#### **ORIGINAL ARTICLE**



# Elective Laparoscopic Cholecystectomy Is Better than Conservative Treatment in Elderly Patients with Acute Cholecystitis After Percutaneous Transhepatic Gallbladder Drainage

Seung Jae Lee<sup>1</sup> · In Seok Choi<sup>1</sup> · Ju Ik Moon<sup>1</sup> · Dae Sung Yoon<sup>1</sup> · Sang Eok Lee<sup>1</sup> · Nak Song Sung<sup>1</sup> · Sung Uk Kwon<sup>1</sup> · In Eui Bae<sup>1</sup> · Seung Jae Roh<sup>1</sup> · Won Jun Choi<sup>1</sup>

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## Abstract

**Background** It is unclear whether cholecystectomy is beneficial after percutaneous transhepatic gallbladder drainage (PTGBD) in elderly patients with acute cholecystitis (AC).

**Methods** This single-center, retrospective study included 202 patients aged >80 years with AC without common bile duct (CBD) stones who underwent PTGBD between January 2010 and December 2019.

**Results** One hundred and forty-two patients underwent elective laparoscopic cholecystectomy (ELC), and 60 underwent conservative treatment, specifically PTGBD removal (PTGBD-R) in 36 patients and PTGBD maintained (PTGBD-M) in 24 patients. The postoperative major complication (POMC) rate in the ELC group was 8.5%. The cumulative incidence for recurrence of biliary events (BE) in the PTGBD-R group was 22.2%. The cumulative incidence for PTGBD-related complication in the PTGBD-M group was 70.8%. Mortality after initial treatment was not significantly different between the three groups (2.8% vs. 2.8% vs. 8.3%, p=0.381). In multivariate analysis, a Charlson age comorbidity index  $\geq$ 6 and body mass index  $\leq$ 19 were significant risk factors for POMC after ELC, and a closed cystic duct was a significant risk factor for recurrent BE after PTGBD-R.

**Conclusion** ELC is recommended in AC after PTGBD for selected patients aged >80 years without CBD stones due to the high recurrence rate of BE after PTGBD-R and the difficulty associated with PTGBD-M.

**Keywords** Acute cholecystitis · Aged, 80 and over · Percutaneous transhepatic gallbladder drainage · Laparoscopic cholecystectomy · Conservative treatment

# Introduction

Acute cholecystitis (AC) is a common biliary disease that is best treated with early cholecystectomy <sup>1</sup>. Currently, laparoscopic cholecystectomy (LC) is recognized as the only definitive treatment for AC<sup>2</sup>. The most common cause of AC is gallbladder (GB) stones, and the prevalence of GB stones increases significantly with age <sup>3</sup>. Despite the risk of complications related to procedure such as bleeding, catheter displacement, bile leakage, and abscess formation, percutaneous transhepatic gallbladder drainage (PTGBD) is an alternative treatment to avoid urgent surgery in high-risk patients and can be a temporary initial treatment before LC<sup>4,5</sup>. In particular, as elderly patients with AC have more underlying diseases, the rate of performing LC after PTGBD as an initial treatment is over 50% of all patient performed LC<sup>°</sup>. However, it is unclear whether cholecystectomy should be performed after PTGBD in elderly patients with AC. Elderly patients typically have a prolonged postoperative hospital stay, high rates of in-hospital mortality, and substantially high rates of discharge to sites other than home . Due to the limited number of studies on risk factors for postoperative complications or mortality after LC in elderly patients with AC, it is difficult to identify the patients who should not undergo surgery. Recently, several risk factors for recurrent biliary events (BE) after PTGBD without definitive treatment have been

<sup>☑</sup> In Seok Choi choiins@kyuh.ac.kr

<sup>&</sup>lt;sup>1</sup> Department of Surgery, Konyang University Hospital, Konyang University College of Medicine, 158, Gwanjeodong-ro, Seo-gu, Daejeon 35365, South Korea

reported <sup>4,8</sup>. However, there are also limited studies on the natural course of AC in elderly patients with PTGBD without cholecystectomy.

