



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

## CLINICAL—LIVER, PANCREAS, AND BILIARY TRACT

# Cholecystectomy or Gallbladder In Situ After Endoscopic Sphincterotomy and Bile Duct Stone Removal in Chinese Patients

JAMES Y. W. LAU,\* CHON-KAR LEOW,\* TERENCE M. K. FUNG,\* BING-YEE SUEN,\* LY-MEE YU,†  
PAUL B. S. LAI,\* YUK-HOI LAM,\* ENDERS K. W. NG,\* WAN YEE LAU,\* SYDNEY S. C. CHUNG,\*  
and JOSEPH J. Y. SUNG<sup>§</sup>

\*Department of Surgery, †Centre for Clinical Trials and Epidemiological Research, and <sup>§</sup>Department of Medicine & Therapeutics, Prince of Wales Hospital, the Chinese University of Hong Kong, Hong Kong SAR, China

See editorial on page 270.

**Background & Aims:** In patients with stones in their bile ducts and gallbladders, cholecystectomy is generally recommended after endoscopic sphincterotomy and clearance of bile duct stones. However, only approximately 10% of patients with gallbladders left in situ will return with further biliary complications. Expectant management is alternately advocated. In this study, we compared the treatment strategies of laparoscopic cholecystectomy and gallbladders left in situ. **Methods:** We randomized patients (>60 years of age) after endoscopic sphincterotomy and clearance of their bile duct stones to receive early laparoscopic cholecystectomy or expectant management. The primary outcome was further biliary complications. Other outcome measures included adverse events after cholecystectomy and late deaths from all causes. **Results:** One hundred seventy-eight patients entered into the trial (89 in each group); 82 of 89 patients who were randomized to receive laparoscopic cholecystectomy underwent the procedure. Conversion to open surgery was needed in 16 of 82 patients (20%). Postoperative complications occurred in 8 patients (9%). Analysis was by intention to treat. With a median follow-up of approximately 5 years, 6 patients (7%) in the cholecystectomy group returned with further biliary events (cholangitis, n = 5; biliary pain, n = 1). Among those with gallbladders in situ, 21 (24%) returned with further biliary events (cholangitis, n = 13; acute cholecystitis, n = 5; biliary pain, n = 2; and jaundice, n = 1; log rank,  $P = .001$ ). Late deaths were similar between groups (cholecystectomy, n = 19; gallbladder in situ, n = 11;  $P = .12$ ). **Conclusions:** In the Chinese, cholecystectomy after endoscopic treatment of bile duct stones reduces recurrent biliary events and should be recommended.

Endoscopic sphincterotomy and stone extraction have gained wide acceptance in the management of bile duct stones. Complete stone removal after endoscopic sphincterotomy can be achieved in >90% of cases with low morbidity and negligible mortality.<sup>1</sup> After endoscopic removal of bile duct stones, the need for cholecystectomy in patients with concomitant gallstones is disputed. Many contend that endoscopic management of bile duct stones with gallbladders left in situ is definitive in elderly and high-risk patients. Retrospective and prospective series have suggested that further biliary complications occur in 4%–24% of patients after varying periods of follow-up, and the rate of subsequent cholecystectomy is 5.8%–18%.<sup>2–8</sup> As a treatment of the complication of biliary pancreatitis, ablation of the sphincter allows free passage of stones into the duodenum. Endoscopic sphincterotomy may in itself be definitive in prophylaxis against further attacks.

Many advocate for a single-stage cholecystectomy and bile duct exploration as the primary treatment of bile duct stones. The strategy was compared with endoscopic treatment in 2 randomized studies. Hammarstrom et al<sup>9</sup> randomized 83 patients and found that recurrent biliary-related events occurred in 28% of patients initially treated by endoscopy compared with 5% in those who underwent open cholecystectomy and bile duct exploration. In a similar study involving 98 patients with a mean age of 80 years, recurrent biliary symptoms occurred in fewer patients treated by operation (3 of 48 vs 10 of 50).<sup>10</sup> Both studies concluded that surgery would

*Abbreviations used in this paper:* ERCP, endoscopic retrograde cholangiopancreatography.

© 2006 by the American Gastroenterological Association  
0016-5085/06/\$32.00

doi:10.1053/j.gastro.2005.10.015

be preferable in the treatment of bile duct stones. We argue that the added cholecystectomy during open surgery in these 2 trials could explain the fewer recurrent biliary events. In a European multicenter study, a single-stage laparoscopic cholecystectomy and bile duct exploration was compared with a 2-stage endoscopic sphincterotomy followed by laparoscopic cholecystectomy in patients with bile duct stones.<sup>11</sup> A single-stage approach led to shorter hospitalization. Long-term follow-up data in these patients were lacking. Skill in laparoscopic bile duct explorations remains sparse and confined to a few expert centers. Although open or laparoscopic cholecystectomy and bile duct exploration may be appropriate as a treatment of uncomplicated bile duct stones, many patients present with acute cholangitis or pancreatitis. In these emergencies, endoscopic therapy is preferred and leads to better outcome.<sup>12,13</sup> Endoscopic sphincterotomy is likely to prevail as the primary treatment of bile duct stones. The real issue is the need for subsequent cholecystectomy, particularly among older patients. We therefore compared the 2 treatment strategies of early elective cholecystectomy or leaving gallbladders in situ in patients >60 years after endoscopic sphincterotomy and removal of bile duct stones.

