

Prospective Comparative Study to Evaluate Intra-Operative and Post-Operative Parameters in Patients Undergoing Laparoscopic Cholecystectomy at Different Intervals after Endoscopic Retrograde Cholangiopancreatography

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Abstract

Background: Choledocholithiasis develops in about 10–15% of patients with gallbladder stones. For patients with cholelithiasis and choledocholithiasis open exploration of the bile duct was the principal treatment for almost 100 years. But with advancement in endoscopic instrumentation and expertise, endoscopic retrograde cholangiopancreatography has evolved as the primary choice of treatment for biliary stones and it is successful in more than 90% of patients. Currently, the most accepted protocol in these cases involves endoscopic clearance of CBD followed at a later date by laparoscopic cholecystectomy. But there is no consensus regarding the exact time gap between these two procedures. Faced with the frequent problem of a 'difficult' laparoscopic cholecystectomy in these cases, the current study was undertaken to attempt to define the ideal time gap between the two procedures for the best possible outcome.

Methods: In this study, 30 patients underwent ERCP with or without sphincterotomy followed at various intervals by elective laparoscopic cholecystectomy. According to these intervals, the patient's data were assigned to one of the two groups : group A (<3 weeks) or group B (>3 weeks). A prospective comparative study was conducted to compare intra-operative parameters and post-operative outcomes of laparoscopic cholecystectomy done at different intervals after endoscopic retrograde cholangiopancreatography to decide upon the optimal timing for the surgery.

Results: Overall rate of partial or subtotal cholecystectomy including all patients was 16.7% with significantly higher in delayed group B. Need for a drain was significantly higher as the interval between ERCP and LC progressed (*p value 0.014*). The mean duration of surgery for group A was 91.75 min and for group B was 127.78 min and this difference was statistically significant at *p value < 0.05*. A lower incidence of post-operative jaundice, bleeding, bile leak and wound infection was observed in group A than in the group B. Overall, statistically significant higher complication rates were observed in late period group B than in the early period group A. Patients in group B had more prolonged post-operative hospital stay with a mean of 5.0 days (SD 3.08).

Conclusion: We recommend early laparoscopic cholecystectomy after ERCP for common bile duct disease could well be an answer in reducing rate of subtotal or partial cholecystectomy, duration of surgery, post-operative complications and post-operative hospital stay.

Keywords: ERCP, laparoscopic cholecystectomy, different intervals.

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Background

Gall-stone disease is almost as old as mankind and with changing lifestyle and dietary habits has contributed to increasing incidence. With wider and easier availability of sonography, it has definitely contributed to the exponential rise in the diagnosis of gall-stone disease. Choledocholithiasis develops in about 10–15% of patients with gall bladder stones. [1]

For patients with cholelithiasis and choledocholithiasis, open exploration of the bile duct was the principal treatment for almost 100 years. But with the advancement in endoscopic instrumentation and expertise, endoscopic retrograde cholangiopancreatography has evolved as the primary choice of treatment for biliary stones [2] and it is successful in more than 90% of patients. [3]

Currently, the most accepted protocol in these cases involves endoscopic clearance of CBD followed at a later date by laparoscopic cholecystectomy. However, endoscopic retrograde cholangiopancreatography can induce complications including biliary pancreatitis, cholangitis and cholecystitis. [4] The use of contrast in endoscopic retrograde cholangiopancreatography also elicits an inflammatory reaction around common bile duct while sphincterotomy leads to ascending bacterial colonization causing inflammation and scarring of the hepatoduodenal ligament leading to adhesions and frozen Calot's triangle. [5] These complications may affect a subsequent laparoscopic cholecystectomy leading to intra-operative difficulties and complications, conversion to open cholecystectomy, partial or subtotal cholecystectomy and longer operative durations. [6]

According to recent studies, better outcomes were observed if laparoscopic cholecystectomy is performed early (<72 hours). [7] Contrarily, some studies claimed that delaying laparoscopic cholecystectomy after ERCP and postponing the operation for about 6 weeks allows gall bladder area to 'cool off' and give time to recover from acute illness, provides for better operating conditions due to less inflammation in gallbladder area. [8,9] On the other hand, some studies found timing of cholecystectomy after endoscopic retrograde cholangiopancreatography has no impact on its outcome. [10]

Most authors share the opinion that laparoscopic cholecystectomy should be performed shortly after ERCP. [9,11,12] But there is no consensus regarding the exact time gap between these two procedures. In our institution a current standard of care for treatment of patients with choledocholithiasis with cholelithiasis is ERCP with or without sphincterotomy and extraction of stones followed by laparoscopic cholecystectomy. Faced with the frequent problem of a 'difficult' laparoscopic cholecystectomy in these cases, the current study was undertaken to attempt to define the ideal time gap between the two procedures for the best possible outcome.

