Assessment of different timing for early laparoscopic cholecystectomy in acute calcular cholecystitis: a multicentric prospective cohort study

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Background
The ideal timing for early laparoscopic cholecystectomy (ELC) continues to be controversial in patients with acute calcular cholecystitis (ACC). This research was constructed to identify the effects of different ELC timing in ACC on surgical outcomes in terms of safety and efficacy.
Patients and methods
This multicentric analysis involved 939 successive patients with ACC ELC. Patients were divided into three groups according to the timing of the surgery: from the onset of symptoms within the first 3 days (group 1), between 4 and 7 days (group 2), and beyond 7 days (group 3). The primary outcome was the incidence of postoperative morbidity.
Results
The median operative time, the time to reach a critical view of safety, and the time of dissection of gall bladder were significantly more in G3. The conversion rate and blood loss were significantly more in G3. No statistical difference among the three groups was observed regarding the rate of postoperative morbidity and postoperative stay. The grade of cholecystitis, cystic duct diameter greater than 5 mm, method of closure of cystic duct, and development of intraoperative complications were the independent factors of the development of postoperative complications. Age greater than 60 years, gall bladder status, grade of adhesions, cystic duct diameter greater than 5 mm, and development of intraoperative complications were the independent factors of conversion.
Conclusion
ELC was performed safely at any time after the onset of ACC. ELC beyond seven days was associated with more blood loss, increased operative time, and increased conversion rate.

Keywords:
acute cholecystitis, bile duct injury, bile leakage, conversion rate, critical view of safety, laparoscopic cholecystectomy

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Introduction

Gallstones are a common disease and present in 20% of the patients with symptomatic disease as acute calcular cholecystitis (ACC), with a large range in severity [1–6]. In 2007, the first international Tokyo Guidelines for ACC addressed the frequency, treatment, and management of AC, which was revised in 2013 (TG13), with the last version of Tokyo Guidelines being 2018 (TG18) [7,8].

The diagnostic criteria for TG13/TG18 advised the diagnosis of AC based on clinical appearance, laboratory examination, and radiological indications and graded AC into three grades of inflammation: mild (grade I), moderate (grade II), and serious (grade III). The TG13/TG18 proposed that AC's effective management was supported by AC's grade [7,8].

LC is currently ACC's foremost proven management, though the optimum timing of the surgery from the start of the presentation continues to be contentious. Some prospective trials have confirmed that early laparoscopic cholecystectomy (ELC) is feasible for ACC as opposed to delayed laparoscopic cholecystectomy (DLC) [1–6]. In several previous studies, ELC causes more blood loss and longer operating time or increased postoperative morbidity compared with late LC. Other studies found that there was no significant difference between intraoperative morbidities within the ELC compared with DLC. Other studies also reported mixed morbidity outcomes in early and late cholecystectomy [2–5].

Many prospective studies have reported that ELC for ACC is safe compared with DLC in intraoperative and postoperative complications, with a shorter hospital stay, lower costs, and also the chances of repeated attacks [2–6].

Many surgeons have expected a 'golden 72 h statute' as a suitable time to conduct ELC [9–14]. With improved capacity in highly advanced laparoscopic surgery, ELC was anticipated after 72 h, and lots of randomized and nonrandomized trials tested its safety within the first 7 days with the short hospital stay [13–17].

Few trials, none of which have been randomized, examined the effects of ELC in patients who presented exclusively after 7 days from the onset of ACC [9,10]. This research was designed to determine the different timing of ELC in ACC regarding safety and efficacy (within the first 3 days, after 3–7 days, and after 7 days from the onset of symptoms).

Patients and methods

Study design

It is a multicenter comparative prospective study of patients who received ELC for ACC. The details included successive patients with ACC who underwent ELC in Gastrointestinal Surgical Center (Mansoura University), Minia University Hospital Egypt, Khamees Meshat General Hospital, and Aseer Central Hospital, Aseer Area, KAS, from April 2018 to March 2020. The criterion for inclusion included patients with ACC. Exclusion requirements included pregnancy, acalculous cholecystitis, preoperatively or intraoperatively diagnosed common duct stones, cholangitis, biliary pancreatitis, American Society of Anesthesiologists (ASA) score 4, and patients originally scheduled for DLC with failed medical treatment. The data were prospectively documented into a computerized archive. Consent was signed from all patients to be included in this research, after proper explanation of ACC's character and also potential treatment strategies with its complications. IRB approved the analysis in all centers. The study was registered in ClinicalTrial.gov ID NCT04405713.

