

A Retrospective Comparative Study Between Early (≤ 72 hrs) and Late (> 72 hrs) Laparoscopic Cholecystectomy after ERCP in St. Paul's Hospital Iloilo

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Objective: The study was performed to assess and compare the effect of early (≤ 72 hours) and late (> 72 hours) laparoscopic cholecystectomy after Endoscopic retrograde cholangio pancreatography (ERCP) in terms of duration of operation, conversion to open cholecystectomy, intraoperative complicating factors, duration of hospital stay from the date of ERCP, hospital expenses, and presence of postoperative complications.

Methods: This is a retrospective study from 2010 up to July 2019. Outcomes (duration of operation, rate of conversion, intraoperative complicating factors, length of hospital stay, hospital expenses and post-operative complications) were compared between patients who had ERCP then cholecystectomy within 72 hours (Early Group) and those who had ERCP then cholecystectomy after more than 72 hours (Late Group).

Results: A total of 19 patients were included in this study. There were 10 patients in the Early Group and 9 in the Late Group. Early laparoscopic cholecystectomy after ERCP had a shorter statistically significant duration of hospital. Shorter operative time, fewer intraoperative complicating factors, no conversion to open cholecystectomy, cheaper hospital expenses and no post-operative complications were also noted in the Early Group as compared to the Late Group.

Conclusion: Early laparoscopic cholecystectomy is safe and results in a shorter hospital stay compared to late laparoscopic cholecystectomy.

Key words: early laparoscopic cholecystectomy, cholecystectomy after ERCP, choledocholithiasis, cholecystolithiasis

Gallstones afflict 10% to 20% of adult populations in developed countries. It is estimated that more than 20 million persons in the United States have gallstones.¹ In the Philippines, thousands of new gallstone cases are diagnosed each year and cholecystectomy (open or

laparoscopic) is one of the most common abdominal operations done locally.

Choledocholithiasis, or common bile duct stones, are classified by their point of origin, with primary common duct stones arising de novo in the bile duct and secondary common duct stones passing from the gallbladder into the bile duct.² Incidence of co-existing common bile duct (CBD) stones in patients undergoing cholecystectomy for cholelithiasis is 3.4 - 15%.^{3,4}

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.⁵ Currently in patients with cholelithiasis with choledocholithiasis, the ideal treatment is endoscopic retrograde cholangiopancreatography (ERCP) removal of duct stone and laparoscopic cholecystectomy. But when to do and whether one can do it simultaneously or one after another and what interval should be there, that is always controversial.⁶

Some studies have reported that early laparoscopic cholecystectomy (within 72 hours) improves the outcome and reduces morbidity.^{7,8,9} One study would mention that delaying laparoscopic cholecystectomy has an incidence of 20% biliary complications.³

On the other hand, some studies claim that delaying laparoscopic cholecystectomy after ERCP allows the gallbladder area to recover from the acute illness.^{10,11} Other studies also reported that the outcome after laparoscopic cholecystectomy following

ERCP is independent of interval between these two procedures.^{10,12,13}

Although Philippine College of Surgeon (PCS) recent guidelines is recommended to do early laparoscopic cholecystectomy after ERCP¹⁴, the practice is still institution based as well as patient and surgeon's preference. This retrospective study is aimed to assess and compare the effect of early and late laparoscopic cholecystectomy after ERCP in the locality of Iloilo City.

This study aimed to provide baseline data on the effect of early vs. late laparoscopic cholecystectomy after ERCP in terms of duration of operations, rate of conversion, intraoperative complicating factors, length of hospital stay, hospital expenses and post-operative complications. This will also help surgeons in Iloilo City in establishing the optimal timing of laparoscopic cholecystectomy after ERCP.

Methods

This was a 9 year and 6 month retrospective study involving data of all patients admitted at St Paul's Hospital Iloilo who had a preoperative diagnosis of choledochocystolithiasis from January 2010 up to June 2019. The patients included in the study had undergone Endoscopic Retrograde Cholangiopancreatography (ERCP) followed by laparoscopic cholecystectomy. Provisional diagnosis of choledochocystolithiasis was based on signs and symptoms (history of jaundice), abnormal liver function tests and dilated common bile duct (CBD) and presence of CBD stones on ultrasound.