## Materials and Methods

### Participants

This study was a prospective, randomized, controlled trial. The Ethics Committee at the Chinese University of Hong Kong approved the study protocol. Consecutive patients who underwent endoscopic sphincterotomy and complete removal of bile duct stones at the Prince of Wales Hospital were eligible for trial entry if they met all of the following criteria: (1) they were older than 60 years, (2) they received complete endoscopic sphincterotomy (defined by free bile flow and passage of a fully bowed sphincterotome with a 25-mm wire), (3) there was radiological evidence of an intact gallbladder containing gallstones, and (4) there was no previous hospitalization for cholecystitis. In patients with cholangitis, we initially decompressed the bile duct by inserting a nasobiliary catheter or a short stent across the sphincter to avoid aggravating systemic sepsis and contaminating the gallbladder. Definitive stone removal was performed after sepsis resolution. Complete clearance of the bile duct was ensured by obtaining a balloon occlusion cholangiogram at the end of procedure. Patients were excluded if there was evidence of concomitant intrahepatic ductal stones, radiological evidence of recurrent pyogenic cholangitis, no consent to trial entry, or intercurrent malignancy with a limited life span or if they were deemed unfit for cholecystectomy (those belonging to American Society of Anesthesiologists grade IV or V).

### Interventions and Randomization

Eligible patients were invited to participate in the trial before their hospital discharge. With informed consent, the managing physician contacted the research office at the Department of Surgery by phone. After verifying all inclusion criteria and the patient's demographic data, a research nurse at the office then disclosed the next numbered assigned treatment from a computer-generated random list. Patients assigned to laparoscopic cholecystectomy underwent surgery as soon as practical. Patients recovering from severe cholangitis and pancreatitis were allowed a period of convalescence before returning for operation. Those with comorbid illnesses received medical treatment to optimize their conditions before undergoing operation.

After their hospital discharge, patients in the respective treatment groups were seen in our clinic every 3 months. Blood tests and abdominal ultrasound scans were repeated if clinically indicated. Those who did not return for scheduled clinic follow-up were contacted by telephone to ascertain their well-being. A telephone hotline was available to participants for emergency consultation.

### Outcomes

The primary end points were recurrent biliary events presenting with cholangitis, pancreatitis, jaundice, complicated gallstones presenting with biliary colic, as defined by the Rome II criteria, or cholecystitis.<sup>14</sup> Secondary end points included mortality from all causes, adverse events, and outcomes after cholecystectomy.

### Sample Size Calculation and Statistical Methods

The sample size was estimated on the assumption that after endoscopic sphincterotomy, cholecystectomy would reduce recurrent biliary complications from 20% to 5%. To detect such a difference ( $\alpha = .05$ ;  $\beta = .2$ ) by using a 2-sided log-rank test, 89 patients would be required in each group, assuming a 10% loss during follow-up.

Analysis was by intention to treat. The Kaplan–Meier method was used to determine the times to events and death. The log-rank test was performed to compare the recurrent biliary events and deaths between the 2 groups. A Cox regression model was used to adjust for bile duct size between groups.<sup>15</sup> Adverse events and outcomes after cholecystectomy in either treatment group were compared by using the Fisher exact test or Mann–Whitney *U* test when appropriate. Analysis based on the treatment actually received was also performed as a sensitivity analysis.

## Results

### Participant Flow

Between July 1997 and December 2000, 305 patients presented with bile duct stones and were referred for endoscopic retrograde cholangiopancreatogra-