Management of ACC

ACC specific diagnosis followed the Tokyo Guidelines with local physical signs, systemic symptoms, leukocytosis, and ACC radiological signs. During this study, ACC's management protocol within the centers was to try to perform ELC for the patients who had ACC once admitted regardless of the onset of an ACC attack. The patients were divided into three categories that supported the ACC inception.

The patients were divided into three groups with respect to the timing of the surgery: G1, within the first 3 days; G2, after 3–7 days; and G3, after 7 days from the onset of ACC.

LC was done by a traditional four-port technique, establishing the critical safety view (CVS) [18]. In selected cases with unclear anatomy, suspect of passed stone to the common bile duct, dilated cystic duct, or dilated common bile duct, intraoperative cholangiogram was performed. If conversion to open cholecystectomy was needed, a proper subcostal incision was done. The consultant surgeon with laparoscopic surgery expertise performed the procedures.

Patients were monitored using ACC guidelines followed by administration of postoperative antibiotic therapy: for mild ACC, antibiotic therapy was stopped within 24 h of surgery and continued for 4–7 days when other manifestations (perforation, gangrene GB or pericholecystic collection) were identified. For 1 week after LC, moderate or severe ACC cases were administered antibiotic therapy. The antibiotic therapy was prolonged for a total of 2 weeks if bacteremia was present.

At the pathological examination, all of the gallbladders removed were established as ACC.

Data collection

The data included the following items: demographic data, previous ACC attacks, previous abdominal operations, ACC onset, ACC grade, leukocytic count, liver function, serum amylase, surgical date, operative data, postoperative complication, postoperative complications in compliance with the Clavien-Dindo classification [19], hospital stay duration, and hospitalization costs.

Outcomes

The primary outcome was postoperative morbidity rate. Postoperative morbidity is defined as any complication that occurs within the 30th day of postoperative operation. Conversion rate, blood loss, operating times, technical difficulties, the cost–benefit relationship of each treatment line, and hospital stay were the secondary outcomes.

Statistical analysis

For categorical variables, descriptive data were presented as counts and percentages; continuous variables were represented as median and variance. The statistical study was carried out using the χ^2 method to evaluate categorical variables and also the analysis of variance one-way method for continuous variables. The significant differences were considered at a P value of less than 0.05 on both sides. The statistical analyses were conducted for Windows using SPSS 17 (SPSS Inc., Chicago, Illinois, USA).

Results

Patient characteristics

Between April 2018 and March 2020, 6820 patients underwent LC, among whom 939 patients (13.8%) met the ACC criteria. Patients in the study included 353 males (37.6%)) and 586 females (62.4%), with a median age of 46 years. The majority of patients (86%) had either 1 or 2 ASA grading scores.

The patients were divided into three groups with respect to the timing of the surgery: G1 included 557 patients who underwent surgery within the first 72 h, G2 included 258 patients who underwent surgery between 72 h and seven days, and G3 included 124 patients who underwent surgery beyond 7 days from the symptom onset.

Preoperative data

Baseline characteristics were similar in age, sex, BMI, comorbidity, and laboratory investigation, among the three groups (Table 1).

Intraoperative data

LC has been converted to open cholecystectomy in 52 patients (5.5%). The conversion rate was significantly more in group III.

The CVS was reached in 906 patients (96.5%). CVS was achieved in most cases in the three groups but with no statistical differences. The median time to achieve CVS is significantly longer in GIII patients (Table 2).