ERCP was conducted by board certified gastroenterologists. Patients were selected from the annual census of the St. Paul's Hospital Digestive and Disease Center and Department of Surgery while charts were retrieved from the Record Section. Patients were divided into an Early Group (early laparoscopic cholecystectomy ≤ 72 hrs.) and a Late Group (late laparoscopic cholecystectomy > 72 hrs.). Conventional laparoscopic cholecystectomies (4 ports) were performed. This study was submitted and evaluated by the Institutional Review Board of St Paul's Hospital Iloilo. The anonymity of all information was observed and maintained.

Patients with malignancy, failed ERCP and placement of biliary stents during ERCP, cholecystectomy with IOC/CBD exploration were excluded from the study. Patients were operated by PCS, PSGS, and PALES certified trained surgeons.

Duration of operation was measured from the start of the first incision to the time the last incision was closed. Conversion rate is the count of operations that were converted from laparoscopic to open cholecystectomy. Intraoperative complicating factors are intraoperative findings noted that could contribute to a more difficult surgery. The length of hospital stay was measured from the day of ERCP until the patient was discharged from the hospital. Hospital expenses are the total hospital expenses excluding the professional fee and deductions from Philhealth and private insurances. Calculations were not corrected for inflation. Post-operative complications were noted that would also affect the treatment and post operative course as well as lengthen the duration of hospital stay.

Descriptive statistics was used to summarize the post-operative outcomes of the patients included in the study. Frequency and proportion were used for categorical variables and mean and standard deviation for scalar variables. The Fisher exact test and two-sample T-test were used to compare the two timings of laparoscopic cholecystectomy procedure relative to the clinical outcome of procedure. The level of significance was set at 0.05 threshold for significance.

Missing data were neither replaced nor estimated during the analysis. All data analyses were performed using STATA 12. (StataCorp. 2011. Stata Statistical Software: Release 12. College Station, TX: StataCorp LP).

Results

There were 454 cases of ERCP done from 2010 up to June 2019; however, only 19 cases were included in this study. Other cases were excluded due to the following reasons: ERCP was done as OPD, laparoscopic cholecystectomy was not done in this institution, failed ERCP, cholecystectomy with IOC/CBD exploration. Among these 19 cases, 10 patients had ERCP then

cholecystectomy within 72 hours (Early Group) and 9 cases had ERCP then cholecystectomy after 72 hours (Late Group). (Figure 1).

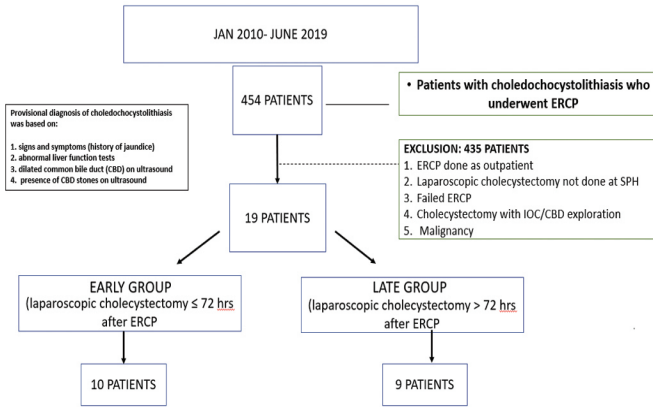


Figure 1. Flowchart for screening patients.

The Early Group had 5 males and 5 females with a mean age of 47.6 years while the Late Group included 5 males and 4 females with a mean age of 45.7 years. All patients were admitted under pay accommodation except for one who was admitted under service accommodation. This patient was included in the Late Group. (Table 1) Seven patients had jaundice, 2 in the Early Group and 5 in the Late Group. Elevation of liver function test was noted in all (100%) the Late Group patients while

8 (80%) in the Early Group patients. CBD dilatation on ultrasound were noted in 11 patients, 8 (80%) in the Early Group and 3 (33%) in the Late Group. Presence of choledocholithiasis on ultrasound were noted in 3 (30%) and 2 (22%) patients for the Early Group and Late Group, respectively. (Table 2).