Methodology

This study was designed as a prospective comparative study with an aim of including all patients with cholelithiasis with choledocholithiasis, who fulfil the selection criteria

for the study population and visited General Surgery OPD during study period. Thirty patients were included in the study. The study was conducted on patients presented to General Surgery OPD of Central Referral Hospital, associated to Sikkim Manipal Institute of Medical Sciences, Gangtok between Oct 2018 and April 2020 with follow up of 2 weeks or the period until the patient resumed their normal work. Due approval of the hospital ethics committee was obtained before commencing the study. All patients were randomized between the two groups using a computer-generated random number list and referred to the gastroenterology department for ERCP. All patients returned to the surgery department for laparoscopic cholecystectomy after an interval assigned according to the group. In Group A, laparoscopic cholecystectomy was performed within 3 weeks after ERCP and in Group B, laparoscopic cholecystectomy was performed after 3 weeks (21 days). A prospective comparative study was conducted to compare intra-operative parameters and post-operative outcomes of laparoscopic cholecystectomy done at different intervals after endoscopic retrograde cholangiopancreatography to decide upon the optimal timing for the surgery.

Data Analysis

All the information was gathered and entered into SPSS version 25.0 and analyzed. The demographic variables of the patients included in this study were analyzed using simple descriptive statistics. Parametric data have been measured as means and standard deviations. Non-parametric data are measured as frequencies and percentages. When comparing normally distributed groups, the chi-square test was used. Student's t-test was used to compare the mean values of groups. Pearson correlation was used to correlate between time since ERCP to LC and the mean duration of surgery, hospital stay and return to normal work. A p-value of 0.05 or less was taken as significant.

Results

To investigate potential effects of the time lapse between ERCP and LC; patients were divided into two groups

- Group A : LC was performed within 3 weeks after ERCP
- Group B : LC was performed after 3 weeks (21 days)

Pre-operative parameters (Table 1)

Table 1:

	Group A < 3 weeks (21 days)	Group B > 3 weeks	P
No. of patients	12	18	
Interval between ERCP and LC (Days) (mean \pm SD)	13.33 \pm 6.97	61.22 \pm 42.45	
Age (years)(mean \pm SD)	44.66 \pm 15.48	43.94 \pm 13.70	
Male/Female	1/11	3/15	0.511
Liver function test (mean)			
a) TB	1.14	1.01	0.596
b) GGT	116.85	100.03	0.492
c) ALP	143.23	129.40	0.702
d) AST	28.26	34.81	0.168
e) ALT	36.99	36.77	0.978

- Mean age of the patients in the study was 44.23 years and of which mean age of patients in Group A and B were 44.7 and 43.9 years respectively. Male to female ratio in study group was 1:6.5. The distribution in male and female in Group A was 1:11 while in Group B it was 1:5.
- On USG abdomen cholelithiasis was diagnosed in all 30 patients. CBD dilatation was seen in 19 of the 30 patients (63.33%) and ultrasound was able to pick up CBD stones in 11 patients (36.66%). IHBR dilatation was observed in 21 patients (70%). 23 out of 30 patients underwent MRCP either for doubtful cases or to confirm the diagnosis.
- The mean interval between ERCP and laparoscopic cholecystectomy was 13.33 days for group A with SD of 6.97 and it was 61.22 days for group B with SD of 42.45. The mean interval between ERCP and laparoscopic cholecystectomy for group B other than two patients (outlier) was 49 days with SD of 4.95. In group B mean interval between ERCP and laparoscopic cholecystectomy was more due to delay in follow-up by the patient.

Intra-operative findings (Table 2)

- In group B, higher level of adhesions i.e. fibrous adhesions were encountered more, which could cause more intra-operative difficulties.
- In 16 patients, there was difficulty in Calot's triangle dissection of which, 12 patients belonged to the group B and 4 from the group A.
- Cholecystitis was observed in 4 patients in group A and 12 patients in group B.
- Cystic duct clipping was difficult in 3 patients of group A and 6 patients in group B.
- All patients underwent laparoscopic cholecystectomy with no conversion to open surgery. 5 patients (27.8%) in group B underwent partial or subtotal cholecystectomy. Overall rate of laparoscopic partial or subtotal cholecystectomy including all patients was 16.7%.
- Patients who required sub-hepatic drain were in group B (7 patients i.e. 38.9%) and no patient in group A required drain insertion.
- Mean duration of surgery was 91.75 minutes in group A and 127.78 minutes in group B.

