Available online at www.sciencedirect.com

SciVerse ScienceDirect

Journal of the Chinese Medical Association 75 (2012) 560–566

www.jcma-online.com

Original Article

The relationship between gallbladder status and recurrent biliary complications in patients with choledocholithiasis following endoscopic treatment

Tzung-Jiun Tsai [a,b,c], Kwok-Hung Lai [a,b,*], Chiun-Ku Lin [a,b], Hoi-Hung Chan [a,b,d], E-Ming Wang [a,d], Wei-Lun Tsai [a,b], Jin-Shiung Cheng [a,b,c], Hsien-Chung Yu [a,b], Wen-Chi Chen [a,b], Ping-I Hsu [a,b]

[a] *Division of Gastroenterology, Department of Internal Medicine, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan, ROC*
[b] *National Yang-Ming University School of Medicine, Taipei, Taiwan, ROC*
[c] *Division of Gastroenterology, Department of Internal Medicine, Kaohsiung Veterans General Hospital Tainan Branch, Tainan, Taiwan, ROC*
[d] *Department of Biological Sciences, National Sun Yat-Sen University, Kaohsiung, Taiwan, ROC*

Received December 21, 2011; accepted April 16, 2012

Abstract

Background: Endoscopic methods are currently the treatment of choice for patients with common bile duct (CBD) stones, but subsequent management of the intact gallbladder for patients following endoscopic treatment is still controversial. The primary aim of this study was to discover the association between gallbladder status and recurrent biliary complications for patients with CBD stones after endoscopic treatment. Additionally, we also sought to determine risk factors for recurrent biliary complications in these patients.
Methods: The records of 1625 patients with CBD stones following endoscopic treatment were reviewed. A total of 681 patients were enrolled and subsequently categorized into four groups: Group 1 ($n = 201$), calculous gallbladder; Group 2 ($n = 140$), acalculous gallbladder; Group 3 ($n = 175$), elective cholecystectomy after endoscopic treatment; and Group 4 ($n = 165$), prior cholecystectomy. The basic demographics and recurrent biliary complications during follow-up among these four groups were analyzed by Chi-square test, ANOVA, Kaplan-Meier analysis, and log-rank test.
Results: During the median follow-up period of 34 months, 133 patients (20%) with recurrent biliary complications were identified. The recurrence rates of Groups 1, 2, 3, and 4 were 29%, 11%, 15%, and 19%, respectively. Kaplan-Meier analysis showed that patients with calculous gallbladder had a significantly higher rate of recurrent biliary complication. In multivariate analysis, patients with a history of cirrhosis, juxta-papillary diverticulum, calculous gallbladder, CBD size $\geq$1.5 cm, and endoscopic management with endoscopic sphincterotomy were at a higher risk for developing biliary complications ($p = 0.029$, $p = 0.039$, $p < 0.001$, $p = 0.002$, $p = 0.021$, respectively.)
Conclusion: Patients with cholecystolithiasis and CBD stones had a higher incidence of recurrent biliary complications. For some of these patients, elective cholecystectomy following endoscopic treatment may be considered. However, routine elective cholecystectomy in patients with normal gallbladder is not appropriate because of the low recurrence of biliary complications. Whether gallbladder function affects the biliary clearance and biliary complications requires further research.

Keywords: cholangitis; choledocholithiasis; endoscopic sphincterotomy; gallstones; pancreatitis

1. Introduction

Endoscopic management of common bile duct (CBD) stones, including endoscopic sphincterotomy (ES) and endoscopic balloon dilation (EBD), is a common and widespread

* Corresponding author. Dr. Kwok-Hung Lai, Division of Gastroenterology, Kaohsiung Veterans General Hospital, 386, Ta-Chung 1st Road, Kaohsiung 813, Taiwan, ROC.
E-mail address: khlai@vghks.gov.tw (K.-H. Lai).

1726-4901/$ - see front matter
http://dx.doi.org/10.1016/j.jcma.2012.08.003

choice of treatment. However, recurrent biliary complications arising from endoscopic management varies from 4% to 24%.[1] Dilated bile duct, juxtapapillary diverticulum (JPD), brown pigmented stones, lithotripsy during treatment, pneumobilia after ES, and calculous gallbladder *in situ* have all been proposed as possible risk factors for recurrent biliary complications,[2] but such risk factors can vary from study to study, and between different populations.

