ORIGINAL ARTICLE

THE EFFECT OF TIME INTERVAL BETWEEN ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATICOGRAPHY AND LAPAROSCOPIC CHOLECYSTECTOMY

Gouda El-labban,[1] Emad Hokkam,[1] Mohamed Adel,[1] Nader El-Nemr,[2] Mohamed Abdu[2]

[1]Department of General Surgery, [2]Department of medicine, Faculty of Medicine, Suez Canal University, Egypt

Correspondence to: Gouda El-labban, Email: ellabbang@yahoo.com

Abstract

Aim: The appropriate time for laparoscopic cholecystectomy (LC) following endoscopic retrograde cholangiopancreaticography (ERCP) in patients with obstructive choledolithiasis is controversial. We aim to compare early versus delayed LC after ERCP in patients with calcular obstructive jaundice as regards conversion rate, postoperative morbidity and hospital stay.

Methods: this study that was conducted on 124 patients who underwent LC after ERCP due to calcular obstructive jaundice. Patients were randomly classified to two groups; in the first group (early group, n=62) LC was performed within 72 hours after ERCP, while in the second group (delayed group, n = 62) LC was performed after 6 weeks.

Results: Conversion to open cholecystectomy was significantly more incident when LC was delayed for more than 6 weeks after ERCP (22.6% in delayed group versus 6.5% in early group). The duration of surgery and the postoperative hospital stay in the early group was significantly shorter than that of the delayed group (42.3± 10.6 minutes versus 72.2± 16.8 minutes and 1.1 ± 1.9 day versus 3.5 ± 1.2 days respectively). No statistically significant difference was found between both groups as regarding the postoperative morbidity.

Conclusion: Performing LC as early as possible (within 72 hours after ERCP) lowers the conversion rate to open cholecystectomy thus decreasing the anticipated postoperative morbidity and prolonged hospital stay.

Keywords: Laparoscopic cholecystectomy, choledocholithiasis, endoscopic sphincterotomy.

INTRODUCTION

In western countries and Japan, 10-15% of all patients with gallstones have coexisting common bile duct (CBD) stones. CBD stones can also be formed in the absence of gallbladder stones, and such primary stones are more common in East Asian countries than in the Western world.(1) ERCP is a useful diagnostic and therapeutic modality in CBD stones, endoscopic sphincterotomy (ES) has been widely accepted as the standard procedure for the treatment of (CBD) stones.(2,3) Although, surgery after successful ES for CBD stones remains controversial, many authors advocate it because nearly 55% of patients with CBDS have symptoms and half of them have complications.(4,5)

Moreover, many randomized studies have reported much higher incidence of biliary complications reaching 28% in those patients who not undergoing cholecystectomy after ES(6-8) while, other studies showed

that the cumulative risk for death is 21% within 5 years versus 5.8% for patients allocated to planned cholecystectomy).[9-11]

The ideal management of CBD stones is preoperative endoscopic retrograde cholangiopancreaticography (ERCP), followed by LC with intraoperative cholangiography or intraoperative ERCP to assure the complete clearance of CBD[4] The time interval between ERCP and LC is a matter of debate. Some retrospective[11-13] and other prospective[14] studies have investigated this issue without sharp clue or definite conclusion. The interval usually varies from days[15] to months.[9,10,16] It is widely accepted to operate early, within a short time following ERCP, but the exact time is not clear.[4] The influence of timing is thought to be due to possible inflammation during ERCP that caused by bile duct cannulation, contrast agent infusion and sphincterotomy.[17]

It is suggested that bile is infected with bacteria after disruption of Oddi's sphincter by sphincterotomy and stone extraction during ERCP. Also the procedure leads to an inflammation around the gallbladder, including the hepatoduodenal ligament, making cholecystectomy more risky.[10] This inflammatory response reaches its peak 2 to 6 weeks after ERCP. Accordingly, the risk of a LC in a patient undergoing ERCP is minimized if he was operated as early as possible in the first two weeks.[13]

The aim of the present study is to evaluate the effect of time interval between LC and ERCP in patients with calcular obstructive jaundice on conversion rates, postoperative morbidity and hospital stay.

