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Early Versus Delayed Laparoscopic Cholecystectomy after Endoscopic Common Bile Duct Stones Management

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ABSTRACT

Background: Stone removal by endoscopic retrograde cholangiographic method (ERC) is a well-established procedure prior to laparoscopy cholecystectomy (LC) in patients with gall bladder stones (GBS).

Objective: To compare the outcomes of early versus delayed LC after endoscopic common bile duct stones clearance in cases of combined GBS and CBDS.

Patients and Methods: This comparative study included 28 patients who had undergone ERCP for CBDS and were then admitted for LC either early or delayed after ERCP from May 2020 to December 2020 at Zagazig University Hospitals. Patients had been divided into two groups: Group 1 (early group 14 patients) where LC was performed within 72 hrs after ERCP and Group 2 (delayed group 14 patients) where LC was performed after 6weeks from ERCP.

Results: The mean operative time was shorter in the early group: 45.29 minutes (range: 29 - 60 minutes) than in the delayed group: 59.57 minutes (range: 40 - 92 minutes) which represented a significant difference in favor of the early group. As regards postoperative complications there was a statistically non-significant difference between both groups.

Conclusion: an early LC after ERCP for the management of cholecystocholedecholithiasis is a safe, effective, and time-saving technique with a low rate of postoperative complications.

Keywords: Laparoscopic Cholecystectomy, Endoscopic retrograde cholangiography.

INTRODUCTION

In an Egyptian priestess' mummy from around 1500 BC, researchers discovered gallbladder stones (GBS). In adults, it affects 10–15% of the population, with symptoms reported by 20% of those who have it. Approximately 3.4-18.8% of those experiencing symptoms will eventually develop coexisting common bile duct stones (choledocholithiasis or CBDS). Patients with cholelithiasis have a higher risk of developing choledocholithiasis as they get older [(1)]. When GBS enters the common bile duct (CBD), it results in choledocholithiasis. Since ERC is an established method for obtaining ductal clearance before laparoscopic cholecystectomy (LC), cholecystectomy is a reasonable method for reducing the number of recurrent biliary stones [(2)]. LC is the gold standard treatment for GBS management, and it has become the most common laparoscopic procedure worldwide since it was first performed in France and America in the 1980s [(3)].

Endoscopic retrograde cholangiopancreatography (ERCP) is widely accepted by gastroenterologists and surgeons, but the rate of conversion to open cholecystectomy is higher in patients who have undergone this procedure [(4)]. Laparoscopic procedures are more difficult to perform after ERCP because of the contamination of the bloodstream with bacteria during the procedure, resulting in inflammation, cholangitis, and adhesions around the gallbladder and the hepatoduodenal ligament, which makes the procedure more difficult [(5)].

There is little evidence to support the idea that LC (performed immediately after an ERCP) causes recurrences in the gallbladder [(6)].

The best time to perform LC after an emergent ERCP for the treatment of combined choledocholithiasis is still up for debate. Although some research suggests that laparoscopic bile duct exploration combined with an early interval LC or a single-stage LC treatment has better outcomes; Since few surgeons have the necessary training, equipment, or time to perform LC on patients with gallstones and choledocholithiasis immediately after an ERCP, this is the treatment of choice for many of these patients. According to some researchers, time intervals do not affect the outcome of laparoscopic procedures [(7)].

It was the goal of this work to compare the outcomes of early versus delayed LC after endoscopic common bile duct stones clearance in cases of combined GBS and CBDS.

PATIENTS AND METHODS

This study was undertaken in the period between May 2020 to December 2020 Department of General Surgery, Zagazig University Hospitals, It included 28 patients with cholecystolithiasis after doing ERCP and ES for their Ex-concomitant CBDS as the first stage of their whole management and assigned for the second stage i.e. laparoscopic cholecystectomy.

Ethical consent:

Zagazig University's research ethics council approved the study as long as all participants signed informed consent forms and submitted them to ZU-IRB#6759. We adhered to the Helsinki Declaration, which is the ethical norm for human testing established by the World Medical Association.