Although some studies reported that an intact calculous gallbladder is a risk factor for recurrent biliary complications, patient with an acalculous gallbladder may still develop similar complications.[3−5] In some Asian studies, routine cholecystectomy following ES does not reduce the incidence of recurrent biliary complications.[6−8] However, 15% to 37% of patients after ES whose gallbladder is left *in situ* will develop symptoms requiring cholecystectomy during a follow-up period ranging from 17 months to over 5 years.[9−12] Therefore, in some reports, cholecystectomy is recommended after bile duct clearance in patients with a calculous gallbladder.[9,11,13] The management of patients having acalculous gallbladder after bile duct clearance remains controversial. In one Asian study, patients with an acalculous gallbladder subsequent to initial clearance of the bile duct had a lower rate of recurrence of bile duct stones.[14]

Unlike patients from western countries, the major component of common bile duct stones in Chinese patients is bilirubinate. Therefore, the role of gallbladder status in recurrent biliary complications may differ.[12,15,16]

The aim of this retrospective study was to find the relationship between different gallbladder statuses and recurrent biliary complications for patients with CBD stones following endoscopic treatment, and also to evaluate whether elective cholecystectomy can effectively reduce biliary complications.

2. Methods

2.1. Patients

We enrolled 1625 consecutive patients admitted to Kaohsiung Veterans General Hospital from January 1991 to December 2008 with CBD stones, who received either ES or EBD and successful clearance of the bile duct stones. Patients with concomitant malignancies, prior Billroth II gastrectomy, incomplete clearance of bile duct and a follow-up period of <6 months were excluded. Consequently, a total of 681 patients were included in this study. These patients were categorized into four groups according to the gallbladder status: Group 1, intact gallbladder with stones; Group 2, intact gallbladder without stones; Group 3, elective cholecystectomy following endoscopic treatment; and Group 4, cholecystectomy before endoscopic treatment.

2.2. Procedures

Standard endoscopic treatment was performed using a side-viewed endoscope (JF1T-20, JF-240, JF1T-30; Olympus Optical Corporation, Tokyo, Japan). The stone number, stone size (the largest diameter), and the CBD size were measured by endoscopic retrograde cholangiography. For ES, sphincterotomy was done using a wire-guided sphincterotome (Olympus Optical Corporation). For EBD, a dilated balloon catheter (Olbert, 8 mm and 10 mm in diameter and 4 cm in length; CRE, 6−8 mm, 8−10 mm, 10−12 mm, 12−15 mm, 15−18 mm, 18−20 mm in diameter and 5.5 cm in length; Microvasive, Boston Scientific Corporation, Watertown, MA, USA) was passed over the guide wire into the bile duct after guidewire insertion as ES. The size of the balloon was determined by the stone size and did not exceed the maximum diameter of the CBD. The balloon was gradually inflated with sterile saline at a pressure according to the manufacturer's instructions, and balloon inflation was halted whenever the patient experienced discomfort. The stones in the common bile duct were then removed using a Dormia basket after ES or EBD, with or without use of a mechanical lithotriptor (BML-4Q; Olympus Optical). If the first treatment resulted in incomplete removal of all stones, a second stone extraction attempt was performed within 7 days. All patients were observed in the hospital for at least 24 hours following endoscopic treatment.

2.3. Follow-up

During endoscopic treatment, the general data and the endoscopic findings, including the presence of JPD, stone size, and stone numbers, were recorded. Stone removal was declared complete if the final cholangiogram showed no residual stones. After clearance of the bile duct and normalization of liver function, each patient was routinely advised to have regular follow-up evaluations that included an interview, biochemical testing of liver function (total serum bilirubin, albumin, alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase), and transabdominal ultrasonography (US) every 3 to 6 months. Follow-up for patients with an intact gallbladder occurred every 3 months, and patients having previous cholecystectomy before endoscopic treatment or elective cholecystectomy after endoscopic treatment were followed up every 6 months. If any biliary symptoms developed between visits, the patient was advised to contact us immediately. Endoscopic retrograde cholangiography was performed if US demonstrated echogenic foci within the bile duct or significant dilatation of the common bile duct in comparison with previous US, or if abnormal liver function tests developed accompanied by typical biliary pain.

All complicating biliary events that occurred during follow-up were recorded, including acute cholecystitis, cholangitis, biliary colic, recurrent CBD stones, and acute pancreatitis.

