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Outcome in Patients Undergoing Laparoscopic Cholecystectomy Following ERCP; Does Timing of Surgery Really Matter?

Diwakar Sahu [1]; Mittu John Mathew [1]; Prasanna Kumar Reddy [1,*]

[1]Registrar, Department of Surgical Gastroenterology and Minimal Access Surgery, Apollo Hospitals, Chennai, Tamil Nadu, India

*Corresponding author: Prasanna Kumar Reddy, Registrar, Department of Surgical Gastroenterology and Minimal Access Surgery, Apollo Hospitals, Chennai, Tamil Nadu, India. Tel: +91-4428290200, Fax: +91-4428294429, E-mail: drpkreddyapollo@gmail.com

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Background: Laparoscopic cholecystectomy (LC) is the gold standard treatment for cholelithiasis.

Objectives: Our study intended to evaluate whether timing of surgery is of any influence on the course of the laparoscopic cholecystectomy (LC) following Endoscopic Retrograde Cholangio-Pancreatography ERCP/Endoscopic sphincterotomy (ES) and to identify and assess various factors that can affect the outcome in these patients.

Patients and Methods: Data of 77 patients treated for choledochocystolithiasis with ERCP/ES followed by LC were reviewed. Patients were classified into four groups, group A (n = 29): LC performed within 24 hours after ERCP; group B (n = 20): LC performed after 24 hours to 7 days; group C (n = 12): LC done between 8 to 28 days; group D (n = 16): LC done after 28 days of ERCP. Primary outcome was operating time and secondary outcomes included intra- or post-operative complications, hospital stay and hospital expenses.

Results: Mean operative time was shortest in group A (57.1 minutes) and longest in group B [63.4 (P = 0.131)]. Mean hospital stay was shortest in group A (2.1 days) and longest in group C (5.7 days) (P = 0.003). Hospital expenses were minimal in group A (P = 0.001). Male sex, serum bilirubin level, White blood cell (WBC) count, duration of ERCP/ES procedure, contracted gall bladder and large calculus size on Ultrasonography (USG) were significantly associated with primary outcome.

Conclusions: LC can be performed within 24 hours of ERCP/ES with favorable outcome and less expenses. Timing of LC after ERCP/ES is not significantly associated with outcome of the procedure. Male sex, serum bilirubin level, WBC count, ERCP/ES procedure duration, contracted gall bladder and large size of gall bladder calculus on imaging are significantly associated with difficulty in surgery.

Keywords: Choledocholithiasis; Cholelithiasis; Laparoscopic Cholecystectomy

1. Background

Laparoscopic cholecystectomy (LC) is the gold standard treatment for cholelithiasis. Incidence of co-existing common bile duct (CBD) stones in patients undergoing cholecystectomy for cholelithiasis is 3.4 - 15% (1, 2). Endoscopic retrograde cholangiopancreatography (ERCP) with or without sphincterotomy is widely accepted as the diagnostic and therapeutic modality for patients with CBD calculus. With ERCP, CBD stone extraction is successful in up to 97% of patients (3). Several treatment protocols have been proposed for management of patients with concomitant gallstones and CBD stones, like two stage approach (LC + pre or post ERCP), single-stage (LC + Laparoscopic CBD exploration) and LC with intra-operative ERCP. Laparoscopic cholecystectomy following ERCP has been accepted as treatment modality for gall stone disease with CBD stones. The rate of conversion of LC after ERCP is higher than elective LC for uncomplicated cholelithiasis (4, 5). Numerous recent studies have reported that early LC improves the outcome and reduces morbidity (6, 7). The possible explanation could be that ERCP causes cholangitis, leading to inflammation and adhesions around extrahepatic biliary tree, thus making a laparoscopic procedure more difficult. This inflammatory response will be more evident 2 to 6 weeks after ERCP. Also, during the interval of cholecystectomy after ERCP, patients can have recurrent biliary complications, as high as 20% (3). Several recent studies have reported that the outcome after LC following ERCP is independent of interval between these two procedures (8, 9).

2. Objectives

Our present study was intended to evaluate whether interval between ERCP and LC has any influence on the outcome after surgery. Also, we identified and assessed various factors that can affect the outcome in these patients.

3. Patients and Methods

A retrospective study was conducted on 77 patients, who underwent LC after ERCP for choledocholithiasis from January 2011 to December 2013 at our institute. Data including patient's demographics, preoperative investigations, ERCP outcomes and complications, intra-operative findings, postoperative complications, hospital stay