Inclusion criteria: Patients with cholecystolithiasis who recently underwent ERCP for choledocholithiasis, whether in our hospital or referred from another one, within the last 72 hours, cholecystolithiasis patients who have undergone ERCP for choledocholithiasis in our hospital or another one for six weeks or more, and patients >18 years.

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Exclusion criteria: Patients<18 years, patients unfit for general anesthesia, patients with severe malnutrition, a history of cholecystectomy, liver cirrhosis, and patients who had been subjected to the previous ERCP for reasons other than CBDS management.

All patients were subjected to:

Full history: Name, age, sex, residence, medical history of chronic and metabolic diseases, date of examination and/or admission, contact information, and other habits of medical interest.

Clinical examination: General examination, Local examination, and Neurovascular examination were done.

Imaging studies: Pelvi-abdominal ultrasound examinations and MRCP was done for three patients with elevated serum bilirubin, ALP, and GGT to confirm that their CBD had been completely eliminated from the stones in which they were found.

Laboratory investigations: CBC and blood sugar profile. Liver function tests include serum bilirubin, albumin, alkaline phosphatase, GGT, SGPT, and SGOT. Renal function tests include serum urea and creatinine. Coagulation profile includes PT, APTT, INR, C-reactive protein, and ESR.

Patients were scheduled to be operated upon in two groups:

Group (A) for early LC within 72 hrs after ERCP and Group (B) for delayed LC (6 weeks or more) after ERCP. Our primary outcome was to measure the conversion rate to open procedure as it is the main index of operative difficulty of LC and secondary outcomes were the operative time, intra and post-operative complications, and hospital stay.

Operative technique:

As soon as the patient had been placed in the supine position and had received general anesthesia with an endotracheal tube, the patient was secured to the operating table, and the following steps were carried out to create an aseptic surgical field in case an open procedure was required.

Establishment of pneumoperitoneum and insertion of first and second ports:

An upper umbilical incision was made and the Veress needle was inserted to induce pneumoperitoneum.

Exploratory laparoscopy:

The first and most important step is a thorough diagnostic laparoscopy, during which any omental or bowel adhesions or injuries that may have occurred during port insertion were excluded and the GB area was examined for the presence of adhesions.

Insertion of the 3rd and 4th ports under direct vision:

Three 5 mm ports were used for exploratory laparoscopy; the 3rd port was inserted just below the right costal margin, and the 4th 5 mm port was inserted at the umbilicus in the right anterior axillary line.

Hepatocystic triangle dissection and creation of a critical view of safety:

The anterior and posterior leaflets of the peritoneum were opened. To obtain the critical view of safety, which is defined as (1) Hepatocystic triangle removal of fibrous and fatty tissue, (2) In the base of the GB, there are only two tubular structures (3) Anatomical dissection to view cystic plate in the lower third of GB.

Clipping and division of cystic duct and artery:

Confidence was restored in the rest of the procedure once the surgeon had achieved an adequate critical view of safety. Clipped proximally two clips and distally one, both structures were carefully transected.

Dissection of the gallbladder from the liver:

Two minutes of abdominal deflation to 8 mmHg and diathermy or harmonic scalpel hemostasis ensured that venous bleeding was not missed because of the high intra-abdominal pressure during the procedure (15 mmHg)

Extraction of the gallbladder and placement of a drain:

A claw forceps extraction of the GB from the abdomen was used in some patients and a retrieval bag in others; in one patient, the GB ruptured during extraction in the group that was delayed and the peritoneum and port site was irrigated and suctioned with normal saline after the stones were removed with an ovum forceps. Tube drain No.18 was used as needed in intraperitoneal (GB bed) situations (2 in early and 7 in delayed group).

Removal of trocars and wound closure:

Except for the umbilical port, which was lifted until the abdomen was completely deflated, all trocars were removed under direct visualization. Subcuticular or interrupted stitching is used to close all trocar sites.