PATIENTS AND METHODS

Between the period of May 2008 to May 2010, a total of 124 patients assigned for ERCP and subsequent cholecystectomy were recruited from the outpatient clinic of General Surgery department, Suez Canal University Hospital, Ismailia, Egypt. All of the included patients were subjected to complete evaluation through detailed history, complete physical examination and laboratory investigations. Randomization was done using computer-generated random number sequences in concealed envelopes with block randomization design. Informed consent was given, and patients not willing to undergo randomization were not included in the study. The study design was approved by the local research ethics committee while an informed consent was obtained from each patient before inclusion into the study.

The indications for ERCP were the presence of stones in common bile duct at ultrasonographic examination and suspicion of choledocholithiasis based on the presence of certain predictors (jaundice, dilated CBD, elevated serum bilirubun and elevated alkaline phosphatase).[18] Patients with evidence of inflammation (cholecystitis, pancreatitis, cholangitis), known allergy to contrast media and possible intra-abdominal adhesions (history of abdominal operation and peritonitis) were excluded from the study.

Endoscopic sphincterotomy was performed after the diagnosis of obstructive choledocholithiasis has been established by ERCP (Fig. 1). A balloon or basket attached to catheter's end was passed into the CBD allowing stone removal (Figs. 2,3). Cholangiography was done at the end of the procedure to assure the complete clearance of CBD. Stenting of the CBD was performed in case of any suspicious about its patency.

After ERCP, the patients were randomly classified using the even and odd numbers technique into two groups; in the first group (Early group, n=62), LC was performed within 72 hours, while in the second group (delayed group, n = 62), LC was performed after 6 weeks. The procedure was conducted using the standard 4-trocar technique with the patient under general anesthesia and endotracheal tube. Clipping and division of cystic duct and artery was done followed by dissection of the gall bladder from its hepatic bed. Drain was inserted in all patients. All the ERCP procedures were performed by single endoscopist while all the cholecystectomies were performed by the same surgical team.

The operating time was calculated from the start of the incision until placement of the last suture. The outcome was the rate of conversion from laparoscopic to an open procedure, complications of ERCP with endoscopic sphincterotomy and LC, hospital stay and mortality rate. All patients were followed up at 3 and 6 months and they were instructed to notify the surgeon if there are any biliary symptoms.

Gathered data were processed using SPSS version 15 (SPSS Inc., Chicago, IL, USA). Quantitative data were expressed as means ± SD while qualitative data were expressed as numbers and percentages (%). Student t test was used to test significance of difference for quantitative variables while Chi Square and Fisher's exact tests were used to test significance of difference for qualitative variables. A probability value (p-value) < 0.05 was considered statistically significant.

RESULTS

Patients in both groups (early and delayed) were matched to each other as regarding age, sex, laboratory and ultrasonographic characteristics. The mean age was 40.9 years and 42.6 years in early and delayed groups respectively. Most of the patients were females in both groups. The most common laboratory finding was elevated serum alkaline phosphatase (ALP) (77.4% in early group and 83.9% in late group). Dilated common bile duct was evident by ultrasound among 82.3% of patients in early group and 75.8 in late group. The sociodemographic and clinical data are summarized in Table 1.

Table 1. Baseline characteristics of the patients.

		Early group *(n=62)*	Delayed group *(n=62)*	P-value
Age (years) mean ± SD		40.9 ± 12.8	42.6 ± 11.3	0.6 (NS)
Sex	Male	30 (48.4%)	26 (41.9%)	0.7 (NS)
	Female	32 (51.6%)	36 (58.1%)	
Elevated bilirubin level		20 (32.3%)	24 (38.7%)	0.9 (NS)
Elevated serum ALP levels		48 (77.4%)	52 (83.9%)	0.7 (NS)
Elevated serum GGT levels		46 (74.2%)	50 (80.6%)	0.6 (NS)
Dilated CBD by US		51 (82.3%)	47(75.8%)	0.7 (NS)
CBD stone by US		45 (72.6%)	42 (67.7%)	0.9 (NS)

Normal values:

- Bilirubin, total: 0.2-1.3 mg/dL.
- Alkaline phosphatase (ALP): 38-126 U/L.
- GGT: 8-78 U/L.
- Normal CBD diameter in adults ≤ 8mm.

