecystectomy within 7 days of admission, while 50 underwent interval laparoscopic cholecystectomy after initial conservative management.

The mean age of patients included in group I was 42.7 ± 10.75 , while it was 42.08 ± 11.2 in group II. This difference was found to be non-significant. 37 of 50 patients were females (74%) and 13 were males (26%) in group I, while 38 of 50 patients were females (76%) and 12 were males (24%) in group II. This difference was found to be non-significant. 7 of 50 (14%) of patients were diabetic in group I, while 5 of 50 (10%) were diabetic in group II. This difference was found to be not significant. 5 of 50 (10%) of patients in group I were hypothyroid while 7 of 50 (14%) in group II were hypothyroid. This difference was again found to be not significant. 9 of 50 (18%) of patients in both the groups were hypertensive. In group I, 42 of 50 (84%) presented with RUQ pain, 6 of 50 (12%) presented with vomiting, 34 of 50 (68%) had history of dyspepsia, 4 of 50 (8%) had fever, 1 of 50 (2%) had jaundice, 5 of 50 (10%) suffered from biliary colic at the time of admission with acute cholecystitis.

In group II, 44 of 50 (88%) presented with RUQ pain, 6 of 50 (12%) presented with vomiting, 33 of 50 (66%) had history of dyspepsia, 5 of 50 (10%) had fever, 1 of 50 (2%) had jaundice, 5 of 50 (10%) suffered from biliary colic at the time of admission with acute cholecystitis. These differences were found to be non-significant.

Mean Hb was found to be 11.9 ± 2.57 g/dL, mean WBC $13700 \pm 4067.04 \times 10^6/L$, Polymorphs $76.24 \pm 11.43\%$, Total Bil was 0.86 ± 0.45 mg/dL, ALP was 115.72 ± 22.73 U/L in group I at the time of admission. These parameters were 11.76 ± 2.55 g/dL, $12480 \pm 3380.56 \times 10^6/L$, $75.82 \pm 11.4\%$, 0.9 ± 0.39 mg/dL, 115.42 ± 23.3 U/L respectively in group II. This difference was found to be non-significant.

31/50 (62%) patients in group 1 had a single calculus in gall bladder,

while 19/50 (38%) had multiple calculi in group I. 22/50 (44%) had thick walled gall bladder, 20/50 (40%) had peri-cholecystic edema in group I. In group II, 29/50 (58%) had a single calculus, while 18/50 (36%) had multiple calculi in gall bladder, 20/50 (40%) had a thick walled Gall bladder, while 19/50 (38%) had peri-cholecystic edema. The above differences were found to be non-significant.

Intraoperatively, in group I, 33/50 (66%) patients were found to have an empyema of gall bladder, while only 18/50 (36%) in group II had the same. Thus the incidence of empyema was significantly high in the early group compared to the delayed group. Incidence of perforated Gall bladder was 2/50 (4%) of cases in each group.

Severe adhesions were seen in 18/50 (36%) cases in group I, while in 21/50 (42%) cases in group II. This difference was found to be non-significant. In group I, gross adhesions at Calot's noticed in 8/50 (16%) cases, which was significantly higher in the delayed group, ie 18/50 (36%).

None of the patients in the early group had a contracted gall bladder, while 10/50 (20%) in the delayed group were found to have a contracted gall bladder intraoperatively. This difference was found to be statistically significant. Only 3/50 (6%) cases in group I were modified to open cholecystectomy as compared to 10/50 (20%) in group II. This difference was found to be statistically significant.

Mean operative time for group I and group II were 51.4 ± 16.93 , 72.0 ± 25.25 respectively. This difference was again found to be statistically significant. Mean post-operative stay in group I was found to be 2.16 ± 1.78 , while in group II was 3.20 ± 2.96 . This difference was found to be statistically significant. In group I, 10/50 (20%) of patients suffered from shoulder pain, 4/50 (8%) had wound infection post surgery, 1/50 (2%) suffered from UTI, 2/50 (4%) experienced post-operative haemorrhage, post-operative bile leak noticed in 1/2 (2%) of cases. The incidence of above complications were 12/50 (24%), 2/50 (4%), 2/50 (4%), 1/50 (2%) respectively in the delayed group. These differences were found to be statistically not significant. 3/50 (6%) of patients in both groups were re admitted for management of complications.