Intraoperative blood loss was considerably greatest in group III (P=0.0001). The median operative time was

Table 1 Preoperative data

	Group 1 [*n* (%)]	Group 2 [*n* (%)]	Group 3 [*n* (%)]	*P* value
Age (years)	42 (35–55)	43 (37–59)	42 (35–57)	0.35
<60	443 (79.5)	194 (75.2)	92 (74.2)	0.24
>60	114 (20.5)	64 (24.8)	32 (25.8)	
Sex				
Male	214 (38.4)	99 (38.4)	40 (32.3)	0.42
Female	343 (61.6)	159 (61.6)	84 (67.7)	
BMI				
<25	254 (45.6)	133 (51.6)	56(45.2)	0.25
>25	303 (54.4)	125 (48.4)	68 (54.8)	
Comorbidity				
DM	115 (20.6)	85 (22.5)	35 (28.2)	0.18
Hypertension	116 9208)	60 (23.3)	30 (24.2)	0.59
BA	42 (7.5)	29 (11.2)	8 (6.3)	0.15
Cardiac	40 (7.2)	17 (6.6)	14 (11.3)	0.23
Clinical picture				
Pain	557 (100)	258(100)	124 (100)	1
Fever	236 (42.4)	114 (44.2)	84 (51.6)	0.17
Jaundice	70 (12.6)	29 (11.2)	11 (8.9)	0.49
Murphy sign	415 (74.5)	184 971.3)	87 (70.2)	0.47
WBC	13 (11–17)	14 (12–18)	14 (13–17)	0.241
Serum albumin (g/dl)	4 (3.7–4.3)	4 (3.9–4.1)	4 (4)	0.338
SGPT (IU/dl)	45 (30–50)	44 (31–52)	44 (29–51)	0.752
Serum bilirubin (mg/dl)	0.9 (0.8–1.5)	0.9 (0.8–1.4)	1 (0.8–1.)	0.721

DM, diabetes mellitus; SGPT, serum glutamic pyruvic transaminase; WBC, white blood cells.

Table 2 Intraoperative data

	Group 1 [*n* (%)]	Group 2 [*n* (%)]	Group 3 [*n* (%)]	*P* value
Severity of cholecystitis				
Acute cholecystitis (not obstructed)	135 (42.2)	14 (5.4)	21 (16.9)	0.0001
Mucocele	369 (62.2)	188 (72.9)	60 (48.4)	
Pyocele	43 (7.7)	46 (17.8)	38 (30.6)	
Gangrenous	10 (1.8)	10 (3.9)	5 (4)	
Grade of cholecystitis				
G 1	325 (58.3)	123 (47.7)	53 (42.7)	
G II	223 (40)	121 (64.9)	59 (47.6)	0.0001
G III	9 (1.6)	14 (5.4)	12 (9.7)	
Adhesion				
No adhesion	77 (13.8)	26 (10.1)	5 (4)	
Filmy easy dissected	250 (44.9)	84 (34.6)	35 (28.2)	0.0001
Pericholecystectomy adhesion with clear anatomy	174 (31.2)	101 (39.1)	50 (40.3)	
Marked adhesion with unclear anatomy	56 (10.1)	47 (18.2)	34 (27.4)	
Liver cirrhosis	26 (4.7)	20 (7.8)	10 (8.1)	0.128
GB stone number				
Single	112 (20.1)	49 (19)	28 (22.6)	0.206
Multiple	445 (79.9)	209 81)	96 (77.4)	
Stone in cystic duct	27 (4.8)	24 (9.3)	7 (5.6)	0.047
Stone in Hartman	394 (70.7)	219 (84.9)	94 (75.8)	0.0001
Critical view of safety	542 (97.3)	274 (95.7)	117 (94.4)	0.202
Diameter of cystic duct				0.0001
Intraoperative cholangiogram	62 (11.1)	21 (8.1)	30 (24.2)	0.0001
Normal CBD	42	7	17	
Dilated CBD	16	13	10	
CBDS	4	0	3	
BDI	0	1	0	
Method of closure of cystic duct				
Single clip	379 (68)	151 (58.5)	59 (47.6)	
Overlapping clip	91 (16.3)	55 (21.3)	30 (24.2)	0.001
Ligature	44 (7.9)	23 (8.9)	18 (14.5)	
Stapler	43 (7.7)	29 (11.2)	17 (13.7)	
Conversion rate	23 (4.1)	16 (6.2)	13 (10.5)	0.017
Cause of conversion				
Marked adhesion	10	10	6	0.551
Bleeding	12	5	5	
CBD injury	1	1	1	
Colonic injury	0	0	1	
Blood loss	50 (30–50)	200 (50–500)	150 (100–400)	0.0001
Intraoperative complications				
Bleeding	15 (2.7)	5 (1.9)	5 (4)	0.159
Colonic injury	0	0	1 (0.8)	
Rupture gall bladder	44 (7.9)	18 (7)	14 (11.3)	
CBD injury	1 (0.2)	1 (0.4)	1 (0.8)	
Drain	337 (67.7)	210 (81.4)	98 (79)	0.0001
Widening of port and closure	446 (80.1)	233 (90.3)	101 (81.5)	0.001
Operative time	60 (55–70)	60 (60–90)	70 (60–90)	0.0001
Time to reach critical view of safety	15 (12–18)	15 (15–19)	16 (15–20)	0.0001
Time for dissection of GB from bed	30 (25–30)	35 (25–45)	35 (30–54)	0.0001
Time for extraction	5 (4–5)	5 (4–6)	5 (5–7)	0.004