The aim of this study was to compare the safety and effectiveness of cholecystectomy and conservative treatment in patients with AC aged >80 years without common bile duct (CBD) stones and identify the risk factors for postoperative major complications (POMC) after LC and recurrent BE after conservative treatment.

# **Materials and Methods**

# Patients

From January 2010 to December 2019, patients with AC aged >80 years who received PTGBD at Konvang University Hospital were evaluated. Patients with pancreatobiliary malignancies or CBD stones were excluded from the study. A total of 202 patients were included in this study. The diagnosis of AC was based on the Tokyo Guidelines 2018 (TG18). Imaging findings were confirmed by abdominal ultrasonography (USG), computed tomography (CT), or magnetic resonance cholangiopancreatography (MRCP). The severity of AC was also classified based on the TG18<sup>°</sup>. We divided the study population into three groups based on their treatment algorithm and retrospectively reviewed the patient demographics, disease characteristics, and treatment outcomes: group 1, elective laparoscopic cholecystectomy (ELC); group 2, conservative treatment with PTGBD removal (PTGBD-R); and group 3, conservative treatment with PTGBD maintained (PTGBD-M) (Fig. 1).

This study was approved by the Institutional Review Board of Konyang University Hospital, and the requirement for informed consent was waived due to the retrospective design of the study (IRB No. 2021-01-015).

## **Decision-Making Process Regarding Treatment**

After consultation with an anesthesiologist and a hepatobiliary-pancreatic (HBP) surgeon, patients who were

at high risk of surgery, such as those with poor European Cooperative Oncology Group performance status and severe underlying diseases, or patients who refused the surgery underwent conservative treatment. The decision of whether to remove or maintain PTGBD was made by consulting a gastroenterologist and an HBP surgeon based on the patient's general condition and disease characteristics.

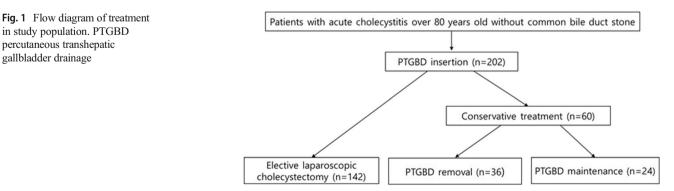
# Definition of Recurrence of BE and PTGBD-Related Complications

Recurrent BE was defined as recurring AC, acute cholangitis, and acute biliary pancreatitis requiring hospitalization. Acute cholangitis is diagnosed based on Tokyo Guidelines 2018<sup>10</sup>. The diagnosis of acute pancreatitis was based on the Atlanta criteria<sup>11</sup>.

We defined a PTGBD-related complication as PTGBD malfunction or self-removal requiring hospitalization or emergency room visits for re-insertion or repositioning of PTGBD.

#### **Definition of Demographics and Treatment Outcomes**

The general condition and physical fitness of each patient was evaluated using the Charlson age comorbidity index (CACI)<sup>12</sup> in all patients and the American Society of Anesthesiologists physical status (PS) classification in patients who underwent ELC. The cystic duct patency was classified as open, closed, or not checked by cholangiography in PTGBD. The presence of GB stones was confirmed by imaging studies using USG, CT, or MRCP. The surgery duration was calculated as the time from skin incision to skin closure. Blood loss estimates were obtained from the surgical records. The total hospital stay was defined as the number of days between admission and discharge. Postoperative hospital stay was defined as the number of days of hospital stay after ELC. Post-PTGBD hospital stay was defined as the number of days of hospital stay after PTGBD insertion. Postoperative complications were graded according to the Clavien-Dindo classification . POMC was defined as a level greater than grade III of the Clavien-Dindo



classification. Mortality after initial treatment was defined as postoperative mortality in the ELC group and mortality related to BE after index admission in the conservative group.