and cost were reviewed and tabulated. Computed tomography (CT) and Magnetic resonance cholangiopancreatography (MRCP) were performed in selected cases, where other investigations were less informative. Provisional diagnosis of choledocholithiasis was based on symptoms and signs, abnormal liver function tests and diagnostic imaging studies like abdominal ultrasound, CT scan and MRCP. Patients with gallstone pancreatitis, failed ERCP and carcinoma of gall bladder were excluded from the study. The interval between ERCP and LC was determined by various factors, including logistical factors, patient's clinical condition, availability of OT and patient's preference. A written informed consent was taken from all the patients for both the procedures. Approval was obtained from local ethical committee for the study. Endoscopic sphinterotomy (ES) with or without stenting was performed under sedation. LC was performed using the standard four port technique. The operating time was calculated from the start of the incision to placement of the last suture. The operative time, intra-operative findings, postoperative complications, hospital stay and expenses were taken into account. The operative ease or difficulty was mainly determined by condition of gall bladder and amount of inflammation and adhesions around it. Severity of adhesions was based on four-point grading scale, as suggested by Hugh et al: 1) no adhesions, 2) mild adhesions, 3) severe adhesions encasing gallbladder, and 4) severe adhesions involving other structures (10). After surgery, patients were followed up at interval of 1 week, 1 month and 6 months. Patients were classified into four groups; group A (n = 29): LC was performed within 24 hours after ERCP, group B (n = 20): LC was performed after 24 hours to 7 days, group C (n = 12): LC was done after 7 days to 28 days and group D (n = 16) wherein LC was done 28 days after ERCP. In patients belonging to group A, both procedures were done during the same hospital stay. In rest of the groups, patients were discharged after ERCP and were re-admitted for LC. All surgeries were performed by the same surgeon, who was a senior laparoscopic surgeon with 20 years of vast experience in the field of laparoscopy. Primary outcome was duration of surgery and secondary outcomes were intra- or post-operative complications, hospital stay and hospital expenses. LC was classified as easy or difficult based on whether duration of surgery is less or more than 60 minutes respectively. Statistical analysis was performed with the use of SPSS 18.0 version. All the continuous variables were assessed for the normality. If variables were normally distributed, they were expressed as mean ± standard deviation (S.D), otherwise as median. Comparison of continuous variables which were normally distributed was done by independent sample t-test or ANOVA, based on number of groups. Comparison of not normally distrusted variables was done by Mann-Whitney test or Kruskal-Wallis test, based on number of groups. Categorical comparisons were done by either Chi-square or Fisher's exact test. P value <0.05 was considered statistically significant.

4. Results

Total 78 patients with cholecystodocholithiasis were subjected to ERCP/ES followed by laparoscopic cholecystectomy. One patient was diagnosed with carcinoma of gall bladder on histological examination. So, total 77 patients were recruited in the present study. Maximum patients were in group A (n = 29) and lowest were in group C (n = 12). The mean age was 49.5 years (range: 17 - 74 years). Thirty-five patients were male and 42 were female. The demographic characteristics of patients, belonging to all the four groups, were more or less comparable. Following ERCP, 5 patients developed pancreatitis and three cholangitis. Ten patients had no CBD stones on ERCP.

Mean operative time was shortest in group A: 57.1 minutes (range: 35 - 90 minutes) and longest in group B: 63.4 minutes (range 40 - 85 minutes) (P value = 0.131). The number of patients with severe adhesions around gall bladder (grade 3 and 4) was highest in group A (n = 6) and lowest in group D (n = 3). Patients who required subhepatic drain were maximum in group A and minimum in group C (P = 0.087). Mean hospital stay was shortest in group A (2.1 days), longest in group C (5.7 days) and on comparing the groups, P value was significant (P = 0.003). Hospital expenses were minimal in patients belonging to group A and highest in group C patients (P < 0.001). The comparative evaluation is shown in Table 1.

Table 1. Comparative Evaluation of Peroperative Parameters Among Various Groups

S. No.	Parameters	Group A (n = 29)	Group B (n = 20)	Group C, (n = 12)	Group D, (n = 16)	P Value
1.	Mean operative time (in mins)	57.1 ± 3.9	63.4 ± 2.3	61.8 ± 4.8	59.3 ± 3.7	0.131
2.	Adhesion around Gall Bladder (Grade 3 and 4), No. (%)	6 (20.6)	5 (25)	3 (25)	3 (18.7)	0.227
3.	Drain (No. of patients), No. (%)	11 (37.9)	8 (40)	5 (41.6)	6 (37.5)	0.087
4.	Mean hospital stay (in days)	2.1 ± 1.3	4.6 ± 1.7	5.7 ± 1.9	5.4 ± 2.1	0.003
5.	Mean Cost (in INR)	1.10 ± 2.4	1.64 ± 3.1	1.82 ± 2.8	1.71 ±2.9	< 0.001

All patients underwent laparoscopic cholecystectomy with no conversion to open surgery. Only three patients had complications in form of biliary leak from cystic duct stump (group A), postoperative bleeding (group B) and subhepatic residual collection (group D). On analysis of various pre-operative factors, shown in table 2, it was evident that male sex, serum bilirubin level, WBC count, duration of ERCP procedure, contracted/shrunken gall bladder and large gall bladder (G.B) calculus size (>15 mm) on ultrasound were significantly associated with primary outcome duration of surgery).