CBD, common bile duct; GB, gall bladder.

60 min (60–75). The median operative time was significantly longer in group III (*P*=0.0001) (Table 2).

The overall rate of intraoperative complications was 105 (11.2%), including three cases of bile duct injury (BDI), which was managed intraoperatively by axial repair in two cases and one case by hepaticojejunostomy. There was no significant difference among the three groups regarding intraoperative complications (Table 2).

Postoperative data

There was no significant difference among the three groups regarding postoperative stay, the median amount of drain, and the overall complications (Table 3).

In 63 (6.7%) patients, one or more complications occurred. The foremost common problems were intra-abdominal collection developed in 42 (4.5%) patients, biliary leakage in 17 (1.8%) patient, and obstructive jaundice in 11 (1.17%) patient. There was no significant difference among the three groups regarding postoperative complications (Table 3).

Regarding predictor factors for the development of postoperative complication, univariate analyses demonstrated five variables, including the grade of cholecystitis, conversion to open cholecystectomy, cystic duct diameter greater than 5 mm, method of closure of cystic duct, and development of intraoperative complications. Multivariate analysis identified that grade of cholecystitis, cystic duct diameter greater than 5 mm, method of closure of cystic duct, and development of intraoperative complications were the independent factors of development of postoperative complications (Table 4).

Regarding predictor factors for conversion to open cholecystectomy, univariate analyses demonstrated eight variables, including age greater than 60, diabetes, gall bladder status, the grade of cholecystitis, the grade of adhesions, cystic duct diameter greater than 5 mm, development of intraoperative complications, and time of surgery. Multivariate analysis identified that age greater than 60 years, gall bladder status, the grade of adhesions, cystic duct diameter greater than 5 mm, and development of intraoperative complications were the independent factors of conversion (Table 5).

Table 3 Postoperative data

	Group 1	Group 2	Group 3	*P* value
Postoperative stay	2 (2)	2 (2)	2 (2–3)	0.065
Amount of drain	60 (50–100)	50 (50–95)	55 (50–100)	0.29
Time for removal of drain	1 (1–2)	1 (1)	1 (1–2)	0.022
WBC (10^3/ml)	11 (10–12)	11 (8–12)	11 (8–12)	0.303
Number of patients developed complications [*n* (%)]	35 (6.3)	18 (7)	10 (8.1)	0.758
Clavian–Dindo classification				
Grade I	5	3	2	0.9507
Grade II	10	6	4	
Grade III	20	9	4	
Grade IV	0	0	0	
Grade V	0	0	0	
Bile leakage [*n* (%)]	9 (1.6)	5 (1.9)	3 (2.4)	0.818
Source				
Cystic duct	4	4	2	
Gall bladder bed	3	1	1	
Accessory duct	2	0	0	
Bleeding [*n* (%)]				
Source	5 (0.9)	1 (0.4)	0	0.44
Cystic artery	2	1	0	0.865
Bed	1	0	0	
Port	2	0	0	
Postoperative jaundice	6 (1.1)	4 (1.6)	1 (0.8)	0.777
Postoperative pancreatitis	1 (0.2)	0	1 (0.8)	0.268
Abdominal collection	18 (3.2)	16 (6.2)	8 (6.5)	0.084
Wound infection	14 (2.5)	15 (5.8)	17 (13.7)	0.0001
Chest complications	6 (1.1)	4 (1.6)	1 (10.8)	0.777
DVT	2 (0.4)	3 (1.2)	3 (.4)	0.064
Pulmonary embolism	4 (0.7)	3 (1.2)	3 (.4)	0.244
Reoperation	5 (0.9)	1 (0.4)	0	0.44
Readmission	13 (2.3)	5 (1.9)	4 (3.2)	0.738
Cause of readmission				
Collection	8	2	3	
Obstructive jaundice	2	3	1	
Biliary pancreatitis	3	0	0	