# **Statistical Analysis**

Continuous variables were summarized as mean and standard deviation (SD) and were compared using the Student's t-test or analysis of variance. Categorical variables were presented as counts and percentages and were compared using the chisquare test. Multivariate analyses were performed using a logistic regression model to identify the risk factors for major postoperative complications and recurrent BE. All tests were two-sided, and p-values <0.05 were considered statistically significant. The analyses were performed using SPSS version 24 (SPSS Inc., Chicago, IL, USA).

## Results

## **Study Cohort**

Patient demographics, disease characteristics, and treatment outcomes of all patients are shown in Table 1. Among the 202 patients included, 142 underwent ELC, and 60 underwent conservative treatment. Among the 60 patients, 36 had PTGBD-R, and 24 had PTGBD-M. Patients in the PTGBD-R group were older (83.9 vs. 88.7 vs. 86.7%, p<0.001) than those in the ELC and PTGBD-M groups. Patients in the PTGBD-M group had a higher CACI (4.9 vs. 5.7 vs. 5.8%, p<0.001) than patients in the other two groups. Calculous cholecystitis was most common in the PTGBD-M group (64.5% vs. 30.6% vs. 70.8%, p<0.001). There were no statistically significant differences in AC severity based on TG18. Total hospital stays (14.5 vs 15.8 vs 12.4 days, p=0.486) and post-PTGBD hospital stays (14.3 vs14.8 vs 11.9 days,

Table 1 Comparison of patient demographics, disease characteristics, and treatment outcomes based on the treatment algorithm

Variable	ELC (n=142)	PTGBD-R (n=36)	PTGBD-M (n=24)	p-value
Age, mean years (SD)	83.9 (3.6)	88.7 (5.5)	86.7 (4.6)	< 0.001
Female, n (%)	78 (54.9)	19 (52.8)	17 (70.8)	0.309
BMI, mean kg/m <sup>2</sup> (SD)	23.1 (3.4)	22.4 (3.7)	21.9 (4.5)	0.215
Charlson age comorbidity index, mean (SD)	4.9 (0.9)	5.7 (1.2)	5.8 (1.1)	< 0.001
Charlson age comorbidity index ≥6, n (%)	30 (21.1)	16 (44.4)	13 (54.2)	< 0.001
Admission to ICU, n (%)	25 (17.6)	10 (27.8)	7 (29.2)	0.227
GB stone, n (%)	91 (64.5)	11 (30.6)	17 (70.8)	< 0.001
Initial WBC count, mean 10 <sup>3</sup> /m <sup>3</sup> (SD)	13.1 (5.3)	14.4 (7.4)	19.5 (9.2)	< 0.001
Initial platelet count, mean 10 <sup>3</sup> /m <sup>3</sup> (SD)	212.7 (82.9)	218.1 (75.3)	198.8 (64.8)	0.644
Initial PT, mean INR (SD)	1.16 (0.15)	1.22 (0.36)	1.25 (0.21)	0.062
Initial creatinine level, mean mg/dL (SD)	1.07 (0.47)	1.19 (0.72)	1.03 (0.34)	0.398
Initial total bilirubin level, mean mg/dL (SD)	1.81 (1.59)	1.46 (1.17)	1.95 (1.39)	0.372
Initial AST level, mean IU/L (SD)	124.4 (221.4)	91.0 (131.7)	185.0 (498.1)	0.384
Initial ALT level, mean IU/L (SD)	80.6 (119.2)	76.9 (174.9)	138.7 (420.1)	0.361
Initial CRP level, mean mg/dL (SD)	13.7 (11.2)	13.6 (10.2)	14.5 (10.4)	0.939
Severity of AC based on TG18, n (%)				0.132
Mild	76 (53.5)	17 (47.2)	8 (33.3)	
Moderate	49 (34.5)	15 (41.7)	15 (62.5)	
Severe	17 (12.0)	4 (11.1)	1 (4.2)	
Total hospital stay, mean days (SD)	14.5 (11.6)	15.8 (7.2)	12.4 (10.6)	0.486
Post-PTGBD hospital stay, mean days (SD)	14.3 (12.6)	14.8 (6.9)	11.9 (10.8)	0.603
Postoperative hospital stay, mean days (SD)	6.0 (8.2)	-	-	-
Postoperative major complication, n (%)	12 (8.5)	-	-	-
Relapse of biliary event after PTGBD removal, n (%)	-	8 (22.2)	-	-
PTGBD-related complication after discharge, n (%)	-	-	17 (70.8)	-
Mortality after initial treatment, n (%)	4 (2.8)	1 (2.8)	2 (8.3)	0.381