The mean duration of operation in the Early Group is 99.9 minutes and 118.8 minutes in the Late Group. Only 1 patient (in the Late Group) was converted from laparoscopic to open cholecystectomy due to severe adhesion and difficulty identifying the critical view of safety. Four intraoperative complicating factors were noted in all patients, 1 was noted in the Early Group (gangrenous gallbladder) while 3 were present in the Late Group (two dense pericholecystic adhesion and one gallbladder empyema). Hospital expenses were noted to be lower in the Early Group (Php97,576) than in the Late Group (Php103,709). Three postoperative complications were noted in the Late Group and none in the Early Group. Complications were urinary tract infection, diarrhea, and elevation of SGPT with mild scleral icterus. These patients were managed accordingly and were discharged improved. Among all parameters, only the total number of hospital stay from the time of ERCP up to date of discharge was statistically significant (p-value<0.05). It was noted that the length of hospital stay in the Early Group (4.5 days) was lowered compared to the Late Group (8.9 days). (Table 3).

Table 1. Demographic characteristics between early and late laparoscopic cholecystectomy.

Demographic characteristics	Laparoscopic cholecystectomy Mean ± SD; Frequency (%)		p-value
	Group A: Early (N=10)	Group B: Late (N=9)	
Accommodation			
Pay	10 (100)	8 (88.9)	0.474 ²
Service	0 (0.0)	1 (11.1)	
Age	47.6 ± 19.8	45.7 ± 17.5	0.825 ¹
Sex			
Male	5 (50.0)	5 (55.6)	1.000 ²
Female	5 (50.0)	4 (44.4)	

Statistical tests used: ¹Two-sample t-test; ²Fisher's exact test

Table 2. Clinical characteristics between early and late laparoscopic cholecystectomy.

Clinical characteristics	Laparoscopic cholecystectomy Mean \pm SD; Frequency (%)		p-value
	Group A: Early (N=10)	Group B: Late (N=9)	
Jaundice			
Absent	8 (80.0)	4 (44.4)	0.170 ²
Present	2 (20.0)	5 (55.6)	
Liver Function Test			
Normal	2 (20.0)	0 (0.0)	0.474 ²
Abnormal	8 (80.0)	9 (100.0)	
CBD Dilation			
Absent	2 (20.0)	6 (66.7)	0.070 ²
Present	8 (80.0)	3 (33.3)	
CBD Stones			
Absent	7 (70.0)	7 (77.8)	1.000 ²
Present	3 (30.0)	2 (22.2)	

Statistical tests used: ¹Two-sample t-test; ²Fisher's exact test

Table 3. Comparison of early and late laparoscopic cholecystectomy by post-operative outcomes.

Post-operative outcomes	Laparoscopic cholecystectomy Mean \pm SD; Frequency (%)		p-value
	Group A: Early (N=10)	Group B: Late (N=9)	
Duration of operations (mins)	99.9 \pm 41.6	118.8 \pm 37.3	0.314 ¹
Rate of conversion			
None	10 (100.0)	8 (88.9)	0.474 ²
Yes	0 (0.0)	1 (11.1)	
Intraoperative complicating factors			
Absent	9 (90.0)	6 (66.7)	0.303 ²
Present	1 (10.0)	3 (33.3)	
Duration of stay (days)	4.5 \pm 1.1	8.9 \pm 3.1	0.0006 ¹
Post-operative complications			
Absent	10 (100.0)	6 (66.7)	0.087 ²
Present	0 (0.0)	3 (33.3)	
Hospital expenses	97,576.8 \pm 30,980.8	103,709.6 \pm 32,479.5	0.679 ¹

Statistical tests used: ¹Two-sample t-test; ²Fisher's exact test; Boldface indicates significance at $\alpha=0.05$

Early and late cholecystectomy were further examined to determine whether these were predictors to post-operative outcome pertaining to length of hospital stay. It was found that the timing of cholecystectomy is a significant predictor that could lead to either shorter or longer length of hospital stay. The duration of stay of the patients who underwent late laparoscopic cholecystectomy is 4.39 (95% CI: 2.19 to 6.59) days longer as compared to early laparoscopic cholecystectomy. The length of stay increased by 4.39 days when late laparoscopic cholecystectomy was done. The difference in the mean duration of hospital stay between early and late laparoscopic cholecystectomy is statistically significant ($p=0.0006$). (Table 3).