DVT, deep venous thrombosis; WBC, white blood cells.

Table 4 Variables affecting the overall complication rate on univariate and multivariate analysis

	Univariate analysis			Multivariate analysis			
	No complications [*n* (%)]	Complications [*n* (%)]	*P* value	95 CI		OR	*P* value
Age (years)							
<60	48 (76.2)	681 (77.7)	0.776				
>60	15 (23.8)	195 (22.3)					
Sex							
Male	30 (47.6)	323 (36.9)	0.089				
Female	33 (52.40	553 (63.1)					
BMI <25	29 (46)	414 (47.3)	0.85				
BMI >25	34 (54)	462 (52.7)					
DM							
Yes	12 (19)	196 (22.4)	0.538				
No	51 (81)	680 (77.6)					
Severity of cholecystitis							
Acute cholecystitis (not obstructed)	9 (14.3)	161 (18.4)	0.425				
Mucocele	44 (69.8)	573 (65.4)					
Pyocele	10 (15.9)	117 (13.4)					
Gangrenous	0	25 (2.9)					
Grade of cholecystitis							
G 1	4 (6.3)	497 (56.7)					0.0001
G II	37 (58.7)	366 (41.8)	0.0001	63.137	907.735	239.398	0.0001
G III	22 (34.9)	13 (1.5)		10.839	76.819	28.855	0.0001
Adhesion							
No adhesion	4 (6.3)	104 (11.9)					
Filmy easy dissected	20 (31.7)	349 (39.8)	0.188				
Pericholecystectomy adhesion with clear anatomy	27 (42.9)	298 (34)					
Marked adhesion with unclear anatomy	12 (19)	125 (14.3)					
Liver cirrhosis	3 (4.8)	53 (6.1)	0.677				
Conversion	10 (15.9)	42 (4.8)	0.0001	0.254	1.884	0.692	0.471
Intraoperative cholangiogram	10 (15.9)	103 (11.8)	0.332				
Cystic duct diameter							
<5 mm	17 (27)	595 (67.9)	0.0001	3.071	16.944	7.213	0.0001
≥5 mm	46 (73)	281 (32.1)					
Method of closure of cystic duct							
Single clip	27 (42.9)	562 (64.2)					0.026
Overlapping clip	21 (33.3)	155 (17.7)	0.0001	0.005	0.400	0.044	0.006
Ligature	14 (22.2)	71 (8.1)		0.007	0.570	0.056	0.014
Stapler	1 (1.6)	88 (10)		0.004	0.345	0.038	0.004
Intraoperative complication	21 (33.3)	84 (9.6)	0.0001	1.152	5.277	2.465	0.02
Time of surgery							
<3 days	35 (55.6)	522 (59.6)					
3–7 days	18 (28.6)	240 (27.4)	0.758				
>7 days	10 (15.9)	114 (13)					

CI, confidence interval; DM, diabetes mellitus; OR, odds ratio.

Discussion

In recent years, the skills, instrument, and postoperative care of laparoscopic surgery have advanced. This improvement encourages the surgeon to change many protocols and guidelines for managing many diseases and diminishing LC contraindications in ACC. Although there is a careful discussion of the benefits of ELC for patients with ACC, the ideal timing of ELC is still debatable [19–23].