*ELC* elective laparoscopic cholecystectomy, *PTGBD* percutaneous transhepatic gallbladder drainage, *PTGBD-R* PTGBD removal, *PTGBD-M* PTGBD maintenance, *AC* acute cholecystitis, *TG* 18 Tokyo Guidelines 2018, *SD* standard deviation, *BMI* body mass index, *ICU* intensive care unit, *GB* gallbladder, *WBC* white blood cell, *CRP* c-reactive protein

p=0.603) were similar in all three groups. The postoperative major complication (POMC) rate in the ELC group was 8.5%. The recurrence rate of BE after drainage tube removal in the PTGBD-R group was 22.2%. The PTGBD-related complication rate after discharge in the PTGBD-M group was 70.8%. There were no significant difference in biliary event-related mortality after index treatment (2.8% vs. 2.8% vs. 8.3%, p=0.381).

#### Elective Laparoscopic Cholecystectomy

The POMC group had a greater proportion of patients with body mass index (BMI)  $\leq 19$  (33.3% vs. 10.0%, p=0.017),

CACI  $\geq$ 6 (66.7% vs. 16.9%, p<0.001), and moderate or severe AC (75.0% vs. 43.8%, p=0.038) compared to patients in the non-POMC group (Table 2). Additionally, the duration of postoperative hospital stay was significantly greater in patients with POMC (25.3 vs. 4.2 days, p<0.001) than these in the non-POMC group. In multivariate analyses, CACI  $\geq$ 6 and BMI  $\leq$ 19 were identified as significant risk factors for POMC after ELC (Table 3).

### **Conservative Treatment with PTGBD-R**

At the time of analysis, the median follow-up was 23.2 months, and the cumulative incidence for recurrence of BE

 Table 2
 Comparison of patient demographics, disease characteristics, and treatment outcomes based on incidence of major complications in the elective laparoscopic cholecystectomy group