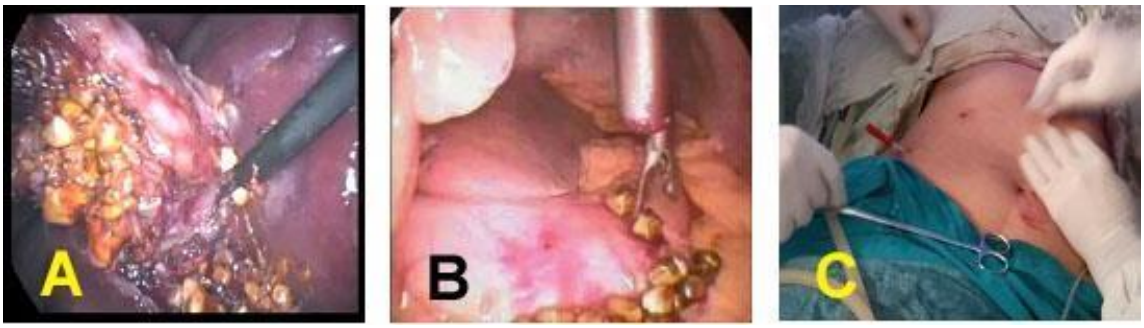

Figure (1): (A) Rupture of GB during dissection, (B) Extraction of stones, and (C) Drain fixation.

Follow-up: Following surgery, all patients were examined clinically (at 1, 2, 4 weeks postoperatively) and radiologically.

Statistical analysis:

The collected data were coded, processed, and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi-square test ($\chi 2$) to calculate the difference between two or more groups of qualitative variables. Quantitative data were expressed as mean ± SD (Standard deviation). Independent samples t-test was used to compare two independent groups of normally distributed variables (parametric data). P-value < 0.05 was considered significant.

RESULTS

The study was carried out on 28 patients: 14 within each group. There was a statistically non-significant difference between both groups regarding age and gender **(Table 1).**

Table (1): Comparison between both groups regarding age and gender

Parameter	Groups		Test	
	Early LC Group	Delayed LC Group	t/$\chi 2$	P-value
	N=14	N=14		
Age (years):				
Mean ± SD Range	37.071 ± 5.771 28 – 49	37.786 ± 11.437 20 – 59	-0.209	0.836
Gender:				
Female-Male	10 (71.4%) 4 (28.6%)	12 (85.7%) 2 (14.3%)	Fisher	0.648

There was a statistically non-significant difference between both groups regarding recurrent biliary colic and PEP: Three patients within the delayed LC group complained of recurrent biliary colic and no patient within the early LC group had. Only one patient within the delayed LC group had PEP and no patient within the early LC group had. No other post-ERCP complications had been detected in both groups **(Table 2).**

Table (2): Comparison between the studied groups regarding post ERCP complaints and complications

Post-ERCP complaints / complications	Groups		Test	
	Early LC Group	Delayed LC Group	t/χ^2	p-value
	N=14	N=14		
Recurrent biliary colic:				
No Yes	14 (100%) 0 (0%)	11(78.6%) 3 (21.4%)	Fisher	0.222
PEP:				
No Yes	14 (100%) 0 (0%)	13 (92.9%) 1 (7.1%)	Fisher	>0.999

There was a statistically significant difference between both groups regarding operative time. Mean operative time was significantly higher among the delayed LC group **(Table 3).**

Table (3): Comparison between the studied groups regarding operative time:

Operative time (in minutes)	Groups		Test	
	Early LC Group	Delayed LC Group	T	p-value
	N=14	N=14		
Mean ± SD Range	45.286 ± 8.471 29 – 60	59.571 ± 15.291 40 – 92	-3.058	0.006*

There was a statistically non-significant difference between both groups regarding intraoperative complications, bile duct injury, GB rupture, or intraoperative bleeding. GB rupture happened in 3 patients all in the delayed group: 2 during dissection from its bed and one during extraction from the abdomen. Only one patient within the delayed group had intraoperative bleeding. No patient within either group had converted to open surgery or bile duct injury **(Table 4).**

Table (4): Comparison between the studied groups regarding intraoperative complications

