

# Laparoscopic Cholecystectomy after Endoscopic Retrograde Cholangiopancreatography: The Optimal Timing for Operation

<sup>1</sup>Samir A Ammar, <sup>2</sup>Mohamad Abdel Bar, <sup>3</sup>Mohy El Shafy

## ABSTRACT

**Background:** In patients with choledochocystolithiasis (CCL), early laparoscopic cholecystectomy (LC), within 72 hours, is recommended after endoscopic stone extraction. The objective of this study is to investigate LC for CCL within 24 hours of endoscopic retrograde cholangiopancreatography (ERCP) to determine its feasibility and safety.

**Materials and methods:** Group I, those patients who had LC within 24 hours after ERCP was compared with group II, those who had LC after 24 hours, but within 72 hours. Primary outcome was the conversion rate from LC to open cholecystectomy. Secondary outcomes were duration of LC, postoperative morbidity and hospital stay.

**Results:** Of 60 consecutive patients, 31 were in group I and 29 were in group II. There were no differences in groups I vs II in demographics, laboratory or ultrasonographic findings. The hospital stay in group I was significantly shorter than that of group II ( $2.5 \pm 1.5$  vs  $4 \pm 2$  days respectively). There was no statistically significant difference in operative time, conversion to open cholecystectomy or postoperative morbidity between both groups.

**Conclusion:** LC for CCL within 24 hours after ERCP is feasible and safe with short hospital stay.

**Keywords:** Laparoscopic cholecystectomy, Gallstones, Common bile duct stones, Timing of operation.

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## INTRODUCTION

Symptomatic cholecystolithiasis is one of the most common gastrointestinal surgical entities, and a considerable amount of patients present with complications of gallstone

disease. There is no consensus on the correct strategy for the care of simultaneous gallbladder and common bile duct (CBD) stones. Many therapeutic options are available, including laparoscopic, endoscopic, percutaneous and open traditional techniques, either through a combination of these treatments or by conducting them in a stepwise sequence. Endoscopic retrograde cholangiopancreatography (ERCP) remains the preferred approach at most centers for managing patients with suspected CBD stones.<sup>1,2</sup> A CBD clearance can be carried out by ERCP with endoscopic sphincterotomy (ES) before laparoscopic cholecystectomy (LC) in many cases, and it is the most common strategy used in the majority of hospitals worldwide.<sup>1</sup>

The safety of early LC after ES for choledochocystolithiasis (CCL) has already been investigated in observational and randomized studies; early LC, within 72 hours, has a better outcome than delayed.<sup>3-8</sup> Early elective LC should be carried out for all surgically fit patients, regardless of age, since it may prevent biliary complaints related to GB stones, further CBD procedures or emergency surgery, which is a more difficult procedure with poorer results.<sup>9</sup> However, no clinical trials address LC within 24 hours after ERCP. The purpose of this study is to evaluate feasibility and safety of LC within 24 hours after ES for CCL.

## MATERIALS AND METHODS

This prospective randomized study was carried out in the period from January 2011 to January 2014 at Department of Surgery, Assiut University Hospital, Egypt. All patients of 18 years and older who underwent successful ERCP and ES and stone extraction for choledocholithiasis and who had radiologically proven residual gallbladder stones were eligible for inclusion. Patients were divided into two groups: Group I, those patients who had LC within 24 hours after ES and group II, those who had LC after 24 hours, but within 72 hours of ERCP.

Our exclusion criteria were, contraindication or failure of ERCP, previous abdominal operations, associated comorbidities, pregnancy, or evidence of inflammation: cholangitis [abdominal pain, fever, elevated bilirubin, elevated leukocyte count/C-reactive protein (CRP) and pus drainage after

<sup>1</sup>Assistant Professor, <sup>2</sup>Senior Resident, <sup>3</sup>Professor

<sup>1-3</sup>Department of Surgery, Assiut University Hospital, Assiut Egypt

**Corresponding Author:** Samir A Ammar, Assistant Professor, Department of Surgery, El Gamaa Street, Assiut University Hospitals, Assiut, Egypt, Phone: 02-0882180562 e-mail: samirahmed70@hotmail.com

ES], pancreatitis (upper abdominal pain, elevated leukocyte count/CRP, elevated amylase at least 3 times normal, and elevated lipase levels), and cholecystitis (pain in the right upper quadrant, fever and leukocytosis, in the absence of hyperbilirubinemia).