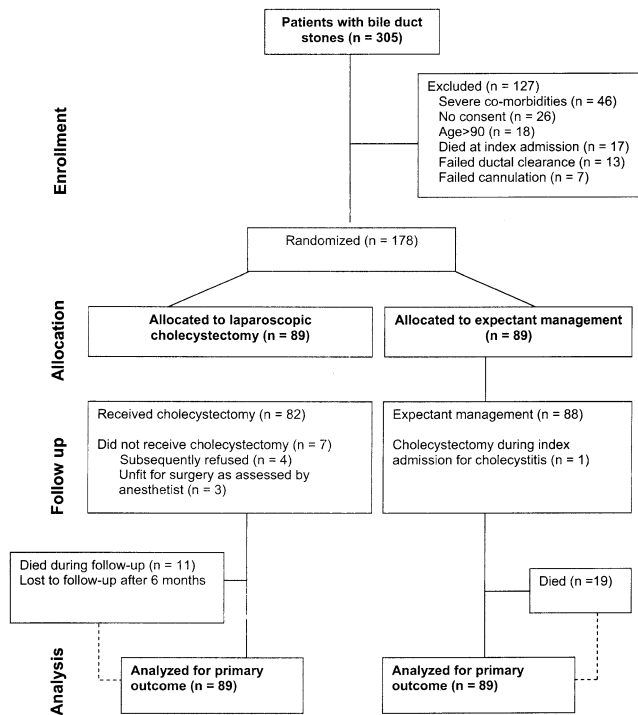


Figure 1. Participant flow diagram.

phy (ERCP) and stone removal. One hundred twenty-seven patients did not participate in the trial for the following reasons: severe comorbid illnesses deemed unfit for cholecystectomy ( $n = 46$ ), no consent ( $n = 26$ ), age  $>90$  years ( $n = 18$ ), failure to clear bile duct with endoscopic means ( $n = 13$ ), and failed bile duct cannulation ( $n = 7$ ); 17 patients died at the index admission. One hundred seventy-eight patients were randomly assigned to undergo elective cholecystectomy ( $n = 89$ ) or expectant management ( $n = 89$ ; Figure 1).

### Recruitment

As of August 1, 2004, the mean follow-up in the cholecystectomy group was 65.5 months, compared with 58.5 months in the gallbladder-in-situ group. All except 3 patients assigned to cholecystectomy completed 36 months of follow-up. Contact with these 3 patients was lost at 23, 30, and 32 months.

### Baseline Data

The 2 groups were comparable in their baseline characteristics. A larger mean bile duct size was observed in the gallbladder-in-situ group (Table 1).

### Primary Outcomes

Analysis was by intention to treat. Of patients who completed a 3-year follow-up period, a reduction in recurrent biliary complications by 15.1% (95% confi-

dence interval, 5.1%–25%;  $P = .004$ ) was observed with cholecystectomy when compared with leaving gallbladders in situ (Table 2). At 3 years, 4 of 81 patients (5%) allocated to cholecystectomy had recurrent biliary events, compared with 16 of 80 patients (20%) allocated to the group with gallbladders left in situ. After adjustment for bile duct size, the difference remained significant (hazard ratio, 0.25; 95% confidence interval, 0.10–0.66;  $P = .004$ ).

During the entire follow-up period, 6 patients (7%) in the cholecystectomy group returned with biliary events (cholangitis,  $n = 5$ ; biliary pain,  $n = 1$ ). Two of 6 patients did not receive intended cholecystectomy despite initial randomization. In the gallbladders-in-situ group, 21 (24%) patients developed further biliary events: recurrent bile duct stones with cholangitis in 13, biliary pain and deranged liver function tests in 2, jaundice in 1, and acute cholecystitis in 5 (log-rank,  $P = .001$ ; Figure 2). At 5 years, the cumulative probability of recurrent biliary events in the cholecystectomy group and the gallbladder-in-situ group was 5.8% (95% confidence interval, 2.4%–13.3%) and 25.4% (95% confidence interval, 17.3%–36.5%), respectively.

### Adverse Events, Durations of Hospitalization, and Outcomes After Cholecystectomy

**Cholecystectomy group.** Of 89 patients allocated to laparoscopic cholecystectomy, 7 patients did not receive surgery (4 withdrew and 3 were subsequently considered by anesthesiologists to be unfit for operation). In this group, 82 underwent the intended laparoscopic cholecystectomy at a median of 26 days from the date of first ERCP (range, 1–123 days). Conversions to open cholecystectomy were required in 16 of 82 patients (20%): 13 because of dense scarring at the Calot triangle, 2 because of bleeding, and 1 because of adhesions from a previous gastrectomy. The median postoperative hospital stay in those who underwent cholecystectomy was 3 days (range, 1–16 days). There was no postoperative death.

Complications occurred in 8 patients (10%) in the cholecystectomy group (Table 3): respiratory failure ( $n = 2$ ), acute retention of urine ( $n = 2$ ), infected hepatic cyst ( $n = 1$ ), pleural effusion ( $n = 1$ ), adhesive intestinal obstruction ( $n = 1$ ), and intra-abdominal abscess ( $n = 1$ ). One of the 2 patients with postoperative respiratory failure developed epididymo-orchitis of an undescended testis, which required excision. The patient with adhesive intestinal obstruction returned for a second laparotomy 1 month after cholecystectomy.