Intraoperative complications	Groups		Test	
	Early LC Group	Delayed LC Group	t/χ^2	P-value
	N=14	N=14		
Bile duct injury:				
No	14 (100%)	14 (100%)		
Conversion to open:				
No	14 (100%)	14 (100%)		
GB rupture:				
No Yes	14 (100%) 0 (0%)	11 (78.6%) 3 (21.4%)	Fisher	0.222
Intraoperative bleeding:				
No Yes	14 (100%) 0 (0%)	13 (92.9%) 1 (7.1%)	Fisher	>0.999

There was a statistically non-significant difference between the studied groups regarding the need for drain insertion and the time needed to remove. Only two patients within the early LC group need drain insertion: the first patient for 1 day and the second for 2 days. Seven patients within the delayed LC group need drain insertion: 4 patients for 1 day, 2 patients for 2 days, and 1 patient for 3 days **(Table 5).**

Table (5): Comparison between the studied groups regarding the need for drain insertion and time for drain removal

Need for drain insertion and time for drain removal	Groups		Test	
	Early LC Group	Delayed LC Group	t/χ2	p-value
	N=14	N=14		
Need for drain insertion:				
No	12 (85.7%)	(50%)	Fisher	0.103
Yes	2 (14.3%)	(50%)		
Time for drain removal:				
Mean ± SD	1.5 ± 0.267	1.57 ± 0.426	-1.063	0.299
1st POD	1 (7.1%)	4 (28.4%)		
2nd POD	1 (7.1%)	2 (14.2%)	Fisher	0.596
3rd POD	0(0%)	1 (7.1%)		

There was a statistically non-significant difference between both groups regarding postoperative complications. No patient within either group needs readmission. 3 patients within the delayed LC group had postoperative complications; the first one had postoperative bile leak up to the 3rd POD, the second patient had reactionary bleeding in the zero POD's night and the third patient had wound infection in the site of umbilical port in the 5th POD **(Table 6).**

Table (6): Comparison between the studied groups regarding postoperative complications

Postoperative complications	Groups		Test	
	Early LC Group	Delayed LC Group	χ^2	P-value
	N=14	N=14		
Bleeding:				
No Yes	14 (100%) 0 (0%)	13 (92.9%) 1 (7.1%)	Fisher	>0.999
Bile leak:				
No Yes	14 (100%) 0 (0%)	13 (92.9%) 1 (7.1%)	Fisher	>0.999
Readmission:				
No	14 (100%)	14 (100%)		
Wound infection:				
No Yes	14 (100%) 0 (0%)	13 (92.9%) 1 (7.1%)	Fisher	>0.999

There were no abnormalities detected in all patients after 1, 2, and 4 weeks except only one patient in the delayed group by abdominal examination had wound infection at the site of umbilical port after the first week of follow up and managed by repeated dressings and removal of stitches with oral Augmentin 1gm/12 hours for seven days **(Table 7).**

Table (7): Comparison between the studied groups regarding postoperative follow up

Follow up timing and parameters		Groups	
		Early LC Group	Delayed LC Group
		N=14	N=14
After 1week	**History**	NAD	NAD
	Examination	NAD	1 patient (7%) developed port site infection
	Laboratory	NAD	NAD
	Ultrasonography	NAD	NAD
After 2weeks	**History**	NAD	NAD
	Examination	NAD	NAD
	Laboratory	NAD	NAD
	Ultrasonography	NAD	NAD
After 4weeks	**History**	NAD	NAD
	Examination	NAD	NAD
	Laboratory	NAD	NAD
	Ultrasonography	NAD	NAD

DISCUSSION

Patients with cholelithiasis who are having their gallbladder removed because of GBS have a 3.4–15% chance of also having CBDS, which is treated with LC, which is the standard procedure. ERC is the standard treatment for CBDS patients. According to most studies, ERCP and LC are safe and effective in the treatment of cholecystolithiasis, with endoscopic CBDS extraction successful up to 97% of the time [8].