2.4. Statistical analysis

All statistical analyses were performed with the SPSS program (version 12.0.1C; SPSS Inc., Chicago, USA). The values were expressed as mean ± SD. Categorical variables were tested by the Chi-square test or Fisher's exact test. The continuous values between four categorical groups were

analyzed by one-way ANOVA. A p-value < 0.05 was considered significant. The cumulative biliary complication rates between the four groups were calculated by the Kaplan-Meier method. We used binary logistic regression for multivariate analysis of the risk factors.

3. Results

The 681 patients in this study were categorized into four groups according to the gallbladder status: Group 1 ($n = 201$), intact gallbladder with stones; Group 2 ($n = 140$), intact gallbladder without stones; Group 3 ($n = 175$), elective cholecystectomy following endoscopic treatment; and Group 4 ($n = 165$), cholecystectomy before endoscopic treatment. The characteristics of the four groups of patients were shown in Table 1. The median follow-up time was 34 months (6–212 months); 68% of all patients were male, 49% of them had a JPD, and 6% were receiving lithotripsy. The mean age was 66 ± 14 years, mean CBD size 1.5 ± 0.5 cm, and mean stone size 1.1 ± 0.5 cm, with 43% of patients having multiple CBDS. There were no significant difference between the four groups in gender, JPD, cirrhosis, total bilirubin level, and the number of stones. We found that patients with prior cholecystectomy on average had a larger stone size (1.3 ± 0.6 cm, $p = 0.004$), a larger CBD size (1.7 ± 0.6 cm, $p < 0.001$), and were more likely to receive lithotripsy (11%, $p = 0.018$). Patients receiving elective cholecystectomy were younger than the other three groups (62 ± 15 year-old, $p < 0.001$).

The interval between endoscopic management and the cholecystectomy was a median of 6 days (1–300). Five patients had the cholecystectomy with an interval of >100 days, three had no recurrent biliary complications, and two had recurrent biliary complications, but the complications all occurred at least 6 months after the surgery.

In total, 133 (20%) biliary complications occurred during the follow-up period. Within the four groups, there were 29% (59/201) of patients in Group 1, 11% (16/140) in Group 2, 15% (26/175) in Group 3, and 19% (32/165) in Group 4 who had biliary complications in the follow-up period ($p < 0.001$). Those biliary complications included recurrent bile duct stone events in 31, 14, 24, and 26 patients in Groups 1, 2, 3, and 4, respectively; 16 acute cholecystitis events occurred in Group 1 patients; biliary colic events occurred in 11, one, two, and three patients of Groups 1, 2, 3, and 4, respectively; and acute pancreatitis occurred in one patient in Group 4 (Table 2). All 16 patients with acute cholecystitis received surgical resection. Three of the Group 1 patients with acute cholecystitis developed gallbladder rupture. One patient died after the operation, and the other 15 patients with acute cholecystitis recovered after surgery. Gallbladder cancer was not observed in these patients. All patients with recurrent bile duct stones were successfully treated with repeated ERCP and stone extraction. Those patients with cholangitis were treated conservatively with antibiotics and the image studies revealed no recurrent bile duct stones. In patients with typical biliary colic, the liver biochemical data was normal, which included total serum bilirubin, albumin, alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase. Only one patient (who had a history of prior cholecystectomy) developed acute pancreatitis, and repeated ERCP did not demonstrate any bile duct stones. He was treated successfully with conservative medical management.

Kaplan-Meier analysis was performed to compare the incidence of recurrent biliary complication between the four groups. It revealed a significantly higher incidence of biliary complications in Group 1 compared to the other three groups ($p < 0.001$) (Fig. 1).

Among the potential risk factors for the occurrence of biliary complications, there were six significant factors (Table 3) noted in univariate analysis: history of cirrhosis, JPD, calculous gallbladder, use of lithotriptor for stone clearance, CBD size ≥1.5 cm, and endoscopic management with ES patients.

In multivariate analysis, patients with a history of cirrhosis, JPD, calculous gallbladder, CBD size ≥1.5 cm, and endoscopic management with ES were at a higher risk for developing biliary complications ($p = 0.029$, $p = 0.039$, $p < 0.001$, $p = 0.002$, $p = 0.021$ respectively, Table 4).

Patients with CBD stones managed with ES had a higher risk of biliary complications compared to the EBD group

Table 1
Characteristics of the four groups of patients following endoscopic treatment for common bile duct stones.