Among 82 gallbladders submitted for histological examination, 10 (12%) showed features of acute chole-

**Table 1.** Baseline Characteristics of Patients

Variable	Cholecystectomy group (n = 89)	Gallbladder-in-situ group (n = 89)
Men, n (%)	43 (48.3)	49 (55.1)
Age (y)		
Mean (SD)	70.9 (7.2)	71.6 (6.8)
Median (range)	70 (60–87)	72.0 (60–89)
ASA grading, n (%)		
I	44 (49.4)	43 (48.3)
II	27 (30.3)	29 (32.6)
III	18 (20.2)	17 (19.1)
Comorbid illnesses, n (%) <sup>a</sup>	42 (47.2)	41 (46.1)
Diabetic mellitus	13	9
Hypertension	24	27
Previous strokes	8	3
Ischemic heart disease	7	7
Chronic renal failure	0	2
Heart failure	2	6
Obstructive airway disease	4	4
Mode of presentation, n (%)		
Cholangitis	35 (39.3)	38 (42.7)
Pancreatitis	31 (34.8)	16 (18.0)
Jaundice only	8 (9.0)	16 (18.0)
Epigastric pain and abnormal liver function tests	13 (14.6)	17 (19.1)
Dilated bile duct on ultrasound alone	2 (2.2)	2 (2.2)
Clinical presentation, n (%)		
Temperature >38°C	17 (19.1)	19 (21.3)
Jaundice	48 (53.9)	53 (59.6)
Confusion	3 (3.4)	2 (2.2)
Epigastric pain	86 (96.6)	78 (87.6)
Septicemic shock	4 (4.5)	3 (3.4)
Chills and rigor	18 (20.2)	16 (18.0)
Positive bile culture	43/61 (70.5)	46/57 (80.7)
Positive blood culture	15/55 (27.2)	14/49 (24.5)
ERCP findings		
Number of stones (%)		
1	36 (40.4)	33 (37.1)
2	6 (6.7)	10 (11.2)
3	6 (6.7)	0
>3	25 (28.1)	35 (39.3)
Sludge only	15 (16.9)	11 (12.4)
Median stone size, mm (range)	5 (2–35)	10 (3–40)
Mean stone size, mm (SD)	8.1 (5.8)	10.2 (7.0)
Mean bile duct size (SD)	11.8 (4.5)	13.3 (4.6)
Filling of gallbladder, n (%)	48 (53.9)	47 (52.8)
Ultrasound findings		
Gallbladder thickness >2 mm, n (%)	15 (16.8)	13 (14.6)
Median gallbladder wall thickness, mm (range)	2 (1–8)	2 (1–6)
ERCP therapy, n (%)		
Initial insertion of nasobiliary drains	25 (28.1)	28 (31.5)
Initial insertion of biliary stents	6 (6.7)	12 (13.5)
ERCP complications, n (%)	4 (4.5)	5 (5.6)
Bleeding	4	4
Pancreatitis	0	1

**Table 1 (continued).** Baseline Characteristics of Patients

Variable	Cholecystectomy group (n = 89)	Gallbladder-in-situ group (n = 89)
Median ERCP sessions (range)	1 (1–3)	1 (1–3)
Previous abdominal surgery	18 (20.2)	18 (20.2)

ASA, American Society of Anesthesiologists.

<sup>a</sup>A patient may have more than 1 comorbid illness.

cystitis. One patient had a mucocele. In addition, 2 other patients had neoplastic lesions in their gallbladders: carcinoma in situ and villous adenoma with moderate dysplasia. In a third patient with adenomyomatosis of the gallbladder, there were features of amyloidosis.

**Gallbladder-in-situ group.** Of 89 patients allocated to the gallbladder-in-situ group, 1 patient had persistent pain after randomization. Laparoscopy on the fifth day after randomization showed acute cholecystitis necessitating cholecystectomy. During follow-up, 16 patients presented with bile duct stones. They underwent further ERCP and removal of bile duct stones. During endoscopy, 1 patient had sphincterotomy stenosis and required extension of sphincterotomy. Five of 16 patients subsequently underwent interval cholecystectomy. Five other patients returned with acute cholecystitis. Four patients were treated by emergency cholecystectomy and 1 by initial percutaneous cholecystostomy followed by interval cholecystectomy. In total, 10 patients received cholecystectomy. Conversion to open surgery was required in 5 of 10 patients (50%). This was higher than the conversion rate in those allocated to elective laparoscopic cholecystectomy ( $P = .045$ ). Their median hospital stay was 4 days (range, 2–24 days). One developed wound infection after surgery. There was no postoperative death.