Discussion

Laparoscopic cholecystectomy 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.¹⁵ Several treatment protocols have been proposed for management of patients with concomitant gallstones and CBD stones, like two stage approach (laparoscopic cholecystectomy + pre or post ERCP), single-stage (laparoscopic cholecystectomy + Laparoscopic common bile duct exploration) and laparoscopic cholecystectomy with intra-operative ERCP. Laparoscopic cholecystectomy following ERCP has been accepted as treatment modality for gall stone disease with CBD stones.^{7,9}

There is a dual hypothesis regarding outcome of laparoscopic cholecystectomy following ERCP. According to recent studies, early laparoscopic cholecystectomy (within 72 hrs.) after ERCP improves the outcome and reduces morbidity.^{8,10} 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. During the interval of cholecystectomy after ERCP, patients can also have recurrent biliary complications, as high as 20%.¹⁶ Another study reported that early laparoscopic cholecystectomy (≤ 72 hrs.) has a significant reduction in the average length of stay, operative time,

complications and rate of conversion to an open procedure as compared to ERCP followed by delayed laparoscopic cholecystectomy in patients with choledocholithiasis.¹⁷ Also in 2 separate randomized trials, they concluded that a wait and see policy is not justified after ERCP, and early laparoscopic cholecystectomy was advised.^{7,24}

On the other hand, some studies claim that delaying laparoscopic cholecystectomy after ERCP allows the gallbladder area to cool off and give time to recover from the acute illness.¹¹ Several recent studies have reported that the outcome after laparoscopic cholecystectomy following ERCP is independent of interval between these two procedures.^{12,13} Also another study pointed out that timing of laparoscopic cholecystectomy after ERCP is not significantly associated with outcome of the procedure. Differences in operative time, adhesions, conversion rate, and complication rate were not statistically significant in terms of timing of laparoscopic cholecystectomy after ERCP.³

In the present study, the mean length of hospital stay from the time of ERCP to the date of discharge after cholecystectomy was lower in the Early Group than in the Late Group by a factor of 2. This statistically significant finding is consistent with other studies.^{13,17,18,19}

Although not statistically significant, duration of operations for the Early Group is shorter by 18.9 min than in the Late Group and is similar with other studies: lesser by 17 min,¹⁷ 26 min,¹⁹ and 12 min¹⁸. The longer operative time in the Late Group could be due to the use of contrast in ERCP that elicits an inflammatory reaction around the common bile duct (CBD) and sphincterotomy leading to bacterial colonization causing inflammation and scarring of the hepatoduodenal ligament. This could lead to adhesions and frozen Calot's triangle.^{7,8} This theory of bacterial colonization is supported by reports that bacteria have been isolated from bile in 60% of patients who underwent ERCP with sphincterotomy.^{8,20} The 72 hour time point was selected because this would correspond to the start of the sub-acute phase of inflammation. The passage of time heightens the inflammatory process around Calot's triangle and provokes adhesion formation following ERCP.^{22,23}

One patient (11.1%) in the Late Group was converted from laparoscopic to open cholecystectomy

which is also noted in other studies in late laparoscopic cholecystectomy with a conversion rate of 6.67%¹⁷ and 2.33%.¹⁹ According to one study, early laparoscopic cholecystectomy done within days following ERCP show conversion rates as low as those for patients with uncomplicated cholelithiasis.²³

Intraoperative complicating factors were more frequently observed in the Late Group, though the difference was not statistically significant. The severity of adhesions increased with the length of the interval from ERCP to cholecystectomy. There was pericholecystic adhesion which is a sign of inflammation and cholecystitis. This could also be attributed to inflammation occurring in contrast material infusion and endoscopic instrumentation of the biliary duct during ERCP.⁹

With the effect of longer operative time and longer hospital stay, 3 patients had post-operative complications in the Late Group. A case of UTI, diarrhea and elevation of SGPT with mild scleral icterus. The 2 post-operative complications (UTI and diarrhea) could not be directly attributed to the operation and could be due to prolonged hospital stay. Hospital expenses were also higher, a difference of around Php6000, in the Late Group because of longer hospital stay.

This study is limited by its small sample size. Only 19 cases were included due to the exclusion criteria previously mentioned. It was also limited in that being a retrospective study, the participants were not randomized to the treatment interventions. Likewise, while surgeries were performed by board-certified surgeons. Their varying levels of skill and technique could affect the length and outcomes of surgery. Other reasons for a delay in the cholecystectomies like post ERCP complications, preoperative preparation/clearance, OR scheduling, surgeon and patient's preference were not reviewed.

Conclusion

This current study suggests that doing early cholecystectomy after ERCP is safe and can result in shorter hospital stays. It is recommended that this research could be continued and be done in a randomized prospective study to validate these results.

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