	Group 1	Group 2	Group 3	Group 4	All	p
n	201	140	175	165	681	
Male gender	66%	74%	65%	70%	68%	0.278
Age (y)	65.9 ± 14.46	68.3 ± 11.84	62.3 ± 14.76	67.2 ± 11.99	65.8 ± 13.62	<0.001
JPD	48%	50%	43%	55%	49%	0.151
DM	20%	13%	17%	12%	16%	0.148
Hypertension	33%	35%	29%	22%	30%	0.060
Cirrhosis	7%	7%	4%	8%	7%	0.446
Lithotripsy (%)	4%	4%	4%	11%	6%	0.018
Stone size (cm)	1.1 ± 0.47	1.2 ± 0.57	1.0 ± 0.52	1.3 ± 0.56	1.1 ± 0.53	0.004
Multiple stones	46%	42%	42%	43%	43%	0.808
CBD size (cm)	1.5 ± 0.51	1.5 ± 0.48	1.4 ± 0.48	1.7 ± 0.56	1.5 ± 0.52	<0.001
Total bilirubin (mg/dL)	4.4 ± 4.34	4.3 ± 4.09	4.4 ± 3.89	3.3 ± 2.81	4.2 ± 3.90	0.088
Follow-up time (months)	33.3 ± 31.28	47.8 ± 40.97	52.2 ± 42.95	50.2 ± 42.44	45.3 ± 39.95	<0.001

CBD = common bile duct; DM = diabetes mellitus; JPD = juxtapapillary diverticulum.

Table 2
Recurrent biliary complications in 4 groups of patients.

	Total $n = 681$	Group 1 $n = 201$	Group 2 $n = 140$	Group 3 $n = 175$	Group 4 $n = 165$
Recurrent CBDS	95	31 (15%)	14 (10%)	24 (14%)	26 (16%)
Acute cholecystitis	16	16	0	0	0
Biliary colic	17	11	1	2	3
Cholangitis	4	1	1	0	2
Acute pancreatitis	1	0	0	0	1
Total	133 (20%)	59 (29%)*	16 (11%)	26 (15%)	32 (19%)

*$p < 0.001$ compared with other three groups (1 *vs.* 2, 1 *vs.* 3, 1 *vs.* 4) by log-rank test. CBDS = common bile duct stones.

(21.8% vs 13.6%, $p = 0.013$). The patients who received these two different treatment modalities were further analyzed according to gallbladder status (Table 5). Only patients with a calculous gallbladder (Group 1) receiving ES had a significantly higher percentage of biliary complication compared to patients receiving EBD (35.5% vs 19.7%, $p = 0.018$). The other three groups showed no statistical difference between ES and EBD. Group 1 patients were further analyzed to see which complication was associated with endoscopic management. Patients in Group 1 with EBD had a reduced CBD stone recurrence rate and a lower incidence of biliary colic compared to ES (Table 6).

4. Discussion

This study demonstrated a higher incidence of recurrent biliary complications in patients with a calculous gallbladder (up to 29%) than in other patients. Although the recurrence of CBDS in patients with a calculous gallbladder did not significantly differ from other patients, 8% of patients developed acute choleycystitis during the follow-up period, and one of them died of sepsis. Ando et al[14] reported that 11% of patients after ES with calculous gallbladder and 2% of patients with elective cholecystectomy had recurrent bile duct stones. In a Dutch study,[11] 47% of those patients with calculous gallbladder developed recurrent biliary events and 37% required a cholecystectomy. In a Chinese study,[13] elective cholecystectomy following endoscopic treatment of bile duct stones reduced recurrent biliary events (by 24% in those with gallbladder *in situ* vs. 7% in those receiving laparoscopic cholecystectomy), so routine cholecystectomy is advisable for those patients with a calculous gallbladder after clearance of the bile duct.

Most of our patients, particularly elderly patients, were unwilling to undergo an operation for symptom relief after endoscopic management; this might be attributable to cultural differences. In our basic patient demographic data, we found patients receiving elective cholecystectomy were younger than in other groups (Table 1). The morbidity rate of cholecystectomy was higher in elderly patients, and even patients with elective cholecystectomy still had recurrent CBD stones.[7] The decision of whether to perform cholecystectomy must also consider the surgical risk to the patients.[1] In those patients with higher operational risk, and those unwilling to receive elective cholecystectomy, close monitoring during follow-up is indicated to avoid lethal complications.[17]