Variable	Total (n=142)	Non-POMC group (n=130)	POMC group (n=12)	p- value
Age, mean years (SD)	83.9 (3.6)	84.0 (3.7)	82.8 (2.6)	0.173
Female, n (%)	78 (54.9)	72 (55.4)	6 (50.0)	0.720
BMI, kg/m <sup>2</sup> $\leq$ 19, n (%)	17 (12.0)	13 (10.0)	4 (33.3)	0.017
Charlson age comorbidity index ≥6, n (%)	30 (21.1)	22 (16.9)	8 (66.7)	< 0.001
ASA PS classification ≥III, n (%)	95 (66.9)	88 (67.7)	7 (58.3)	0.510
Prior abdominal surgery (+), n (%)	23 (16.2)	22 (16.9)	1 (8.3)	0.440
Preoperative ICU admission, n (%)	25 (17.6)	22 (16.9)	3 (25.0)	0.482
Initial WBC count > $18*10^3/m^3$ , n (%)	25 (17.6)	23 (17.7)	2 (16.7)	0.929
Initial platelet count $<10*10^3/m^3$ , n (%)	3 (2.1)	2 (1.5)	1 (8.3)	0.117
Initial PT level >1.5 INR, n (%)	4 (2.8)	4 (3.1)	0 (0.0)	0.538
Initial creatinine level >2 mg/dL, n (%)	8 (5.6)	7 (5.4)	1 (8.3)	0.672
Initial total bilirubin level >2 mg/dL, n (%)	35 (24.6)	31 (23.8)	4 (33.3)	0.466
Initial AST level >36 IU/L, n (%)	65 (45.8)	61 (46.9)	4 (33.3)	0.366
Initial ALT level >38 IU/L, n (%)	52 (36.6)	50 (38.5)	2 (16.7)	0.134
Initial CRP level > 30 mg/dL, n (%)	45/140 (32.1)	39/129 (30.2)	6/11 (54.5)	0.097
Moderate or severe AC based on TG18, n (%)	66 (46.5)	57 (43.8)	9 (75.0)	0.038
Single incision	7 (4.9)	6 (4.6)	1 (8.3)	0.569
Surgery duration, mean minutes (SD)	61.3 (28.7)	60.7 (28.4)	67.9 (32.6)	0.472
Estimated blood loss, mean mL (SD)	32.9 (71.1)	32.2 (72.7)	40.0 (53.0)	0.646
Open conversion, n (%)	4 (2.8)	4 (3.1)	0 (0.0)	0.538
Adjacent organ injury (+), n (%)	3 (2.1)	2 (1.5)	1 (8.3)	0.117
Intraoperative transfusion, n (%)	1 (0.7)	1 (0.8)	0 (0.0)	0.760
Drain insertion (+), n (%)	50 (35.2)	45 (34.6)	5 (41.7)	0.625
Postoperative complication $\geq$ grade II Clavien-Dindo classification, n (%)	34 (23.9)	22 (16.9)	12 (100.0)	< 0.001
Postoperative hospital stay, mean days (SD)	6.0 (8.2)	4.2 (2.8)	25.3 (18.2)	< 0.001
Mortality, n (%)	4 (2.8)	0 (0.0)	4 (33.3)	< 0.001
Pathology				0.919
Acute cholecystitis	69 (48.6)	63 (48.5)	6 (50.0)	
Chronic cholecystitis and others	73 (51.4)	67 (51.5)	6 (50.0)	
Incisional hernia, n (%)	1 (0.7)	1 (0.8)	0 (0.0)	0.760

POMC postoperative major complication, AC acute cholecystitis, TG 18 Tokyo Guidelines 2018, SD standard deviation, BMI body mass index, ICU intensive care unit, WBC white blood cell, CRP c-reactive protein

Table 3	Multivariate analysis of risk factors for postoperative major
complicat	tions in the elective laparoscopic cholecystectomy group

Factor	Multivariate analysis				
	OR (95% CI)				
Charlson age comorbidity	index				
<6	1 (ref)	-			
≥6	10.780 (2.714-42.822)	0.001			
BMI, kg/m <sup>2</sup>					
>19	1 (ref)	-			
≤19	5.394 (1.095-26.569)	0.038			
Severity of acute cholecys	stitis				
TG18 grade I	1 (ref)	-			
TG18 grade II or III	3.903 (0.911–16.723)	0.067			

*TG18* Tokyo Guidelines 2018, *OR* odds ratio, *CI* confidence interval, *BMI* body mass index

was 22.2% (8/36). The 2-year recurrence rate of BE was 24.5% (Fig. 2). Among the eight patients, six had cholecystitis and two had cholangitis. The median duration between PTGBD removal and the recurrence of BE was 5.8 months. Among patients who experienced the recurrence of BE, five were conservatively treated, one underwent LC, one underwent PTGBD re-insertion, and one underwent percutaneous transhepatic biliary drainage insertion. The median retention period of the PTGBD was 14 days. The cystic duct patency rate before PTGBD-R was 86.1% (Table 4). In multivariate analysis, a closed cystic duct on cholangiography in

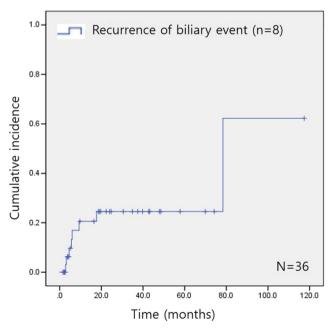


Fig. 2 Cumulative incidence for recurrence of biliary events in the PTGBD removal group. PTGBD percutaneous transhepatic gallbladder drainage