Very few trials, none of which were randomized, examined the effects of ELC in patients who presented after 7 days from the onset of ACC [9,13,23–25]. The study was planned to assess the different ELC timing in ACC (within the first 3 days, after 3–7 days, and after 7 days from the onset of symptoms) concerning safety and feasibility. With respect to the conversion rate and to boost postoperative results, the recommendations for ELC were restricted to the first 72 h from the onset of ACC until last years. However, within the primary 7 days of

Table 5 Variables affecting the conversion rate on univariate and multivariate analysis

	Univariate analysis			Multivariate analysis			
	Conversion group [*n* (%)]	Complete LC [*n* (%)]	*P* value	95% CI		OR	*P* value
Age (years)							
<60	31 (59.6)	698 (78.7)	0.001	1.580	7.729	3.494	0.002
>60	21 (40.4)	189 (21.3)					
Sex							
Male	25 (48.1)	328 (37)	0.108				
Female	27 (51.9)	559 (63)					
BMI <25	20 (38.5)	423 (47.7)	0.195				
BMI >25	32 (61.5)	464 (52.3)					
DM							
Yes	19 (36.5)	189 (21.3)	0.01	0.233	1.113	0.509	0.091
No	33 (63.5	698 (78.7)					
Severity of cholecystitis							
Acute cholecystitis (not obstructed)	4 (7.7)	166 (18.7)					0.016
Mucocele	29 (55.8)	588 (66.3)	0.0001	2.431	241.749	24.243	0.007
Pyocele	16 (30.8)	111 (12.5)		1.143	55.643	7.973	0.036
Gangrenous	3 (5.8)	22 (2.5)		0.485	26.343	3.573	0.212
Grade of cholecystitis							
G 1	15 (28.8)	486 (54.8)	0.001				0.218
G II	34 (65.4)	369 (41.6)		0.033	1.966	0.253	0.189
G III	3 (5.8)	32 (3.6)		0.025	1.357	0.185	0.097
Adhesion							
No adhesion	2 (3.8)	106 (12)					0.003
Filmy easy dissected	19 (36.5)	350 (39.5)	0.0001	1.938	74.690	12.032	0.008
Pericholecystectomy adhesion with clear anatomy	13 (25)	312 (35.2)		1.450	9.164	3.646	0.006
Marked adhesion with unclear anatomy	18 (34.6)	119 (13.4)		1.817	13.831	5.013	0.002
Liver cirrhosis	3 (5.8)	53 (6)	0.951				
Cystic duct diameter							
<5 mm	20 (38.5)	592 (66.7)	0.0001	2.062	10.013	4.543	0.0001
≥5 mm	32 (61.5)	295 (33.3)					
Intraoperative complication	30 (57.7)	75 (8.5)	0.0001	17.950	100.791	42.535	0.0001
Time of surgery							
<3 days	32 (44.2)	534 (60.2)	0.017				0.274
3–7 days	16 (30.8)	242 (27.3)		0.717	5.368	1.962	0.189
>7 days	13 (25)	111 (12.5)		0.382	3.110	1.091	0.871

CI, confidence interval; DM, diabetes mellitus; LC, laparoscopic cholecystectomy; OR, odds ratio.

presentation, several trials confirmed the safety, feasibility, and promising advantages for ELC [12,13,24–27].

Bouassida *et al.* [27] analyzed the outcomes of early versus late cholecystectomy for ACC; in the study, group 1, including 143 patients who underwent LC within 24 h, was compared with group 2, including 350 patients undergoing LC between 25 and 72 hours following the onset of symptoms. The study concluded that LC for ACC significantly decreased the rate of conversion to OC and the length of hospital stay without increasing postoperative morbidity during the first 24 h of onset of symptoms. Shinke *et al.* [26] reviewed the outcomes of early vs late cholecystectomy for ACC, where group 1, which included 193 patients undergoing LC within 3 days, was compared with group 2, which included 40 patients undergoing LC between 4 and 7 days following the onset of symptoms. The study showed that conducting LC after 3 days up to 7 days after the start of ACC is healthy and feasible, with no substantial difference between the two groups in terms of operating time, postoperative morbidity, or overall hospital stay.