### Late Deaths

Late mortality was higher in the gallbladder-in-situ group (11 vs 19; log-rank,  $P = .1$ ; Table 4). Figure 3 shows the Kaplan–Meier curves with the cumulative risk of death in both groups. The cumulative probability of death at 5 years was 9.2% (95% confidence interval, 4.7%–17.6%) for patients allocated to elective cholecystectomy and 21% (95% confidence interval, 13.7%–31.3%) for patients allocated to expectant management. Four deaths in the gallbladder-in-situ group occurred after a recurrent biliary event. Only 1 death was directly attributable to biliary sepsis. This patient died from acute myocardial infarction during a recurrent episode of cholangitis. Other causes of death between groups are listed in Table 4.



**Table 2.** Recurrent Biliary Events in Both Groups of Patients

Variable	Laparoscopic cholecystectomy (n = 89)	Gallbladder in situ (n = 89)	Relative risk (95% CI)	P value
Median follow-up, mo (range)	64.1 (2.6–82.2)	58.5 (0.4–81.1)		
Recurrent biliary events, n (%)				
At 36 mo <sup>a</sup>	4 (4.9%)	16 (20%)	0.25(0.09–0.71)	.004
During the entire follow-up period	6	21		
Cholangitis	5	13		
Pancreatitis	—	—		
Jaundice only	—	1		
Biliary pain and deranged liver function tests	1	2		
Cholecystitis	—	5		

CI, confidence interval.

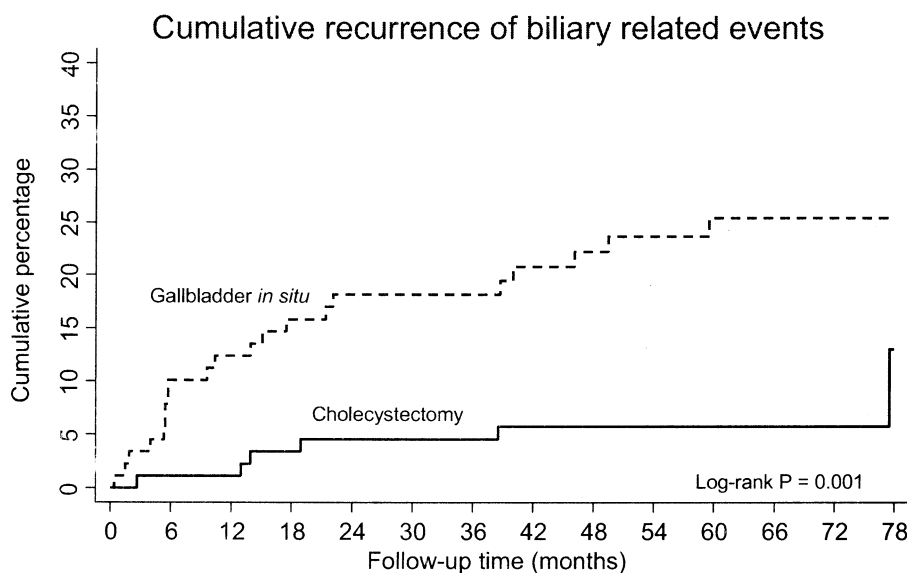
<sup>a</sup>Laparoscopic cholecystectomy, n = 81 (5 dead; 3 lost to follow-up); gallbladder in situ, n = 80 (9 dead); absolute risk reduction, 15.1% (5.1%, 25.0%).

**Sensitivity Analysis**

Sensitivity analysis was performed to assess the treatment effect based on treatment received. At 36 months, 4 recurrent biliary events were observed in the 83 patients who underwent cholecystectomy, compared with 16 of 95 patients with gallbladder in situ (relative risk, 0.29; 95% confidence interval, 0.10–0.82). Results from the survival analysis were also similar (log-rank,  $P = .005$  and  $P = .1$  for recurrent biliary events and late mortality, respectively). These results were consistent with those of the intention-to-treat analysis.

**Discussion**

We showed that, in Chinese patients >60 years of age who underwent endoscopic sphincterotomy and removal of bile duct stones, the addition of cholecystectomy reduced recurrent biliary events. Our randomized trial has a median follow-up of >5 years. The only other randomized study that examined the need for cholecystectomy after endoscopic sphincterotomy came from a Dutch group.<sup>16</sup> Their reported recurrence rate among patients managed expectantly was 47%. They concluded that adding cholecystectomy would be recommended after endoscopic treatment of bile duct stones. Their



Annual no. at risk (events)							
Cholecystectomy	89 (1)	87 (3)	83 (0)	77 (1)	73 (0)	50 (0)	30
GB in situ	89 (11)	77 (5)	69 (0)	64 (3)	54 (2)	43 (0)	25

**Figure 2.** Kaplan–Meier estimates of the likelihood that biliary-related events would recur (cholecystectomy group, solid line; gallbladder-in-situ group, dotted line). GB, gallbladder.