All patients were subjected to complete evaluation through a detailed history, complete physical examination, laboratory investigations, and imaging study (US and/or MRCP). Randomization was done using computer-generated random number sequences. ERCP was performed for all patients under general anesthesia. If CBD stones were found on endoscopic cholangiography, ES was performed and the stones were extracted using either Dormia basket or balloon catheter. Mechanical lithotripsy was done in cases of large stones. Occlusion cholangiography was done at the end of every ERCP to ensure that no missed stones.

Laparoscopic cholecystectomy was done in both groups by the same surgical team using the standard four-port technique. In case of difficulty or complication, conversion to open cholecystectomy was done by a subcostal incision. The decision for conversion could only be taken by the most experienced surgeon in the operating team.

Primary outcome was the conversion rate from laparoscopic to open cholecystectomy. Secondary outcomes were duration of LC (measured from first incision to last skin suture), postoperative morbidity and hospital stay. Complications were recorded during the hospital stay and at the outpatient clinic, which every patient visited after 2 to 4 weeks. All patients were followed up for 6 months and were instructed to notify the surgeon if there were any symptoms suggesting biliary complication.

## STATISTICAL ANALYSIS

Statistical analyses were performed using the Statistical Package for Social Sciences, version 16.0 (SPSS Inc, Chicago, IL, USA). Data are expressed as mean  $\pm$  standard deviation (SD) for continuous variables and percentages for categorical variables. Student t-test was used to analyze continuous variables, whereas chi-square test was used to analyze categorical variables. p-value is considered statistically significant when less than 0.05.

## RESULTS

During the period of the study, out of 65 patients recruited, 60 patients were included in the final analysis. Five patients were complicated by mild post ERCP pancreatitis, 3 in group I and 2 in group II, and excluded from the final analysis. Patients with acute pancreatitis were treated successfully with conservative treatment. No other post ERCP complications were reported.

Laparoscopic cholecystectomy was performed in 31 patients in group I and in 29 patients in group II. The age ranged from 25 to 65 years (mean  $46 \pm 12.8$ ). Both groups were matched to each other as regard age, sex, laboratory and US characteristics (Table 1).

No mortality was recorded in either group. The mean duration of surgery was longer in group 2 than in group 1 ( $48.5 \pm 11.6$ ) vs ( $43 \pm 10.4$ ) but the result did not reach statistical significance. The conversion rates to an open procedure were 6.4 and 10.3% in groups I and II respectively (Table 2). The main reasons for conversion were dense adhesions in Callot's triangle, unclear anatomy and bleeding from the gallbladder bed. The hospital stay was

**Table 1:** Patients' characteristics

Variables	Group I	Group II	p-value
Number of cases	31	29	
Age (years) (mean $\pm$ SD)	$46.2 \pm 11.2$	$47.3 \pm 11.1$	0.7
Sex (female/male)	21/10	21/8	0.69
Proportion of abnormal LFTs (%)	25/31 (80%)	26/29 (89%)	0.3
US findings			
• Dilated CBD diameter ( $> 8$ mm)	29/31 (93.5%)	24/29 (82.7%)	0.19
• CBD stone (s)	28/31 (90%)	23/29 (79.3%)	0.23

LFTs: Liver function tests

**Table 2:** Patients' outcomes

Variables	Group I	Group II	p-value
Operative time (min) (mean $\pm$ SD)	$43 \pm 10.4$	$48.5 \pm 11.6$	0.057
Conversion rate	6.4%	10.3%	0.58
Length of hospital stay (days) (mean $\pm$ SD)	$2.5 \pm 1.5$	$4 \pm 2$	0.001
Postoperative complications			
• Bleeding	0	1/29 (3.4%)	
• Bile leak	1/31 (3.2%)	0	
• Wound infection	0	1/29 (3.4%)	

significantly prolonged among patients in the group II ( $4 \pm 2$  days) vs ( $2.5 \pm 1.5$  days) in group I.

One patient had cystic stump leakage after LC, for which postoperative endoscopic intervention and stent placement was done. This patient did recover completely. Another patient had postoperative blood collection in gallbladder bed and percutaneous pigtail catheter drainage was carried out. Otherwise, the complications in all groups were minor, and responded well to conservative management. During the follow-up period, no biliary symptoms appear in both groups.