 Table 4
 Treatment outcomes in the PTGBD removal group

Variables	Number		
Duration of follow-up, median	23.2 (5.1–46.1)		
months (IQR)			
Retention period of PTGBD, median days (IQR)	14 (10.3–21.5)		
Total hospital stay, mean days (SD)	15.8 (7.2)		
Post-PTGBD hospital stay, mean days (SD)	14.8 (6.9)		
Cystic duct patency before PTGBD removal, n (%)			
Closed	2 (5.6)		
Open	31 (86.1)		
Not checked	3 (8.3)		
Recurrence of biliary event, n (%)	8 (22.2)		
Cholecystitis	6 (16.7)		
Cholangitis	2 (5.6)		
Duration between PTGBD removal and recurrence of biliary event, median months (IQR)	5.8 (3.5–15.6)		
Treatment for relapse of biliary event			
LC	1 (2.8)		
PTGBD re-insertion	1 (2.8)		
ERCP or PTBD	1 (2.8)		
Conservative care	5 (13.9)		
Mortality related to biliary event after initial treatment, n (%)	1 (2.8)		

PTGBD percutaneous transhepatic gallbladder drainage, LC laparoscopic cholecystectomy, ERCP endoscopic retrograde cholangiopancreatography, PTBD percutaneous transhepatic biliary drainage, IQR interquartile range, SD standard deviation

PTGBD was the only statistically significant risk factor for recurrent BE following PTGBD-R (Table 5).

#### **Conservative Treatment with PTGBD-M**

At the time of analysis, the median follow-up was 4.4 months, and the cumulative incidence for PTGBD-related complication was 70.8% (17/24). Among the 17 patients, 10 had PTGBD malfunction, and seven had PTGBD removal. The median number of PTGBD-related complications during the follow-up period was 2. The median duration between discharge and first PTGBD-related complications was 1.3 months. PTGBD reinsertion was performed in all patients with PTGBD-related complications. The cystic duct patency rate before discharge was 62.5% (Table 6).

## Discussion

The management of elderly patients with AC remains controversial. A recent population-based study recommends

Table 5	Multivariate	analysis	of risk	factors	for	recurrence	of	biliary
events aft	er PTGBD rer	noval						

Sex       -         Female       1 (ref)       -         Male $3.342$ ( $0.281-39.702$ )       0         Body mass index, kg/m <sup>2</sup> -         <25       1 (ref)       -         ≥25       2.566 ( $0.163-40.450$ )       0         CACI       -         <6       1 (ref)       -         ≥6       0.163 ( $0.012-2.310$ )       0         Total bilirubin level       -       -         < 2 mg/dL       1 (ref)       -		
Female       1 (ref)       -         Male $3.342$ ( $0.281-39.702$ )       0         Body mass index, kg/m <sup>2</sup> -         <25       1 (ref)       - $\geq 25$ $2.566$ ( $0.163-40.450$ )       0         CACI       -       -         <6       1 (ref)       - $\geq 6$ 0.163 ( $0.012-2.310$ )       0         Total bilirubin level       -       -         < 2 mg/dL       1 (ref)       -	p-value	
Male $3.342 (0.281-39.702)$ 0Body mass index, kg/m2- $<25$ 1 (ref) $\geq 25$ 2.566 (0.163-40.450)0CACI- $<6$ 1 (ref) $\geq 6$ 0.163 (0.012-2.310)0Total bilirubin level- $< 2 mg/dL$ 1 (ref)-		
Body mass index, kg/m <sup>2</sup> - $<25$ 1 (ref)       - $\geq 25$ 2.566 (0.163-40.450)       0         CACI       -       - $<6$ 1 (ref)       - $\geq 6$ 0.163 (0.012-2.310)       0         Total bilirubin level       -       - $< 2$ mg/dL       1 (ref)       -		
$<25$ 1 (ref)       - $\geq 25$ 2.566 (0.163-40.450)       0         CACI       -       - $<6$ 1 (ref)       - $\geq 6$ 0.163 (0.012-2.310)       0         Total bilirubin level       -       - $< 2 mg/dL$ 1 (ref)       -	).339	
≥25 2.566 (0.163-40.450) 0 CACI <6 1 (ref) - ≥6 0.163 (0.012-2.310) 0 Total bilirubin level < 2 mg/dL 1 (ref) -		
CACI       -         <6		
$<6$ 1 (ref)       - $\geq 6$ 0.163 (0.012–2.310)       0         Total bilirubin level       -       - $< 2 \text{ mg/dL}$ 1 (ref)       -	0.503	
≥6 0.163 (0.012–2.310) 0 Total bilirubin level < 2 mg/dL 1 (ref) -		
Total bilirubin level < 2 mg/dL 1 (ref) -		
< 2 mg/dL 1 (ref) -	0.180	
•		
> 2 ma/dI = 0.205 (0.012, 11.942)		
$\geq 2 \text{ mg/dL}$ 0.395 (0.013–11.842) 0	).592	
CRP level		
$\leq$ 20 mg/dL 1 (ref) -		
> 20 mg/dL 1.303 (0.068–25.089) 0	).861	
Severity of AC		
TG grade I 1 (ref) -		
TG grade II/III 0.537 (0.045–6.454) 0	).624	
GB stone		
No 1 (ref) -		
Yes 13.880 (0.958–201.071) 0	0.054	
Cystic duct patency		
Open 1 (ref) -		
Closed 53.836 (1.542–1879.150) 0	0.028	
Duration of PTGBD insertion		
< 14 days 1 (ref) -		
$\geq$ 14 days 1.203 (0.145–9.997) 0		