According to some surgeons, delayed LC is preferred as the standard treatment for patients with gallstones and/or choledocholithiasis following ERCP because they believe that delaying the procedure allows the GB area to cool down and give time to recover from acute illness [7].

According to new research, a combination of laparoscopic CBD exploration with an early interval LC or a single-stage treatment with LC has better outcomes; Patients with gallstones and choledocholithiasis who have undergone ERCP are often given a delayed LC as a standard treatment because of the lack of experience, necessary equipment, or organizational restrictions. However, some researchers believe that time intervals do not affect the outcome of laparoscopic surgery. When it

comes to the timing of LC after emergent ERCP, there is no consensus on the best course of action [7].

Our study was intended to compare early versus delayed LC after ERCP as regards safety, operative time, conversion to OC, postoperative morbidity, hospital stay, and outcomes of the same procedure in the two strategies of management of patients with cholecystolithiasis and choledocholithiasis.

Our study included 28 patients who were randomly divided into 2 groups: the early group (14 patients); 10 females (71.40%) and 4 males (28.30%); their mean age was 37.07 ± 5.77 (range 28-49 years) and delayed group (14 patients); 12 females (85.70%) and 2 males (14.30%), their mean age was 37.77 ± 11.44 (range 20-59 years). There were no significant differences regarding age and gender between both groups (P>0.05) which is in agreement with the study of **Morshed and Shaban** [9] and **Ghnnam** [8].

In the current study 3/14 cases (21%) in the delayed group complained of recurrent biliary colic while waiting for LC after ERCP which is insignificant regarding the number in the delayed group (p = 0.222). This result appears to be in disagreement with the findings of **El-Nakeeb *et al.*** [6] who found that 12.71 percent of patients in the delayed LC group had recurrent biliary symptoms, compared to one patient in the early LC group (P=0.03). They concluded that delayed LC was associated with significantly higher rates of recurrent biliary symptoms. This discrepancy was evident due to the small sample size of our study.

The mean operative time in our study was shorter in the early group 45.29± 8 min. than in the delayed group 59.57 ± 15 min. with a significant difference between them (p=0.006) and this was in agreement and comparable with the results of the studies done by **Gorla *et al.*** [10], where the mean operative time in the early group was shorter 81 ± 31 min. and in the delayed group was longer 101 ± 33 min., **Ghnnam** [8], the mean operative time in the early group was 53.6 ± 32.18 min. and in the delayed group was 79.8 ± 26.3 min.

In our study, no patient had GB rupture due to difficult dissection caused by adhesions in the early group (0%) compared to 3 patients (21%) in the delayed group (in 2 patients during dissection and one during GB extraction). A total of 9 patients (32%) needed placement of drain due to excessive dissection; 2 patients (14%) in the early group and 7 patients (50%) in the delayed group (P-value: 0.103). All these differences were non-significant between both groups regarding these variables.

These results were comparable to those of the study of **Sahoo *et al.*** [11] when it comes to the hepatocystic triangle dissection, 26 patients had difficulty, with 20 of those patients being delayed and six being early. Ten patients in the early group and half of the delayed group's patients (15/32) required drain placement due to excessive dissection.

In our study, no patient had postoperative wound infection in the early group (0%) compared to 1 (7%) patient in the delayed group. No patient had postoperative bile leak in both groups compared to 1 (7%) patient in the delayed group. No patient had postoperative bleeding in the early group compared to 1 (7%) patient in the delayed group. All these differences were found to be statistically non-significant between both groups and the overall complication percentage was 21% and all were in the delayed group. This complication percentage was in agreement with that of **Ghnnam's** [8] study where only 5/86 (5.81%) patients had complications in both groups in the form of a biliary leak from cystic duct stump in two cases one from each group (early group 2.4% and 2.2% in the delayed group), one postoperative bleeding (2.2%) and two wound infections (4.4%) in the delayed group only. Also, our results agreed with that of **Sahoo *et al.*** [11], where surgical site infection was noted in 8/30 (26.67%) cases in the delayed group and 2/30 (6.67%) in the early group.