Roulin *et al.* [10] surveyed 86 patients with ACC. The patients were randomly divided into two groups (42 in ELC and 44 within the DLC group after 6 weeks). The study found that ELC for ACC is reliable even after 72 h of presentation and is related to fewer complications, shorter total hospital stay, and duration of antibiotic therapy, in addition to lower cost in contrast to DLC.

Tan *et al.* [12,13] found that the conversion rate to open cholecystectomy was 21% for patients who presented after 7 days, with insignificant differences in median postoperative stay for this group and longer overall hospital stay. Tan *et al.* [13] studied 83 patients with ACC who had LC with more than 7 days of symptoms dividing the patients into the same LC group of admission and postponed LC after 4–24 weeks. They found that DLC decreased conversion levels to OC and provided shorter hospital stay and suggested DLC after 7 days of symptoms for patients with ACC. Brunée *et al.* [28] analysis included 276 patients who had ACC and underwent ELC. The patients were divided into three groups based on the timing of the surgery: within the first 3 days, between 4 and 7 days, and after 7 days from the onset of the presentation. They found that the rate of conversion, hospital stay, and complication incidence were increased beyond 7 days in patients with symptoms and do not support ELC intervention after 7 days of symptom onset owing to more complicated LC and a substantially increased risk of postoperative morbidity.

TG18 restructured their information and scheduled ELC for patients who may be eligible for LC given the exact duration of the presentation. The data are verified by our analysis. A recent retrospective review of 381 patients who had ACC was performed by Mora-Guzmán *et al.* [9]. Patients were subdivided into two groups with respect to the start of ACC's timing of LC: G1 in the primary 7 days, and GII in 7 days. The study reported negligible differences for conversion rate, operating time, BDI, major postoperative morbidity, postoperative reexploration, hospital stay, readmissions, and costs. The study concluded that ELC is safe to do for patients with ACC.

Hartmann's pouch stones found during LC and lead to mucocele or empyema gall bladder can prevent safe cystic pedicle dissection and increase the risk of BDI. Pushing the stone into the gall bladder, removal of stone, swab dissection, and intraoperative cholangiography are helpful steps to prevent BDI and minimize conversion rate [29].

The recent studies found that the conversion rates to OC varying in the wide range of 1.5–19% [11–14,29–32]. Conversion from LC to OC is considered important to prevent BDI resulting from uncertain anatomy. We suggest conversion before any complications develop. The conversion from LC to open procedure should not be viewed by surgeons as a failure or a complication. Coffin *et al.* [30] found that the conversion rate was 139/2810 (4.95%) cases to OC. Univariate analysis demonstrated that the male sex, age greater than or equal to 65 years, urgent and emergent admissions, and minimally invasive surgical training of the surgeon were predictors of conversion to OC. In multivariate analysis, it was revealed that urgent or emergent admission, male sex, and age greater than or equal to 65 were independent predictors of conversion to OC. Ashfaq *et al.* [31] reported the conversion rate to OC in a difficult cholecystectomy was 70/351 (19.9%) patients. The reasons for the conversion included marked adhesion (46.3%), unclear anatomy (20.9%), and bleeding (9.0%). In multivariate analysis, it was revealed that emergent intervention, previous abdominal surgery, and gangrenous cholecystitis were independent predictors of conversion to OC [32–34].

Brunée *et al.* [28] reported that the overall postoperative complication rate was significantly more in group greater than 7 days between the onset of symptoms and surgery. On univariate analysis, age greater than 60 years, male sex, ASA 3, increased WBC, increased CRP, and delay greater than 7 days between the onset of symptoms and surgery were factors statistically associated with increased morbidity rate.

Conclusion

ELC was performed safely at any time after the onset of ACC. ELC beyond seven days of the onset of ACC was associated with more blood loss, increased operative time, and increased conversion rate. Age greater than 60 years, empyema GB, severe adhesions, dilated cystic duct diameter greater than 5 mm, and development of intraoperative complications were the independent factors of conversion. Grade of cholecystitis, dilated cystic duct diameter greater than 5 mm, method of closure of cystic duct, and development of intraoperative complications were the independent factors of the development of postoperative complications. There was no effect of timing of surgery from the onset of ACC on intraoperative and postoperative complications.

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Conflicts of interest

There are no conflicts of interest.

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