**Table 3.** Rates of Conversion, Duration of Hospital Stay, and Complications After Cholecystectomy in Both Groups of Patients

Variable	Laparoscopic cholecystectomy (n = 89)	Gallbladder in situ (n = 89)	P value
Laparoscopic cholecystectomy received, n (%)	82 (92.1)	10 (11.2)	
Conversion to open surgery, n (%)	16 (20.7)	5 (50)	.045
Total hospital stay			
Mean, SD	12.5, 6.1	8.0, 6.4	<.001
Median (range)	11 (3–35)	6 (2–36)	
Median hospital stay (days) during index admission (range)	4 (1–27)	4 (1–29)	.33
Median hospital stay (days) after cholecystectomy (range)	3 (1–16)	4 (2–24)	.25
Complications from cholecystectomy, n (%)	8 of 82 (9.7)	1 of 10 (10)	.1
Complications			
Urinary retention	1	—	
Pleural effusion	1	—	
Infected hepatic cyst	1	—	
Epididymo-orchitis	1	—	
Respiratory failure	1	—	
Small-bowel adhesion	1	—	
Intraoperative hemorrhage from torn cystic artery	1	—	
Abdominal abscess	1	1	

trial, however, differed from ours in several aspects. First, our trial represented a single-center experience, and consecutive patients with bile duct stones were accounted for. Second, the age distribution of patients included in the other study was much wider, whereas our sample contained patients >60 years. In our opinion, young patients should be offered elective cholecystectomy. Gallstone disease is a risk factor for gallbladder cancers. Third, outcome events in the Dutch trial were predominantly gallbladder related; 31% of patients were operated on for biliary pain and 12% for acute cholecystitis. Cholecystectomies were performed at a median of 11 weeks after sphincterotomy. Our lower rate of recurrences contrasted with that of the Dutch trial. Outcome events in our study were mostly cholangitis. Neither trial

distinguished between primary and secondary bile duct stones.

In most series, cholecystitis generally occurred within the first year of endoscopic sphincterotomy.<sup>2–8</sup> After 2 years, the incidence was comparable to that of uncomplicated gallstone diseases. This was again observed in our study. Laparoscopic cholecystectomy should be performed early to gain maximal efficacy in preventing cholecystitis. In approximately 10% of our patients assigned to cholecystectomy, acute cholecystitis was present at operation. In patients with cholangitis or pancreatitis, gallbladders, being part of the biliary tree, are often found inflamed at early cholecystectomy. Gallbladders may have been contaminated during instrumentation and occlusion cholangiogram at ERCP. In our protocol, we endeavored to reduce such risks by providing initial drainage to the bile duct before definitive removal of stones in patients with cholangitis. After resolution of biliary sepsis, the rate of subsequent cholecystitis is, however, lower. Patients with nonfilling of their gallbladders at ERCP were thought to be at risk of subsequent cholecystitis and biliary pain.<sup>17</sup> Because of the small number of outcome events in our trial, an ancillary analysis would be of limited value.

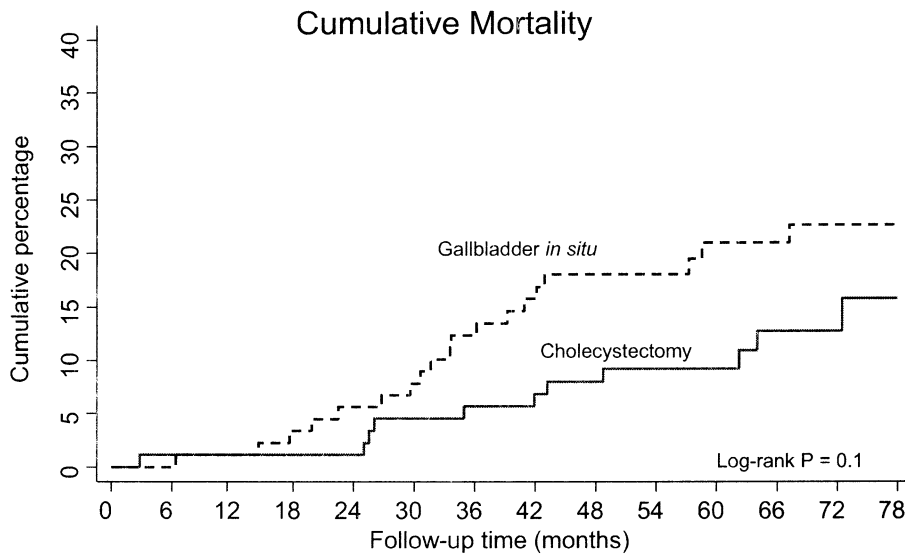
It is conjectural whether endoscopic sphincterotomy itself may lead to acute cholecystitis. Some have suggested that ablation of the sphincter could lead to ascending biliary tract infection from enteric organisms and, thereby, increase the risk of cholecystitis. In a randomized study that compared endoscopic sphincterotomy and balloon sphincteroplasty in the treatment of

**Table 4.** Late Deaths in Both Groups of Patients

Variable	Laparoscopic cholecystectomy (n = 89)	Gallbladder in situ (n = 89)
Death during follow-up (n) <sup>a</sup>	11	19
Event		
Road traffic accident	1	1
Cancer	1	5
Stroke	1	3
Biliary sepsis	0	4
Myocardial infarction	1	1
Chest infection	2	2
Urinary sepsis	1	0
Liver cirrhosis	1	0
Unknown	1	2
SARS	0	1

SARS, severe acute respiratory syndrome.