In our study there was a statistically non-significant difference between the studied groups regarding the length of hospital stay (P =0.596). 13 patients within the early LC group and 11 patients within the delayed LC group stayed in the hospital for 1 day and 1 patient within the early LC group and 2 patients within the delayed LC group stayed for 2 days and only1 patient within the delayed LC group stayed for 3 days. The patients in the delayed group had longer hospital stays than those in the early group despite being statistically non-significant, which may be due to more postoperative complications in the former group.

Compared to other studies hospital stay of our study was closer to **Ghnnam** [8] and shorter than in other studies [11, 12].

CONCLUSION

Early LC after ERCP for the management of cholecystocholedecholithiasis is a safe, effective, and time-saving technique with a low rate of postoperative complications. However, the early LC after ERCP has some definite advantages over delayed LC after ERCP; it does not increase perioperative complications, conversion rate, or lengths of hospital stay. Early LC on the contrary reduces the risk of recurrence and progression of disease in the delay between ERCP.

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REFERENCES

1. **McNicoll C, Pastorino A, Farooq U *et al.* (2020):** Choledocholithiasis. StatPearls [Internet]. https://www.ncbi.nlm.nih.gov/books/NBK441961/
2. **Wang C, Tsai M, Wang Y *et al.* (2019):** Role of cholecystectomy in choledocholithiasis patients underwent endoscopic retrograde cholangiopancreatography. Scientific Reports, 9(1): 1-7.
3. **Sanawan E, Qureshi A, Qureshi S *et al.* (2017):** Effectiveness of ultrasound shear for clipless laparoscopic cholecystectomy versus conventional

unipolar electrocautery in patients with cholelithiasis. Journal of the College of Physicians and Surgeons Pakistan, 27(10): 611-615.

4. **Aziret M, Karaman K, Ercan M *et al.* (2019):** Early laparoscopic cholecystectomy is associated with less risk of complications after the removal of common bile duct stones by endoscopic retrograde cholangiopancreatography. The Turkish Journal of Gastroenterology, 30(4): 336-41.
5. **Köksal A, Eminler A, Parlak E (2018):** Biliary endoscopic sphincterotomy: Techniques and complications. World Journal of Clinical Cases, 6(16): 1073-78.
6. **El Nakeeb A, Ezzet H, Askar W *et al.* (2016):** Early versus late cholecystectomy after clearance of common bile duct stones by endoscopic retrograde cholangiopancreatography: a prospective randomized study. Surgical Laparoscopy Endoscopy and Percutaneous Techniques, 26(3): 202-207.
7. **Şenocak R, Çelik S, Kaymak Ş *et al.* (2020):** Perioperative outcomes of the patients treated using laparoscopic cholecystectomy after emergent endoscopic retrograde cholangiopancreatography for bile duct stones: Does timing matter. Turkish Journal of Trauma and Emergency Surgery, 26(3): 396-404.
8. **Ghnnam W (2016):** Early Versus Delayed Laparoscopic Cholecystectomy Post Endoscopic Retrograde Cholangio Pancreatography (ERCP). JSM Gen Surg Cases Images, 16: 1006-9.
9. **Morshed G, Shaban N (2012):** Early Versus Late Laparoscopic Cholecystectomy Post ERCP. The Medical Journal of Cairo University, 80(2): 689-691.
10. **Gorla G, Augustine A, Madhavan S (2014):** Optimal timing of laparoscopic cholecystectomy after endoscopic retrograde cholangiopancreatography. Journal of Current Surgery, 4(2): 35-39.
11. **Sahoo R, Samal D, Pradhan A *et al.* (2017):** Optimal timing of laparoscopic cholecystectomy after endoscopic retrograde cholangiopancreatography. International Surgery Journal, 4(10): 3504-3506.
12. **Donkervoort S, Van Ruler O, Dijksman L *et al.* (2010):** Identification of risk factors for an unfavorable laparoscopic cholecystectomy course after endoscopic retrograde cholangiography in the treatment of choledocholithiasis. Surgical Endoscopy, 24(4): 798-804.