## DISCUSSION

The last 30 years have seen major developments in the management of gallstone-related disease. ERCP has become a widely available and routine procedure, whilst open cholecystectomy has largely been replaced by a laparoscopic approach, which may or may not include laparoscopic exploration of the common bile duct (LCBDE). In addition, new imaging techniques such as magnetic resonance cholangiography (MRC) and endoscopic ultrasound (EUS) offer the opportunity to accurately visualize the biliary system without instrumentation of the ducts.<sup>1,10</sup>

Cholelithiasis is concomitant with gallstones in approximately 3 to 20% of the patients.<sup>11-16</sup> In the pre-endoscopy and prelaparoscope era, the standard treatment for patients suffering from gallstones accompanied with CBD stones was open cholecystectomy and CBD exploration.<sup>17</sup> Currently, open choledochotomy could still play a role in those cases with an intraoperative unexpected diagnosis of choledocholithiasis, with CBD dilatation or where all other endoscopic, percutaneous and laparoscopic approaches failed.<sup>18</sup> However, open CBD exploration remains the 'gold standard' for selected rare patients, such as those with Mirizzi syndrome, Billroth II anatomy, and those requiring a drainage procedure.<sup>18,19</sup> A Roux-en-Y hepaticojejunostomy, a choledochojejunostomy, or a surgical sphincteroplasty may be indicated for sphincter of Oddi stenosis/dysfunction, primary CBD stones, patients with duodenal diverticula, multiple stones or intrahepatic stones.<sup>10</sup>

With the advent of laparoscopic and endoscopic techniques, several alternative treatments have been developed to treat CCL. An interesting observational study from Sweden reported a so-called 'paradigm shift' from open choledochotomy and cholecystectomy toward bile duct clearance using the endoscopic route and selective LC in patients suffering from CCL.<sup>20</sup> Cholecystectomy is recommended for all patients with CBD stones and symptomatic gallbladder stones, unless there are specific reasons for considering surgery inappropriate.<sup>1</sup>

Endoscopic retrograde cholangiopancreatography remains the preferred approach at most centers for managing patients with suspected CBD stones. However, ERCP is associated with complications such as pancreatitis, hemorrhage, cholangitis, duodenal perforation (5 to 11%) and mortality of up to 1%.<sup>2</sup> Moreover, failure rates of 5 to 10% are reported with ERCP. In the present study, mild post-ERCP pancreatitis occurred in five patients (6.7%); all of them were treated successfully with conservative treatment. In addition, when patients proceed to ERCP, a significant number of them may not have stones.<sup>21,22</sup> ERCP should be performed only in patients who are expected to require an intervention; it is not recommended for use solely as a diagnostic test.<sup>23</sup>

Previous studies have shown that LC after ES is more difficult than LC for uncomplicated cholelithiasis: the conversion rate after a previous ES has been reported to be as high as 8 to 55% vs lower than 5% in patients with uncomplicated disease.<sup>4,8,9,24-28</sup> In this study, the conversion rates to an open procedure were 6.6 and 10.6% in groups I and II respectively. It might be beneficial to have these patients operated on by an experienced laparoscopic surgeon to minimize the risk of conversion and subsequent morbidity.<sup>29</sup> The etiology is thought to be because of disruption of the sphincter of Oddi and subsequent bacterial colonization of the biliary tract leading to inflammation and subsequent scarring of the hepatoduodenal ligament hindering dissection of Calot's triangle. This theory of reflux and bacterial colonization is strengthened by the finding that bile in patients who have undergone a sphincterotomy is colonized in approximately 60% of patients.<sup>30,31</sup>

The technique of combined LC with intraoperative ERCP as a single-step procedure implies some organizational problems concerning the availability of an endoscopic setting and experienced endoscopist in the operating theater whenever needed. Performing ERCP after surgery would raise the dilemma of managing CBD stones whenever ERCP fails to retrieve them because a third procedure would then be needed.<sup>1,32,33</sup> Sequential treatment, ES followed by early elective LC, is a safe procedure, and should be considered as a standard, definitive treatment for CCL.<sup>34</sup>

Laparoscopic cholecystectomy should be performed soon after ES; surgery could be easier if performed early before inflammatory process sets in. This study revealed that the first group stayed in the hospital for a shorter time than the second group ( $2.5 \pm 1.5$  vs  $4 \pm 2$  days). This difference in the length of stay was statistically significant ( $p = 0.001$ ). Such a longer stay will possibly lead to increased cost of health services and could lead to increased incidence of hospital acquired infections. If early LC for acute cholecystitis is

recommended within 24 hours,<sup>35</sup> it should be possible to offer the same standard of care to patients with CCL after ES. These findings have implications for surgical practice. However, patient's condition, organizational facilitation, operator's expertise and local resources should be taken into account in making treatment decisions.

## CONCLUSION

Laparoscopic cholecystectomy for CCL within 24 hours after ERCP is feasible and safe and has become our standard of practice.

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