<sup>a</sup>Absolute risk reduction, 9.0% (−0.6%, 19.0%).



Annual no. at risk (events)

Cholecystectomy	89 (1)	88 (0)	87 (4)	81 (2)	78 (1)	53 (2)	30
GB <i>in situ</i>	89 (1)	88 (4)	84 (6)	78 (5)	67 (2)	54 (1)	33

**Figure 3.** Kaplan–Meier estimates of the likelihood of deaths from all causes (cholecystectomy group, solid line; gallbladder-in-situ group, dotted line).

bile duct stones, acute cholecystitis occurred in 7 of 71 patients treated by sphincterotomy, as compared with 1 of 75 patients assigned to balloon sphincter dilation.<sup>18</sup> Other studies showed that endoscopic sphincterotomy reduces gallbladder filling and increases gallbladder emptying. Augmented gallbladder contractility may in theory reduce the risk of acute cholecystitis.<sup>19,20</sup> The issue is largely unresolved.

There are inherent limitations to our study. First, we arbitrarily recruited patients >60 years. The European Society of Gerontology defined an elderly patient to be someone older than 65. Patients should, however, be assessed by their physiological rather than chronological ages. Using the same argument, we did not impose an upper age limit during recruitment. Second, a significant proportion of our patients, as a result of advanced age or perceived comorbid illnesses, were unwilling to undertake surgery with its attendant risks and, therefore, did not participate. Patients who entered the trial could represent a group with less risk. The scenario is, however, closer to real clinical practice, in which elderly patients are often reluctant to receive cholecystectomy after successful endoscopic sphincterotomy and clearance of bile duct stones. Third, Hong Kong Chinese may have a higher incidence of primary pigment stones when compared with the white population. The inclusion of such patients in our trial may explain the higher rate of recurrent cholangitis and a lower rate of cholecystitis. Our findings may therefore not be extrapolated to the Western population.

We could also argue against routine cholecystectomy. Older patients, particularly those with comorbid illnesses, often prefer an expectant management. In our locality, recurrent events among those with gallbladders left in situ were mostly cholangitis. In this instance, endoscopic removal of bile duct stones seemed to be an adequate alternative. Interval elective ERCP can be a treatment option in patients predicted to develop recurrent bile duct stones.<sup>21</sup> A larger bile duct is the only consistent factor identified.<sup>22</sup> It is interesting to note that none of the recurrent events was pancreatitis. Ablation of the sphincter may have therefore prevented calculous impaction and bile reflux into the pancreatic duct. We did not show a difference in late deaths with cholecystectomy. Many of the patients from both groups died from their comorbid illnesses rather than biliary sepsis.

Laparoscopic cholecystectomy in complicated gallstone diseases is often difficult. Significant scarring is often noted in areas of the Calot triangle and hepatoduodenal ligament. In our series, we report a conversion rate of 20% to open operation in patients assigned to elective cholecystectomy. The conversion rate increased to 50% when laparoscopic cholecystectomy was performed at recurrence. Morbidities in our series were sufficiently low, and mostly complications were minor. The higher procedure-related morbidities are to be borne in mind when we offer surgery to elderly patients with complicated gallstone diseases. The timing of cholecystectomy in patients recovering from cholangitis or pancreatitis has been a subject of controversy. Some surgeons argue



for early cholecystectomy, whereas others urge waiting for inflammation to subside before surgery. In our series, the lead time to surgery was often a practical consideration. Patients often needed a period of recuperation or optimization of medical treatment before returning to surgery.

In conclusion, elective laparoscopic cholecystectomy after endoscopic sphincterotomy reduces recurrent biliary-related events. We recommend laparoscopic cholecystectomy to most patients, except those with prohibitive surgical risks.