NS: No statistically significant difference (p-value > 0.05).

No complications due to ERCP, such as acute pancreatitis, duodenal perforation, bleeding were recorded in either of the groups. During the waiting period, 14 patients in the delayed group (22.6%) developed biliary events in the form of acute cholecystitis (7 patients), recurrent obstructive choledocholithiasis (4 patients) and cholangitis (3 patients). Patients with cholecystitis or cholangitis were managed conservatively by antibiotics and intravenous fluids till the condition stabilize while patients with choledocholithiasis were managed by endoscopic reintervention. Then, all complicated patients were prepared for cholcystectomy in their scheduled time.

On analysis of the intra-operative characteristics, it was found that patients in delayed group have significantly longer duration of surgery (72.2 minutes versus 42.3 minutes for patients in the early group). Conversion to open cholecystectomy was significantly more incident when LC was delayed for more than two months after ERCP. Conversion rate was 22.6% among patients in delayed group versus 6.5% in early group. The main causes for conversion were dense adhesions in Callot's triangle, unclear anatomy and bleeding from the gall bladder bed.

There were no intraoperative complications in either of the groups. Although, the postoperative complications were more common in the delayed group, yet they were minor and insignificant between both groups (3 patients with wound infection and 5 patients with mild fever in the early group compared to 4 and 7 patients respectively in the delayed group). The Postoperative hospital stay was significantly prolonged among patients in the delayed group (3.5 ± 1.2 days versus 1.1 ± 1.9 days in the early group). During the follow up period; no biliary symptoms appear in both groups. The perioperative characteristics are illustrated in Table 2.

Table 2. Conversion rate, operative characteristics and postoperative morbidity.

		Early group (n=62)	Delayed group (n=62)	P-value
Conversion rate		4 (6.5%)	13 (22.6%)	0.02*
Duration of operation (min) mean ± SD		42.3± 10.6	72.2± 16.8	0.001*
Postoperative hospital stay (days) mean ± SD		1.1 ± 1.9	3.5 ± 1.2	0.001*
Postoperative complications				
	Wound infection	3 (3.2%)	5 (8.1%)	0.3 (NS)
	Fever	5 (8.1%)	7 (11.3%)	0.3 (NS)

NS: No statistically significant difference (p-value > 0.05).
* Statistically significant difference (p-value < 0.05).

Fig 1. ERCP showing stone in the common bile duct.

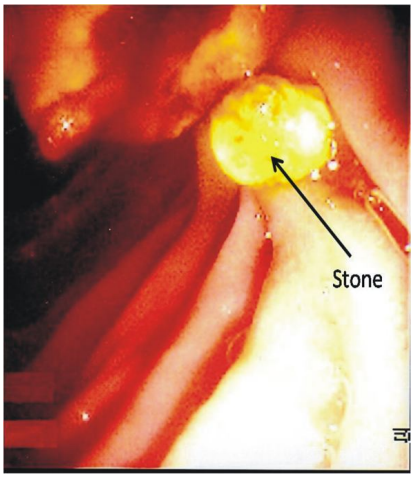

Fig 3. Showing stone extraction.

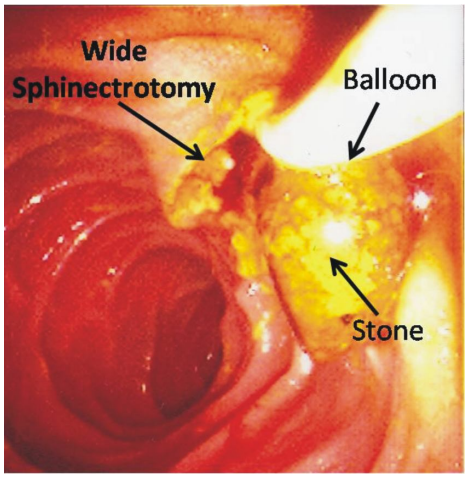

Fig 2. Showing wide sphincterotomy and balloon extraction of the stone.