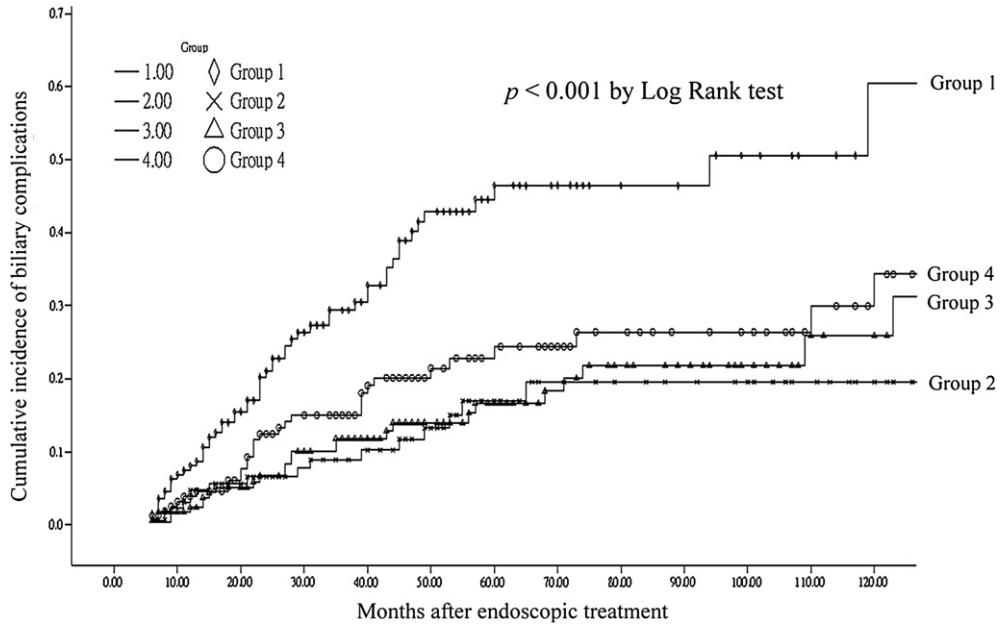

Fig. 1. The cumulative incidences of biliary complications in 4 groups of patients.

Table 3
Univariate analysis of risk factors for recurrent biliary complications.

	Recurrence (*n*)	Nonrecurrence (*n*)	*p*
Gender			
Male	91	373	1.000
Female	42	175	
Age			
≥65	87	357	1.000
<65	46	191	
Hypertension			
Yes	44	159	0.398
No	89	389	
Type 2 DM			
Yes	18	90	0.508
No	115	458	
Cirrhosis			
Yes	15	30	0.030
No	118	518	
JPD			
Yes	76	256	0.034
No	57	292	
Gallstone			
Yes	59	142	0.000
No	74	406	
Lithotripsy			
Yes	13	27	0.040
No	120	521	
Stone number			
≥2	67	229	0.080
Single	66	319	
Stone size			
≥0.8 cm	106	401	0.350
<0.8 cm	25	120	
CBD size			
≥1.5 cm	92	286	<0.001
<1.5 cm	41	261	
Endoscopic management			
ES	103	369	0.013
EBD	27	172	

CBD = common bile duct; DM = diabetes mellitus; EBD = endoscopic balloon dilation; ES = endoscopic sphincterotomy; JPD = juxtapapillary diverticulum.

Table 4
Multivariate analysis of the risk factors for recurrent biliary complications.

	OR	95% CI	*p*
Cirrhosis	2.143	1.083–4.239	0.029
JPD	1.530	1.022–2.290	0.039
Gallbladder stone	2.684	1.773–4.065	<0.001
CBD size ≥1.5 cm	1.943	1.264–2.987	0.002
Lithotripsy	1.848	0.883–3.867	0.103
ES	1.779	1.091–2.902	0.021

CBD = common bile duct; CI = confidence interval; ES = endoscopic sphincterotomy; JPD = juxtapapillary diverticulum; OR = odds ratio.

A Japanese study[16] evaluated the long-term outcome in patients after EBD, and found biliary complications were seen in 12.4% of the cases. The recurrent biliary complications were more frequent in the calculous gallbladder group than in the acalculous gallbladder, elective cholecystectomy, and prior cholecystectomy groups (22.6% vs. 9.2%, 2.8%, and 13.5%, respectively); stone recurrence was seen in 15.6%, 5.9%, 2.4%, and 10.8%, respectively. Our study showed similar rates of recurrent biliary complications of 29%, 11%, 15%, and 19%, and stone recurrence rates of 15%, 10%, 14%, and 16% respectively. Unlike the Japanese study, our patients who underwent elective cholecystectomy had a similar rate of recurrent CBDS as the other groups.