5. Discussion

Several options are available for the treatment of cholelithiasis associated with CBD calculus. The choice is often led by the availability of professional expertise and resources, rather than by superiority of one strategy over another. Single stage treatment by LC combined with CBD exploration is considered as safe alternative. Surgeons with ample expertise in advanced laparoscopy consider laparoscopic CBD exploration (LCBDE) as a better option. But this policy is not widely accepted , probably due to its steep learning curve and equivocal results with other alternatives (11). Another approach consists of LC with intra-operative ERCP/ES (Rendezvous Technique). But because of lack of expertise and organizational restrictions, it is not always possible to perform both procedures simultaneously (12). LC along with the pre-operative ERCP remains the cornerstone and most commonly practiced strategy worldwide for complete management of co-existing gallbladder and CBD stones (13). There is a dual hypothesis regarding outcome of LC following ERCP. According to recent studies, if LC is performed early (< 48 - 72 hours) then outcome is good (6, 7). However, some studies claim that delaying LC after ERCP allows the gallbladder area to cool off and give time to recover from the acute illness (14). But the major drawback of delaying LC is the incidence of biliary complication, which is as high as 20% (3). To the contrary, Donkervoort et al. reported in 2010 that the interval between LC and ERCP failed to influence the outcome of surgery (9). Our practice in managing these cases is to perform LC following ERCP as early as possible and therefore maximum patients were in group A. The primary outcome in our study was duration of surgery, which signifies the difficulty of procedure. On comparing the mean operative time of each group, the P value was 0.131, which is not significant. Previous studies have mentioned conversion rate as the main outcome, but in our study there was no conversion to open surgery (6-9). Also, there were minimal complications. The possible explanation for no conversion and few complications could be the vast experience of the operating surgeon. Abdominal drain was placed in those patients who had intra-operative blood loss more than 100 mL. This need of placing drain during surgery also signifies a difficult procedure, as severe adhesion and inflammation will cause more blood loss. The comparison of number of patients in different groups who required drain was not statistically significant (P = 0.087). The severity of adhesion around gall bladder was independent of interval between ERCP and LC (P = 0.128). Percentage-wise, both group B and C had equal share of patients with severity grade 3 and 4 (each 25%). This contradicts the presumption that the severity of adhesion is maximum between 2nd and 6th weeks. In group A, ERCP and LC was performed within 24 hours, with a minimum interval of 6 hours. In this group, hospital stay (2.1 days; P = 0.003) and expenses (P < 0.001) were lowest and the outcome was comparable to other groups, suggesting that it is a safe practice. Univariate analysis was done to evaluate various risk factors that can influence the duration of surgery. Out of various factors, male sex, serum bilirubin level, WBC count, large size of G.B calculus, ERCP/ES procedure duration and abnormal gall bladder appearance (contracted or shrunken) on ultrasound were found significant (Table 2). These findings indicate that it is mainly pre-existing disease conditions which influence the outcome (difficult surgery). The hypothetical justification of male sex as risk factor could be that anatomical variation of biliary tree is high in males and they have more inflammation and fibrosis during cholecystitis (15). High level of serum bilirubin level and WBC count before ERCP indicate severe inflammation in and around biliary tract. In a similar study by Donkervoort et al. the C-reactive protein, serum bilirubin, severe adhesion and male gender have been associated with adverse outcome (9). Other risk factors in our study like calculus size (> 15 mm) and contracted gall bladder itself are indicative of long standing inflammation. Also, long duration of ERCP procedure again implies chronic pathology of biliary tree. Identification of these risk factors can decrease the complications by optimization of these factors. At the same time, senior surgeon can be involved in dealing such cases. Our study has identified some significant risk factors associated with difficult LC following ERCP. Also, practice of performing LC within 24 hours of ERCP is safe and feasible. Based on above results, we can suggest that in developing nations like ours carefully selected cases can undergo ERCP and LC during same hospital stay, thereby reducing the hospital expenses. On critical note, ours was a retrospective 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. In conclusion, in patients with symptomatic choledocholithiasis, LC can be performed within 24 hours of ERCP/ES with favourable outcome and less expenses. Timing of surgery after ERCP/ES is not significantly associated with outcome of procedure. Male sex, serum bilirubin level, WBC count, ERCP/ES duration, abnormal G.B appearance and large size of G.B calculus on imaging are significantly associated with difficulty of surgery.

Table 2. Univariate Analysis of Various Factors Affecting the Outcome (Duration of Surgery) [a]

Factors	O.T < 60 min (n = 47)	O.T > 60 min (n = 30)	P Value	Odd Ratio
Age, median-52 y			0.68	1.20
≤52, y	21	12		
>52, y	26	18		
Gender			0.0001	0.14
Male	13	22		
Female	34	08		
Diabetes mellitus	15	12	0.63	0.70
ERCP duration ≥32 min, median	12	25	0.0001	0.07
Serum Bilirubin > 8.4 mg/dL, median	17	21	0.007	0.24
WBC count > 12000 mm^3	11	19	0.001	0.80
Alkaline Phoshatase > 108 IU/dL	34	22	0.86	0.95
GGTP > 38 IU/dL	36	24	0.94	0.82
G.B status (contracted)	08	20	0.0001	0.10
G.B calculus size > 1.5 cm	5	18	0.0001	0.08

[a] Abbreviations: ERCP, Endoscopic Retrograde Cholangio-Pancreatography; WBC, White Blood Cell; GGTP, Gamma-Glutamyl Transpeptidase; G.B, Gall Bladder.

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