*PTGBD* percutaneous transhepatic gallbladder drainage, *TG18* Tokyo Guidelines 2018, *OR* odds ratio, *CI* confidence interval, *GB* gallbladder, *AC* acute cholecystitis, *CRP*, c-reactive protein, *CACI* Charlson age co-morbidity index

cholecystectomy unless there are surgical contraindications<sup>15</sup>. However, in clinical practice, PTGBD insertion tends to be preferred as the initial management for urgent LC in elderly patients with AC. Elderly patients often have significant comorbidities and require preoperative risk assessment for general anesthesia. Severe AC, including biliary sepsis, is more common in elderly patients. In the present study, the initial intensive care unit (ICU) admission rate was approximately 20%. Therefore, a study on optimal management after PTGBD insertion is necessary. In the present study, ELC and conservative treatment after PTGBD were compared, and in the case of conservative treatment, treatment outcomes were classified based on whether the PTGBD tube was removed or maintained.

 Table 6
 Treatment outcomes in the PTGBD maintenance group

Variable	Number	
Duration of follow-up, median months (IQR)	4.4 (1.7-8.7)	
Total hospital stay, mean days (SD)	12.3 (10.6)	
Post-PTGBD hospital stay, mean days (SD)	11.9 (10.8)	
Cystic duct patency before discharge, n (%)		
Closed	8 (33.3)	
Open	15 (62.5)	
Not checked	1 (4.2)	
PTGBD-related complication after discharge, n (%)	17 (70.8)	
Malfunction	10 (41.7)	
Removal	7 (29.2)	
Number of PTGBD-related complications, median num- ber (IQR)	2 (1.0–3.5)	
Duration between discharge and first PTGBD-related complication, median months (IQR)	1.3 (0.8–3.2)	
Mortality related to biliary event after initial treatment, $n(\%)$	2 (8.3)	

*PTGBD* percutaneous transhepatic gallbladder drainage, *IQR* interquartile range, *SD* standard deviation

LC is associated with low morbidity and mortality rates <sup>16</sup>. However, negative postoperative outcomes, such as major complications or mortality, appear to be significantly increased in elderly patients. A recent meta-analysis demonstrated that there is a seven-fold increase in perioperative mortality, which increases by ten-fold in patients aged >80 years <sup>17</sup>. In our ELC group, the POMC rate was 8.5%, and the mortality rate was 2.8%. The results were similar to those of other studies on elderly patients <sup>6</sup>. However, there is a lack of studies on the risk factors for POMC after LC in elderly patients with AC. We performed a multivariate analysis of risk factors for POMC, and CACI  $\geq$ 6 and BMI  $\leq$ 19 were statistically significant risk factors for POMC. It was confirmed that the patient's general condition and nutritional status had a greater effect on POMC after ELC than on AC severity.