Gallstones are primarily comprised of cholesterol and bile pigments. In studies focusing on patients from western countries, gallbladder stones are mainly composed of cholesterol (consisting of more than 50% cholesterol).[18] However, in Asian patients, most gallstones are pigmented stones.[15] In western countries, most of the common bile duct stones were secondary, coming from the passage of gallstones in the gallbladder, and primary CBD stones were seen less frequently. In our previous study, bilirubinate was the predominant composition of initial or recurrent CBD stone in Chinese patients,[15] so the role of the gallbladder in recurrent CBDS differs from that role in populations where cholesterol is the major gallstone component.

In the basic demographic data, we also found patients with prior cholecystectomy before endoscopic treatment had larger stones (1.3 ± 0.6 cm, $p = 0.004$), larger CBDs (1.7 ± 0.6 cm, $p < 0.001$), and a higher rate of undergoing lithotripsy (11%, $p = 0.018$). Gallbladder motility is important to deliver bile through the CBD to the duodenum. It also helps to flush out the newly produced stone particles and prevent new stone formation in the bile duct.[14] Patients with prior cholecystectomy may develop bile stasis due to the absence of a "pumping" effect of the gallbladder. These patients also lost their gallbladder storage function, which resulted in larger CBD size and more sizeable stone formation.

In the multivariate analysis, we found patients who had cirrhosis, JPD, gallbladder stones *in situ*, CBD size >1.5 cm, and those who underwent ES for CBD stone removal were at risk of recurrent biliary complications. Most of those factors have been mentioned in previous reports.[2,4,7,14,16] In our study, cirrhosis was a significant risk factor for recurrent biliary symptoms, which was not mentioned in the previous literature. There were 15 cirrhosis patients with recurrent biliary symptoms. Eleven of them had recurrent CBD stones, two had biliary colic pain, and two had cholangitis. We know that cirrhosis is the major risk factor for gallbladder stones with

Table 5
Recurrence of biliary symptoms between two methods of endoscopic management for CBD stones.

	Group 1	Group 2	Group 3	Group 4	Total
ES	35.5% (44/124)	12.5% (13/104)	17.5% (21/120)	20.8% (25/120)	21.8% (103/472)
EBD	19.7% (15/76)	6.3% (2/32)	5.9% (3/51)	17.5% (7/40)	13.6% (27/199)
p	0.018	0.520	0.054	0.712	0.013

CBD = common bile duct; EBD = endoscopic balloon dilation; ES = endoscopic sphincterotomy.

Table 6
Recurrence of biliary complications between two methods of endoscopic management for CBD stones in Group 1 patients.

	Recurrent CBDS	Acute cholecystitis	Biliary colic	Cholangitis	Acute pancreatitis	Total
ES ($n = 124$)	27	7	10	0	0	44
EBD ($n = 76$)	4	9	1	1	0	15
p	0.002	0.117	0.042	0.38	0	0.018

CBD = common bile duct; EBD = endoscopic balloon dilation; ES = endoscopic sphincterotomy.

a prevalence of 29.5%.[19] The increased frequency of gallstone formation in cirrhosis patients might be due to several factors, including reduced hepatic synthesis and transport of bile salts and nonconjugated bilirubin,[20] high estrogen levels,[21] and impaired gallbladder contraction in response to a meal.[22] However, the reason for the recurrent CBD stone formation in cirrhosis patients is unclear. In our study, the number of cases in this subgroup was small, so it requires further large-scale study for a more detailed evaluation.

In our previous study,[23] we found that slower hepatic clearance in quantitative cholescintigraphy is an important factor for stone recurrence, and JPD is responsible for delayed biliary emptying. JPD may also induce bacterial contamination in the bile of patients with a dysfunctional sphincter of Oddi. These might contribute to the cause of the recurrent biliary tract stone formation and biliary complications.

The dilated CBD is commonly contaminated with bacteria[1,24] and has delayed biliary emptying,[23] which may contribute to the pathogenesis of recurrent stones. Clearly, small stone fragments after lithotriopsy may act as nidi,[14] combined with biliary stasis in dilated bile duct, resulting in recurrent stone formation.

Lithotripsy is a documented risk factor for recurrent biliary complications,[14] but it is not a significant factor in our study. The reason might be that the stones in our patient were loose in character, and we only had a small number of patients who received lithotripsy.