DISCUSSION

During the last three decades, major advances in the management of CBD stones have been developed. ERCP is now widespread and is considered a routine step to attain ductal clearance before LC.[19] Few studies have investigated the time interval between the two procedures and produce conflicting results. Some studies[4,13] found that short interval is associated with fewer complications and lower conversion rate to open cholecystectomy while others[11,14] found no association.

In the present study; we evaluated the difference between patients who underwent LC within 72 hours after ERCP and those who underwent LC after 6 weeks of ERCP. The first 72 hours was chosen because the possible inflammatory process produced by ERCP should be at its start without formation of adhesions or development of oedema while after 6 weeks the oedema

subsided and adhesions may be improved or completely resolved.

The present study showed that 22.6% of patients waiting to undergo cholecystectomy after 6 weeks of ERCP had experienced at least one biliary event that require intervention. In accordance to our results; Schiphorst et al[11] showed that one every five patients had experienced recurrent biliary event in his/her wait and see period. However; other authors[9,21] have shown higher rate of recurrent biliary events after sphincterotomy. This difference between studies may come from diversity of time interval between ERCP and cholecystectomy.

Our results show that patients who underwent LC within 72 hours after ERCP have significantly lower conversion rate to open cholecystectomy, shorter hospital stay and shorter operation time when compared to patients who underwent LC after 6 weeks of ERCP. This is in agreement with the results of Salman et al[4] who conducted a randomized trial to compare patients who operated between 24 and 72 h after ERCP and those who operated more than 72 h after ERCP. Another benefit of early LC is avoiding the risk of new stones that may slip down the CBD with time.

The main reasons for conversion to laparotomy were extensive inflammatory adhesions and oedema while intraoperative bleeding is a less likely cause. The same findings were observed by Bostanci et al[14] and Hassanen.[22] Certainly, the conversion rate is affected by experience and skills of the surgeon.[23] In the present study we tried to eliminate this bias by conducting all operations in both groups by one surgical team.

The operating time was longer in patient underwent delayed cholecystectomy possibly due to scarring and fibrosis of the biliary tree and Calot's triangle which make the surgeon very cautious during dissection of the junction between cystic duct, common hepatic duct and CBD. Also patients in this group have significantly longer hospital stay than patients in the early group. This partially due to increased number of patients who underwent open cholecystectomy and the more encountered postoperative complications in the delayed group.

In conclusion, it is recommended to perform LC as early as possible within 72 hours after ERCP to decrease the conversion rate to open cholecystectomy thus decreasing the anticipated postoperative morbidity and prolonged hospital stay.

Acknowledgment: The authors would like to thank prof/ Ahmed Ellabban and prof/Amed Hafez Helmy for their revision of this paper.