DISCUSSION:

Amongst a total of 100 patients admitted from OPD or emergency of Ramakrishna mission sevapratishthan with the diagnosis of acute cholecystitis, 50 underwent early, while 50 underwent delayed cholecystectomy.

In the present study, most of the patients undergoing laparoscopic cholecystectomy for acute cholecystitis were females (75 of 100) while the mean age in both groups was around 42.

This is comparable to many previous studies, for example in a study by Sinha R et al⁷ was found that majority of patients undergoing laparoscopic cholecystectomy were in the 4th decade of life.

At the time of first presentation, 86% suffered from Right upper quadrant pain, 12% had vomiting, while only 9% had fever, 2% even had jaundice at presentation even though the patients with dilated CBD and CBD stones were excluded from the study. Our icteric patients were also found to have raised alkaline phosphatase levels along with raised bilirubin, which may have been due to compression of the bile duct by oedematous or fibrosed gall bladder. It could also have been due to concomitant medical liver disease. Only 10 % of patients on further enquiry had previous symptoms of biliary colic, while 67% had a history of on and off dyspeptic symptoms.

In our study, 3 cases of early cholecystectomy had to be converted to open while 10 of delayed cholecystectomy were opened. The reason for conversion was mostly unclear Calot's, distorted gall bladder anatomy, gangrenous gall bladder, and one case of cystic arterial bleed.

This result was comparable to a number of studies. For example, in a study by Sinha R et al⁷, conversion rate was lower (3.48%) for early group, while it was fairly high 19.5% in delayed group.

Some studies have been performed to establish the overall time for operation in acute cholecystitis. Pessaux P et al⁸ found increased conversion rate when the patient delay was more than 48 hours, and it was the same for Willshor PC et al⁹.

We took the patients for early cases who were admitted for acute cholecystitis and treated them until our next laparoscopy OT was available, i.e. within 3 days of admission. Some patients concealed the fact that they had their pain few days before the admission. So we did have some patients who were more than 4 days old symptomatically. Our slightly high conversion rate might have been the reflection of that reason.

In our study, mean operating time was 52 minutes approximately in early, while the same was around 72 minutes in delayed group. During our study we found problems leading to prolongation of operative time to be fibrous tissue and dense adhesions especially around the calot's in the delayed group. Some other studies have also shown similar results where early cases were easier to deal with and the delayed surgeries being prolonged, for example as shown by a study by Garaibeh et al¹⁰.

Average post operative stay for early group was 2.16, while that for delayed group was 3.20. Also, the delayed group had undergone initial conservative indoor treatment which would make the total hospital stay to be even longer. This was surprisingly in contrast to some studies like that by Lai PB et al¹¹ (early 7.6 versus delayed 11.6 days). They might have excluded the average hospitalization or initial conservative treatment of delayed group. Moreover, initial cost of conservative treatment for delayed group puts a significant economical burden to the patients and the government as well. In this developing country, we should think for a relatively cheap method of performing operation and early lap cholecystectomy in acute case may be an answer.

In our study, no significant differences in complication rate in the two groups were noticed. A total of 22 patients experienced post operative shoulder pain (10 from early and 12 from delayed group). UTI developed in 3 cases (1 of early and 2 of delayed). Wound infection occurred in 6 cases in all, 4 of which belonged to the early while 2 belonged to the delayed group. All these were treated with regular dressing and proper antibiotics, 3 of them even required readmission for administration of intravenous antibiotics. Incidence of wound infection was 0.6% in study by Strasberg et al¹² and 2% in study by Garaibeh et al¹⁰. Major bleeding occurred in 1.38% of cases in a study by Strasberg SN¹². Epigastric vessel injury occurred in a single patient of acute cholecystitis and trocar induced aortic injury occurred in a case by Garaibeh et al¹⁰. Cystic arterial injury in our study was treated by converting to open procedure, and was seen in one case in the delayed group. Postoperative haemorrhage through abdominal drain occurred in 1 and 2 patients respectively in early and delayed group.

We, luckily enough did not encounter the complication of bile duct injury. We did have post-operative bile leak in 3 cases (1 of early and 2 of delayed) which was managed by readmission for ERCP and stenting followed by removal of stent after 4 weeks. Bile leak incidence was 0.4% and biliary injury was 0.2% in Strasberg SM et al¹² Study. Different types of bile duct injuries were encountered in a study by Balasara KP¹³ and showed different types of presentation of these patients. Usually CBD injuries were seen in early group (3.3% Vs 1.4%) in a study by Kamal IA Garaibeh¹⁰. Bile duct injury may be detected few weeks after the initial operation, so, meticulous follow up is necessary.