Patients who underwent ES had significantly more recurrent biliary complications than those who underwent EBD (22% vs 14% $p = 0.013$) in this study, similar to results Yasuda et al (25% vs 10%, $p = 0.0016$).[3] Unlike the traditional EBD method (maximum inflated outer diameter of 8 mm, dilating 1−2 minutes), we used the larger controlled radial expansion balloon for dilation from 3 to 5 minutes.[25] It has a high success rate of stone clearance, fewer complications, it minimizes the use of mechanical lithotripsy, and also has a low stone recurrence rate of 10%.[26] In our previous report, we found 71.6% of patients had loss of the function of the sphincter of Oddi following EBD.[27] The patients after large balloon EBD had less frequent recurrent biliary complication. This was probably due to the fact that the distal bile duct and whole biliary sphincter were dilated simultaneously, facilitating bile drainage and smooth passage of residual stone fragments, or newly formed stone particles.

We subgrouped the patients into four different gallbladder statuses to compare the difference between the patients receiving ES or EBD. We found that patients with a calculous gallbladder who received ES had a significantly higher percentage of biliary complication compared to the patients receiving EBD (35.5% vs 19.7%, $p = 0.018$), and that patients with EBD had reduced recurrent CBD stones and bilairy colic (of any statistical significance). In patients with a calculous gallbladder, recurrent stones might be due to both primary and secondary stones. Patients receiving EBD might have less distal biliary stricture and the primary stone or secondary stones may pass out more casually after the pumping effect of the gallbladder, thus resulting in fewer biliary complications. However, the exact mechanism of this process requires further study to confirm.

There were some limitations to our study. Many patients became symptom-free and did not return for follow-up examinations, so only 42% of total patients were included in this retrospective analysis. We may have underestimated or overestimated the rate of biliary complications, especially the rate of biliary colic. There is a wide variability of biliary emptying in response to food in patients with CBDS following endoscopic treatment.[28] Therefore, further prospective studies are required to examine the relationship between the intact gallbladder function and recurrent biliary complications.

Acknowledgments

This study was approved by the Institutional Review Board, Kaohsiung Veterans General Hospital (VGHKS11-CT6-06).

References

1. Cheon YK, Lehman GA. Identification of risk factors for stone recurrence after endoscopic treatment of bile duct stones. *Eur J Gastroenterol Hepatol* 2006;**18**:461−4.
2. Costamagna G, Tringali A, Shah SK, Mutignani M, Zuccalà G, Perri V. Long-term follow-up of patients after endoscopic sphincterotomy for choledocholithiasis, and risk factors for recurrence. *Endoscopy* 2002;**34**:273−9.
3. Yasuda I, Fujita N, Maguchi H, Hasebe O, Igarashi Y, Murakami A, et al. Long-term outcomes after endoscopic sphincterotomy versus endoscopic papillary balloon dilation for bile duct stones. *Gastrointest Endosc* 2010;**72**:1185−91.
4. Ohashi A, Tamada K, Wada S, Hatanaka H, Tomiyama T, Tano S, et al. Risk factors for recurrent bile duct stones after endoscopic papillary balloon dilation: long-term follow-up study. *Dig Endosc* 2009;**21**:73−7.
5. Kojima Y, Nakagawa H, Miyata A, Hirai T, Ohyama I, Okada A, et al. Long-term prognosis of bile duct stones: endoscopic papillary balloon dilatation versus endoscopic sphincterotomy. *Dig Endosc* 2010;**22**:21−4.
6. Lai KH, Lin LF, Lo GH, Cheng JS, Huang RL, Lin CK, et al. Does cholecystectomy after endoscopic sphincterotomy prevent the recurrence of biliary complications? *Gastrointest Endosc* 1999;**49**:483−7.
7. Saito M, Tsuyuguchi T, Yamaguchi T, Ishihara T, Saisho H. Long-term outcome of endoscopic papillotomy for choledocholithiasis with cholecystolithiasis. *Gastrointest Endosc* 2000;**51**:540−5.