In the previous study, the incidence of recurrent BE ranged from 9.2 to 29.8% <sup>4,8,18–20</sup>. In the present study, the incidence of recurrent BE after PTGBD removal was 22.2%, similar to previously published data. Several risk factors for recurrent BE have been proposed in previous studies, including complicated cholecystitis, prolonged duration of PTGBD, abnormal cholangiography findings, and high initial c-reactive protein levels <sup>4,8,19,20</sup>. Our results indicate that closed cystic duct patency on cholangiography in PTGBD was the only risk factor for recurrent BE after PTGBD-R.

There is a lack of studies on the natural course of AC in PTGBD-M. Indeed, maintaining the PTGBD tube can prevent recurrence of BE; however, it also greatly interferes with the patient's life. In the present study, the incidence of PTGBD malfunction or unintentional removal requiring emergency room visits or inpatient treatment was 70.8%. The median duration between discharge and the first PTGBD-related complication was only 1.3 months. It was confirmed that maintaining the PTGBD tube for a prolonged period is difficult. Conservative treatment with PTGBD-M is not an optimal treatment option for patients aged >80 years with AC.

Mortality after initial treatment occurred in 4 (2.8%), 1 (2.8%), and 2 (8.3%) patients in the ELC, PTGBD-R, and PTGBD-M groups, respectively. In the ELC group, three patients died of pneumonia, and one patient died postoperatively due to the aggravation of heart failure. In the PTGBD-R group, one patient died of biliary sepsis related to recurrent AC. In the PTGBD-M group, two patients died of biliary sepsis related to the unintentional removal of PTGBD. In general, conservative treatment is selected to avoid major complications, such as mortality after surgery. However, in the present study, there was no significant difference in mortality after initial treatment (2.8% vs. 2.8% vs. 8.3%, p=0.381). Therefore, conservative treatment may be considered in patients with a high risk of POMC after ELC. Although not included in this study, conservative treatment may be prioritized rather than cholecystectomy in patients with severe dementia or terminal conditions.

The patient counseling about the benefits and risks of surgery is very important for decision-making of surgery in elder patients. In our institution, before this study was conducted, cholecystectomy was decided based on the personal judgment of a HBP surgeon or a gastroenterologist without clear criteria in elder patients. After this study, we recommended conservative treatment for patients who satisfy both CACI  $\geq$ 6 and BMI  $\leq$ 19. In addition, information on the rate of POMC after LC and rate of BE recurrence after conservative treatment is helpful for elder patients to decide on surgery.

Our study has several limitations. First, this was a retrospective study with a small sample size, and attempts to reduce selection bias or confounding variables may have been insufficient. Second, we excluded patients with CBD stones, since the treatment of CBD stones could result in a more heterogeneous population. However, elderly patients with AC are more likely to have CBD stones and require additional procedures, such as endoscopic retrograde cholangiopancreatography or CBD exploration<sup>7</sup>. Additional studies are needed, including those in patients with CBD stones.

# Conclusion

ELC is recommended after PTGBD for selected patients with AC aged >80 years without CBD stones due to the high recurrence rate of BE after PTGBD-R and the difficulty associated with PTGBD-M. Author Contribution Substantial contributions to the conception or design of the work or the acquisition, analysis, or interpretation of data for the work: Seung Jae Lee, In Seok Choi, Ju Ik Moon, Dae Sung Yoon, Sang Eok Lee, Nak Song Sung, Sung Uk Kwon, In Eui Bae, Seung Jae Roh, and Won Jun Choi

Drafting the work or revising it critically for important intellectual content: Seung Jae Lee, In Seok Choi, and Ju Ik Moon

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Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: Seung Jae Lee and In Seok Choi

#### Declarations

Conflict of Interest The authors declare no competing interests.

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