CONCLUSION AND RECOMMENDATIONS:

Early Lap chole for acute cholecystitis is feasible and safe. Early cholecystectomy is superior to delayed surgery in terms of post

operative and overall hospital stay with no increased requirement for readmission. Furthermore, a reduction of total hospital stay is a major economic benefit to the current health care system. We recommended that early Lap cholecystectomy should be the procedure of choice in treating acute cholecystitis.

Table 1: Distribution of clinical parameters in two groups

		GROUP I	GROUP II	p Value	Significance
Sex	FEMALE	37(74)	38(76)	0.810	Not Significant
	MALE	13(26)	12(24)		
DM	NO	43(86)	45(90)	0.538	Not Significant
	YES	7(14)	5(10)		
HYPOTHYROIDISM	NO	45(90)	43(86)	0.538	Not Significant
	YES	5(10)	7(14)		
HYPERTENSION	NO	41(82)	41(82)	1.000	Not Significant
	YES	9(18)	9(18)		
RUQ Pain	NO	8(16)	6(12)	0.564	Not Significant
	YES	42(84)	44(88)		
Vomiting	NO	44(88)	44(88)	1.000	Not Significant
	YES	6(12)	6(12)		
Dyspepsia	NO	16(32)	17(34)	0.832	Not Significant
	YES	34(68)	33(66)		
Fever	NO	46(92)	45(90)	0.727	Not Significant
	YES	4(8)	5(10)		
Jaundice	NO	49(98)	49(98)	1.000	Not Significant
	YES	1(2)	1(2)		
Biliary colic	NO	45(90)	45(90)	1.000	Not Significant
	YES	5(10)	5(10)		
Age Group (in years)	12-19	1	1		
	20-29	3	5		
	30-39	13	12		
	40-49	25	23		
	50-59	6	6		
	60-69	2	2		
	70-99	1	1		
Bilirubin	<2 mg	50	48		
	2-3 mg	0	2		
	>3 mg	0	0		
Hb%	≥11 g/dL	31	30		
	<11g/dL	19	20		
WBC	>10,000 x 10 ⁶ /L	38	37		
	≤10,000 x 10 ⁶ /L	12	13		
Polymorph	≥70%	42	41		
	<70%	8	9		
ALP	>140 IU/L	6	3		
	≤ 140 IU/L	44	47		

Table 2 Distribution of post-operative complication parameters in two groups

		GROUP I	GROUP II	Total	p-Value	Significance
Intraop Empyema	ABSENT	17(34)	32(64)	49(49)	0.003	Significant
	PRESENT	33(66)	18(36)	51(51)		
Intraop Perforated GB	ABSENT	48(96)	48(96)	96(96)	1.000	Not Significant
	PRESENT	2(4)	2(4)	4(4)		
Intraop Severe Adhesions	ABSENT	32(64)	29(58)	61(61)	0.539	Not Significant
	PRESENT	18(36)	21(42)	39(39)		
Intraop Gross Adhesions at Callots	ABSENT	42(84)	32(64)	74(74)	0.023	Significant
	PRESENT	8(16)	18(36)	26(26)		
Intraop Contracted GB	ABSENT	50(100)	40(80)	90(90)	0.001	Significant
	PRESENT	0(0)	10(20)	10(10)		

Conversion to open	NO	47(94)	40(80)	87(87)	0.037	Significant
	YES	3(6)	10(20)	13(13)		
Shoulder Pain	NO	40(80)	38(76)	78(78)	0.629	Not Significant
	YES	10(20)	12(24)	22(22)		
Wound Infection	NO	46(92)	48(96)	94(94)	0.400	Not Significant
	YES	4(8)	2(4)	6(6)		
Urinary Tract Infection	NO	49(98)	48(96)	97(97)	0.558	Not Significant
	YES	1(2)	2(4)	3(3)		
Post-operative Haemorrhage	NO	48(96)	49(98)	97(97)	0.558	Not Significant
	YES	2(4)	1(2)	3(3)		
Postoperative Bile Leak	NO	49(98)	48(96)	97(97)	0.558	Not Significant
	YES	1(2)	2(4)	3(3)		
Readmission	NO	47(94)	47(94)	94(94)	1.000	Not Significant
	YES	3(6)	3(6)	6(6)		

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