REFERENCES

1. Tazuma S. Epidemiology, pathogenesis, and classification of biliary stones (common bile duct and intrahepatic). Best Pract Res Clin Gastroenterol. 2006;20:1075-83.
2. Helmy H, Abbas M, Youssef Y, Rizk H, Elkhyat H, Elserafry M, et al. The timing of choledocholithotomy and the type of biliary drainage after failed Endoscopic Retrograde Cholangiopancreatography in calcular obstructive Jaundice. Egy J Surg. 2002;4;1088-69.
3. Costi R, DiMauro D, Mazzeo A, Boselli AS, Contini S, Violi V, et al. Routine laparoscopic cholecystectomy after endoscopic sphincterotomy for choledocholithiasis in octogenarians: is it worth the risk? Surg Endosc. 2007;21:41-7.
4. Salman B, Yilmaz U, Kerem M, Bedirli A, Sare M, Sakrak O, et al. The timing of laparoscopic cholecystectomy after endoscopic retrograde cholangiopancreaticography in cholelithiasis coexisting with choledocholithiasis. J Hepatobiliary Pancreat Surg. 2009;16:832-6.
5. Fink AS. Current dilemmas in management of common bile duct stones. Surg Endosc. 1993;7:285.
6. Carr-Locke DL. Cholelithiasis plus choledocholithiasis: ERCP first, what next? Gastroenterol. 2006;130:270-2.
7. Hammarstrom LE, Holmin T, Stridbeck H, Ihse I. Long-term follow-up of a prospective randomised study of endoscopic versus surgical treatment of bile duct calculi in patients with gallbladder in situ. Br J Surg. 1995;82:1516–21.
8. Targarona EM, Ayuso RM, Bordas JM, Ros E, Pros I, Martinez J, Terés J, et al. Randomised trial of endoscopic sphincterotomy with gallbladder left in situ versus open surgery for common bile duct calculi in high-risk patients. Lancet. 1996;347:926–9.
9. Lau JY, Leow CK, Fung TM, Suen BY, Yu LM, Lai PB, et al. Cholecystectomy or gallbladder in situ after endoscopic sphincterotomy and bile duct stone removal in Chinese patients. Gastroenterol. 2006;130:96-103.
10. Boerma D, Rauws EA, Keulemans YC, Janssen IM, Bolwerk CJ, Timmer R, et al. Wait-and-see policy or laparoscopic cholecystectomy after endoscopic sphincterotomy for bile duct stones: a randomised trial. Lancet. 2002;360:761–5.
11. Schiphorst AH, Besselink MG, Boerma D, Timmer R, Wiezer MJ, van Erpecum KJ, et al. Timing of cholecystectomy after endoscopic sphincterotomy for common bile duct stones. Surg Endosc. 2008;22:2046-50.
12. Allen NL, Leeth RR, Finan KR, Tishler DS, Vickers SM, Wilcox CM, et al. Outcomes of cholecystectomy after endoscopic sphincterotomy for choledocholithiasis. J Gastrointest Surg. 2006;10:292–6.
13. De Vries A, Donkervoort SC, van Geloven AA, Pierik EG. Conversion rate of laparoscopic cholecystectomy after endoscopic retrograde cholangiography in the treatment of choledocholithiasis: does the time interval matter? Surg Endosc. 2005;19:996–1001.

14. Bostanci EB, Ercan M, Ozer I, Teke Z, Parlak E, Akoglu M. Timing of elective laparoscopic cholecystectomy after endoscopic retrograde cholangiopancreaticography with sphincterotomy: a prospective observational study of 308 patients. Langenbecks Arch Surg. 2010;395:661-6.

15. Yamashita Y, Takada T, Kawarada Y, Nimura Y, Hirota M, Miura F, et al. Surgical treatment of patients with acute cholecystitis: Tokyo guidelines. J Hepatobiliary Pancreat Surg. 2007;14:91–7.

16. Hamy A, Hennekinne S, Pessaux P, Lada P, Randriamananjo S, Lermite E, et al. Endoscopic sphincterotomy prior to laparoscopic cholecystectomy for the treatment of cholelithiasis. Surg Endosc. 2003;17:872–5.

17. Misra SP, Dwivedi M. Complications of endoscopic retrograde cholangiopancreatography and endoscopic sphincterotomy: diagnosis, management and prevention. Natl Med J India. 2002;15:27-31.

18. Abboud PA, Malet PF, Berlin JA, Staroscik R, Cabana MD, Clarke JR, et al. Predictors of common bile duct stones prior to cholecystectomy: a meta-analysis. Gastrointest Endosc. 1996;44:450-5.

19. Williams EJ, Green J, Beckingham I, Parks R, Martin D, Lombard M, British Society of Gastroenterology. Guidelines on the management of common bile duct stones (CBDS). Gut. 2008;57:1004-21.

20. Renton-Power W. Laparoscopic cholecystectomy: potential for missed pathology. Ann R Coll Surg Engl. 1995;77:233.

21. Reinders JS, Goud A, Timmer R, Kruijt PM, Witteman BJ, Smakman N, et al. Early laparoscopic cholecystectomy improves outcomes after endoscopic sphincterotomy for choledochocystolithiasis. Gastroenterol. 2010;138:2315-20.

22. Hassanen A. Timing of laparoscopic cholecystectomy after endoscopic retrograde cholangiopancreatography. EJS. 2009;28:26-30.

23. Ibrahim S, Hean TK, Ho LS, Ravintharan T, Chye TN, Chee CH. Risk factors for conversion to open surgery in patients undergoing laparoscopic cholecystectomy. World J Surg. 2006;30:1698-704.