## References

- Cotton PB, Geenen JE, Sherman S, et al. Endoscopic sphincterotomy for stones by experts is safe, even in younger patients with normal ducts. *Ann Surg* 1998;227:201–204.
- Escourrou J, Cordova JA, Lazorthes F, Frexinos J, Ribet A. Early and late complications after endoscopic sphincterotomy for biliary lithiasis with and without the gallbladder 'in situ'. *Gut* 1984;27:598–602.
- Ingoldby CJH, El-Saadi J, Hall RI, Denyer ME. Late results of endoscopic sphincterotomy for bile duct stones in elderly patients with gallbladders in situ. *Gut* 1989;30:1129–1131.
- Hansell DT, Millar MA, Murray WR, Gray GR, Gillespie G. Endoscopic sphincterotomy for bile duct stones in patients with intact gallbladders. *Br J Surg* 1989;76:856–858.
- Kullman E, Borch K, Dahlin LG, Liedberg G. Long-term follow-up of patients with gallbladder in situ after endoscopic sphincterotomy for choledocholithiasis. *Eur J Surg* 1991;157:131–135.
- Hill J, Martin DF, Tweedle DEF. Risks of leaving the gallbladder in situ after endoscopic sphincterotomy for bile duct stones. *Br J Surg* 1992;78:554–557.
- Prat F, Malak NA, Pelletier G, et al. Biliary symptoms and complications more than 8 years after endoscopic sphincterotomy for choledocholithiasis. *Gastroenterology* 1996;110:894–899.
- Pereira-Lima JC, Jakobs R, Winter UH, et al. Long-term results (7 to 10 years) of endoscopic papillotomy for choledocholithiasis. Multivariate analysis of prognostic factors for the recurrence of biliary symptoms. *Gastrointest Endosc* 1998;48:457–464.
- 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;82:1516–1521.
- Targarona EM, Perez Ayuso RM, Bordas JM, 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;347:926–929.
- Cuschieri A, Lezoche E, Morino M, et al. EAES multicenter prospective randomised trial comparing two-stage versus single-stage management of patients with gallstone disease and ductal calculi. *Surg Endosc* 1999;13:952–957.
- Lai ECS, Mok FPT, Tan ESY, Chung-Mau L, Sheung-Tat F, Kok-Tjang Y, Wong J. Endoscopic biliary drainage for severe acute cholangitis. *N Engl J Med* 1992;326:1582–1586.
- Fan ST, Lai EC, Mok FP, Lo CM, Zheng SS, Wong J. Early treatment of acute biliary pancreatitis by endoscopic papillotomy. *N Engl J Med* 1993;328:228–232.
- Corazziari E, Shaffer EA, Hogan WJ, Sherman S, Toouli J. Functional disorders of the biliary tract and pancreas. *Gut* 1999;45(Suppl 2):II48–II54.
- Cox DR, Snell EJ. *Analysis of binary data*. 2nd ed. Boca Raton, FL: Chapman & Hall/CRC Press, 1989.
- Boerma D, Rauws EA, Keulemans Y, Janssen I, Bolwerk CJ, Timmer R, Boerma EJ, Obertop H, Huibregtse K, Gouma DJ. Wait-and-see policy or laparoscopic cholecystectomy after endoscopic sphincterotomy for bile-duct stones: a randomised trial. *Lancet* 2002;360:761–765.
- Worthley CS, Toouli J. Gallbladder non-filling: an indication for cholecystectomy after endoscopic sphincterotomy. *Br J Surg* 1988;75:796–798.
- Bergman JJ, Rauws EA, Fockens P, van Berkel AM, Bossuyt PM, Tijssen JG, Tytgat GN, Huibregtse K. Randomised trial of endoscopic balloon dilation versus endoscopic sphincterotomy for removal of bile duct stones. *Lancet* 1997;349:1124–1129.
- Li YF, Weisbrodt NW, Moody FG. Effect of bile diversion and sphincterotomy on gallbladder muscle contractility and gallstone formation. *Am J Surg* 1991;162:31–35.
- Sharma BC, Agarwal DK, Baijal SS, Negi TS, Choudhuri G, Saraswat VA. Effect of endoscopic sphincterotomy on gall bladder bile lithogenicity and motility. *Gut* 1998;42:288–292.
- Lai KH, Lo GH, Lin CK, Hsu PI, Chan HH, Cheng JS, Wang EM. Do patients with recurrent choledocholithiasis after endoscopic sphincterotomy benefit from regular follow-up? *Gastrointest Endosc* 2002;55:523–526.
- Costamagna G, Tringali A, Shah SK, Mutignani M, Zuccala G, Perri V. Long-term follow-up of patients after endoscopic sphincterotomy for choledocholithiasis, and risk factors for recurrence. *Endoscopy* 2002;34:273–279.

---

Received August 18, 2005. Accepted October 5, 2005.

Reprint requests: James Y. W. Lau, MD, Department of Surgery, Fourth Floor, Clinical Science Building, Prince of Wales Hospital, the Chinese University of Hong Kong, 32 Ngan Shing Street, Shatin, New Territories, Hong Kong SAR, China. e-mail: laujyw@surgery.cuhk.edu.hk; fax: (852) 2637-7974.

Supported by a Direct Grant (project code 2040856) from the Chinese University of Hong Kong.