Post-operative parameters (Table 2)**Table 2**

		Groups		P value [χ^2-test]
		A	B	
Adhesion	Absent	3	4	0.256
	Fibrinous	7	6	
	fibrous	2	8	
Difficult Calot's dissection	Absent	8	6	0.073
	Present	4	12	
Cholecystitis	Absent	8	6	0.073
	Present	4	12	
Difficulty in cystic duct clipping	Absent	9	12	0.626
	Present	3	6	
Rate of partial / subtotal cholecystectomy	Absent	12	13	0.046
	Present	0	5	
Conversion to open cholecystectomy	Absent	12	18	*
	Present	0	0	
Need for Drain Insertion	Absent	12	11	0.014
	Present	0	7	
Injury to cystic duct, cystic artery, CBD	Absent	12	18	

	Present	0	0	*
Bowel perforation	Absent	12	18	
	Present	0	0	*
Post-operative complications	Absent	11	10	
	Present	1	8	0.034
Mean duration of surgery (min)		91.75	127.78	0.040[#]
Mean duration of hospital stay (days)		6.67	7.06	0.762 [#]
Mean duration of postoperative hospital stay (days)		2.83	5.00	0.030[#]

- Post-operative complications - In group A, there was one case of post-operative jaundice with no other complications, while in group B there were five cases of bile leak, one post-operative jaundice, one wound infection and one case of bleeding were observed. All post-operative complications resolved spontaneously with conservative management without any need of re-operation in both the groups.
- Mean post-operative stay was 2.83 days in group A, ranging from 1 to 5 days in comparison to 5.0 days in group B, ranging from 2 to 12 days. Patients in group B had more prolonged post-operative hospital stay with a mean of 5.0 days (SD 3.08).
- After discharge all patients were followed for 2 weeks, there were no patients with symptoms of retained stones in the common bile duct or delayed complications.

Discussion

In our study, we found that in group B, the incidence of fibrous adhesions was more frequent, which could cause more intra-operative difficulties. But this difference in adhesions between the two groups was statistically insignificant [(Pearson chi-square test) p value 0.256] and this is in coherence with the results of Salman et al who observed that, there was no statistically significant difference in severity of adhesions between the groups. [5] In 16 patients, there was difficulty in Calot's triangle dissection of which, 12 belonged to the group B and 4 to the group A, but this difference was statistically insignificant [(Pearson chi-square test) p value 0.073] and was consistent with study done by Sahoo R et al. [13]. Cholecystitis was observed in 4 patients in group A and 12 patients in group B. The differences were statistically insignificant [(Pearson chi-square test) p value 0.073]. De Vries et al had also observed that, there was no statistically significant difference in finding cholecystitis between the early and delayed groups. [14]

In our study 5 patients (27.8%) in group B underwent partial or sub-total cholecystectomy. Overall rate of partial or sub-total cholecystectomy including all patients was 16.7% with significantly higher in delayed group B. In our study none of the cases required conversion to open surgery. C. Friis et al when combined the results from the pooled

studies showed an increase in conversion rate as time increased between ERCP and LC, from 4.2% when operated within 24 hours to 14% when operated more than 6 weeks after ERCP ($p < 0.0005$). [15] In our study a total of 23.3% of the patients undergoing LC following ERCP needed placement of a drain and all were in group B. Need for a drain was significantly higher as the interval between ERCP and LC progressed (p value 0.014).

In our study the mean duration of surgery for group A was 91.75 min and for group B was 127.78 min and this difference was statistically significant at p value < 0.05 . Studies by Sahoo R et al, Rajesh K. Patel et al, and Aziret M et al also observed significant difference between early and delayed LC groups in reference to duration of surgery. [13,16,17] Contrarily the studies by Bostanci et al show no significant difference in duration of surgery between early and delayed LC groups.

A lower incidence of post-operative jaundice, bleeding, bile leak and wound infection was observed in group A than in group B. Wound infection, bleeding, bile leak and post-operative jaundice were 1 (5.55%), 1 (5.55%), 5 (27.78%) and 1 (5.55 %) in group B respectively. While in group A post-operative jaundice was 1 (8.33%) and no bleeding, bile leak or wound infection. Transient pancreatitis, retained stone and need for re-operation did not occur in any cases. Overall, a statistically significant higher complication rates were observed in late group B than in early group A.

In our study, patients in group B had more prolonged post-operative hospital stay with a mean of 5.0 days (SD 3.08) and this was in accordance with a study by Donkervoort et al who found significant reduction in the post-operative hospital stay in early group. [18] The reason for a longer post-operative hospital stay was probably due to significantly more post-operative complications and need for drain insertion with drain removal post-operatively in the group B. Comparing the duration of post-operative hospital stay between group A and group B, the difference was significant [(t -test) p value 0.030] in the current study.

Conclusion

Our study concludes that the ideal time to perform laparoscopic cholecystectomy after ERCP is within 3 weeks. The longer the interval between ERCP and laparoscopic cholecystectomy, the greater are the chances of encountering complications and increased rate of sub-total or partial cholecystectomy, prolonged operating time as well as more post-operative hospital stay according to our observations. Our study was a prospective study and the sample size was not large. So, a randomized controlled trial (RCT) with a larger patient population is required to further evaluate our study results. However, these finding still must be validated in larger studies, preferably in a randomized clinical setting. For now, the two-stage procedure is widely accepted ; we believe that the course of a two-stage procedure can be improved further. Given the literature and the analysis of the data in this study, we believe that it is worth expediting laparoscopic cholecystectomy following ERCP.

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