8. Hui CK, Lai KC, Yuen MF, Ng MM, Lam SK, Lai CL. Role of cholecystectomy in preventing recurrent cholangitis. *Gastrointest Endosc* 2002;**56**:55–60.
9. Williams EJ, Green J, Beckingham I, Parks R, Martin D, Lombard M. Guidelines on the management of common bile duct stones (CBDS). *Gut* 2008;**57**:1004–21.
10. Hammarström LE, Holmin T, Stridbeck H, Ihse I. Long-term follow-up of a prospective randomized study of endoscopic versus surgical treatment of bile duct calculi in patients with gallbladder *in situ*. *Br J Surg* 1995;**82**:1516–21.
11. 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.
12. Targarona EM, Ayuso RM, Bordas JM, Ros E, Pros I, Martinez J, et al. Randomised trial of endoscopic sphincterotomy with gallbladder left *in situ* versus open surgery for common bileduct calculi in high-risk patients. *Lancet* 1996;**347**:926–9.
13. 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. *Gastroenterology* 2006;**130**:96–103.
14. Ando T, Tsuyuguchi T, Okugawa T, Saito M, Ishihara T, Yamaguchi T, et al. Risk factors for recurrent bile duct stones after endoscopic papillotomy. *Gut* 2003;**52**:116–21.
15. Tsai WL, Lai KH, Lin CK, Chan HH, Lo CC, Hsu PI, et al. Composition of common bile duct stones in Chinese patients during and after endoscopic sphincterotomy. *World J Gastroenterol* 2005;**11**:4246–9.
16. Tsujino T, Kawabe T, Komatsu Y, Yoshida H, Isayama H, Sasaki T, et al. Endoscopic papillary balloon dilation for bile duct stone: immediate and long-term outcomes in 1000 patients. *Clin Gastroenterol Hepatol* 2007;**5**:130–7.
17. Lai KH, Lo GH, Lin CK, Hsu PI, Chan HH, Cheng JS, et al. Do patients with recurrent choledocholithiasis after endoscopic sphincterotomy benefit from regular follow-up? *Gastrointest Endosc* 2002;**55**:523–6.
18. Carey MC. Pathogenesis of gallstones. *Am J Surg* 1993;**165**:410–9.
19. Conte D, Fraquelli M, Fornari F, Lodi L, Bodini P, Buscarini L. Close relation between cirrhosis and gallstones: cross-sectional and longitudinal survey. *Arch Intern Med* 1999;**159**:49–52.
20. Alvaro D, Angelico M, Gandin C, Ginanni Corradini S, Capocaccia L. Physico-chemical factors predisposing to pigment gallstone formation in liver cirrhosis. *J Hepatol* 1990;**10**:228–34.
21. Stauber RE, Capocaccia E, Eagon PK, Gavaler JS, Van Thiel DH. The effect of portal-systemic shunting on hepatic sex hormone receptors in male rats. *Gastroenterology* 1991;**100**:168–74.
22. Acalovschi M, Dumitraşcu DL, Csakany I. Gastric and gall bladder emptying of a mixed meal are not coordinated in liver cirrhosis–a simultaneous sonographic study. *Gut* 1997;**40**:412–7.
23. Lai KH, Peng NJ, Lo GH, Cheng JS, Huang RL, Lin CK, et al. Prediction of recurrent choledocholithiasis by quantitative cholescintigraphy in patients after endoscopic sphincterotomy. *Gut* 1997;**41**:399–403.
24. Gregg JA, De Girolami P, Carr-Locke DL. Effects of sphincteroplasty and endoscopic sphincterotomy on the bacteriologic characteristics of the common bile duct. *Am J Surg* 1985;**149**:668–71.
25. Liao WC, Lee CT, Chang CY, Leung JW, Chen JH, Tsai MC, et al. Randomized trial of 1-minute versus 5-minute endoscopic balloon dilation for extraction of bile duct stones. *Gastrointest Endosc* 2010;**72**:1154–62.
26. Chan HH, Lai KH, Lin CK, Tsai WL, Wang EM, Hsu PI, et al. Endoscopic papillary large balloon dilation alone without sphincterotomy for the treatment of large common bile duct stones. *BMC Gastroenterol* 2011;**11**:69.
27. Tsai TJ, Lin CK, Lai KH, Chan HH, Tsai WL, Hsu PI. Does preserved sphincter of Oddi function prevent recurrence of bile duct stones in patients after endoscopic balloon dilation? *Gastroenterol J Taiwan* 2008;**25**:61.
28. Chan HH, Lai KH, Lin CK, Tsai WL, Peng NJ, Hsu PI, et al. Impact of food in hepatic clearance of patients after endoscopic sphincterotomy. *J Chin Med Assoc* 2009;**72**:10–4.