

Evaluating Surgical Outcomes in Acute Cholecystectomies

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ABSTRACT

Background and Objectives: This study aimed to identify the predictors of surgical outcomes in acute cholecystitis (AC).

Methods: Patients undergoing cholecystectomy for AC between January 1, 2007 and December 31, 2019 at a single center were retrospectively reviewed. Conversion rate (CR), laparoscopic success rate (LSR), mortality, and bile duct injury (BDI) were evaluated in light of sex, age, ultrasound morphological diagnoses, severity of cholecystitis, performance status, time frame, and introduction of percutaneous transhepatic gallbladder drainage (PTGBD).

Results: A total of 465 patients underwent early cholecystectomy. CR and LSR were 16.89% and 78.28%, respectively; the mortality rate was 1.62%. Increased severity of cholecystitis (grade I vs II vs III) was associated with increased mortality (1.17 vs 2.27 vs 8.33%, P= .183) and CR (7.09 vs 32.93 vs 28.57%, P< .001) and decreased LSR (91.11 vs 61.11 vs 38.46%, P< .001). Surgery within 72 hours had lower mortality (1.41 vs 2.6%, P= .013) with significantly lower CR (14.45 vs 25.71%, P= .008) and higher LSR (81.69 vs 67.53%, P= .008) compared to surgery after 72 hours. Mortality (0 vs 0.92 vs 6.19%, P= .001) and CR (4.2 vs 16.27 vs 39.53%, P< .001) increased with an increase in Charlson comorbidity index (CCI), while LSR decreased (95.8 vs 79.91 vs 50.49%, P< .001).

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Conclusion: CCI and the severity of cholecystitis had the strongest influence on CR and LSR. Cholecystectomies performed within 72 hours were associated with reduced CR and increased LSR. PTGBD is a viable treatment option in elderly high-risk patients.

Key Words: Acute cholecystitis, Conversion rate, Early cholecystectomy, Gallbladder drainage, Laparoscopic cholecystectomy, Percutaneous transhepatic.

INTRODUCTION

Acute cholecystitis (AC) is a common emergency presentation worldwide. The treatment strategy for each patient should be a multidisciplinary decision based on several factors such as the patient's performance status, duration of symptoms, the severity of inflammation, and the availability of equipment and personnel. The Tokyo Guidelines, prepared in 2013 and modified in 2018, 1,2 provide guidance for treatment decision-making. Currently, the management protocol for AC in most centers is based on the flowchart published with these guidelines. Laparoscopic cholecystectomy (LC) is the gold-standard surgical treatment for AC. 3,4 The Tokyo Guidelines 2018 recommend early LC for grade I and II AC.² In the case of grade III inflammation associated with septic symptoms, the suitability for acute LC depends on the patient's performance status. In other cases, general supportive care plus antibiotics and/or percutaneous transhepatic gallbladder drainage (PTGBD) should be considered. These 2 alternative treatment options can serve both as bridging therapies and as definitive solutions. From a surgical perspective, one of the most important aspects of management is to determine the timing of surgery (cholecystectomy). Currently, there is no consensus or robust evidence on the optimal time elapsed since the onset of symptoms prior to which early LC is recommended. Moreover, the Tokyo Guidelines do not offer any specific recommendations in this regard. 1,2,5 A more precise definition of the time frame can help and, in

some cases, simplify the choice of therapeutic pathways and the timing of cholecystectomy. As regards acute surgery, the principal surgical outcomes are the conversion rate (CR), mortality, and, one of the most important morbidity factors, bile duct injury (BDI).

The objectives of the study were to evaluate the factors that potentially impact surgical outcomes during the surgical treatment of AC and to assess the role of introducing PTGBD at our department.

MATERIALS AND METHODS

The study was approved by the Regional Human Biomedical Research Ethics Committee.

All patients who underwent LC for AC between January 1, 2007 and December 31, 2019 were retrospectively reviewed. The data were collected from the patients' medical records and the MedSolution electronic system. Early cholecystectomy was defined as laparoscopic or open surgery for AC performed within 12 days after the onset of symptoms, since acute admission with a diagnosis of cholecystitis indicating urgent cholecystectomy was always within 12 days. After 12 days, conservative treatment and delayed elective cholecystectomy with or without PTGBD were performed. Patients subjected to PTGBD prior to early LC during the same hospital stay were excluded from the study. Following the exclusion, data pertaining to 465 patients who underwent early LC were evaluated. The indications for early LC in patients with radiologically confirmed AC were determined based on the recommendations in the Tokyo Guidelines 2007, 2013, and 2018.^{1,2,6}

The severity of inflammation was determined retrospectively based on the TG18/TG13 severity grading for AC specified in the Tokyo Guidelines 2018.⁷ The severity of the AC-related inflammation was thus classified as grade I (mild), grade II (moderate), or grade III (severe). Based on an abdominal ultrasound (US) scan, AC cases were classified according to several morphological diagnoses: acute acalculous cholecystitis (AAC), acute calculous cholecystitis (ACC), empyema vesicae felleae (EVF), hydrops vesicae felleae (HVF), and covered perforated cholecyst (PC).

The data were disaggregated based on sex, age (18–65 years and >65 years), and performance status for analysis. The American Society of Anesthesiologists (ASA) score (1–6) was determined for each patient.⁸ Based on the Charlson comorbidity index (CCI), the patients were categorized into 3 groups (0, 1–3, 4+).⁹ The rate of BDI and mortality within 1 month after hospitalization were also assessed.

The following endpoints were used to investigate the surgical outcomes of early LC: rates of primary open chole-cystectomy, LC, and conversion from laparoscopy. The CR for LCs (number of converted LCs × 100/[total number of operations — primary open cholecystectomies]) and the laparoscopic success rate (LSR) (number of LCs/total number of operations) were calculated accordingly. Subsequently, the effects of sex, age, performance status (ASA score and CCI), US morphological diagnoses (AAC, ACC, EVF, HVF, and PC), severity of inflammation (grades I, II, and III), and history of surgery (upper and lower abdominal surgery) on CR, LSR, and condition-related mortality were evaluated in each group.

As for the clinical outcome, the impact of time elapsed from the onset of symptoms to early LC (the time frame) on the different endpoints (mortality, CR, and LSR) was analyzed. Based on the daily routine used in our clinic, patients were categorized into 2 groups in terms of time frame: 0-72 hours (n=355) versus >72 hours (n=77).

Lastly, we investigated mortality, CR, and LSR in relation to the introduction of PTGBD. Ultrasound-guided PTGBD was introduced in our department in 2010. Patients subjected to early LC were thus assigned to 2 groups: surgery performed before (2007 to 2009, n=48) and after (2010 to 2019, n=417) the introduction of PTGBD (**Figure 1**).

Statistical Analysis

Descriptive statistics were presented as the mean ± standard deviation of the mean (SD), minimum and maximum for continuous variables and as the count + percentage for categorical variables. Normality was tested by visual interpretations.

Pearson's χ^2 test or Fisher's exact test was used for univariate analysis, as appropriate.

Potential factors influencing the need for conversion during early LC were analyzed using logistic regression (overall model fit was assessed by the Nagelkerke R^2 and goodness of fit was determined by performing the Hosmer–Lemeshow test).

Statistical analysis was performed using R 3.5.1. (R Foundation, Vienna, Austria) and IBM SPSS software (IBM SPSS Statistics for Windows, version 29.0, IBM Corp., Armonk, NY).

RESULTS

A total of 465 patients underwent acute, early cholecystectomy during the study reference period. The patient characteristics and surgical details are summarized in **Table 1**.



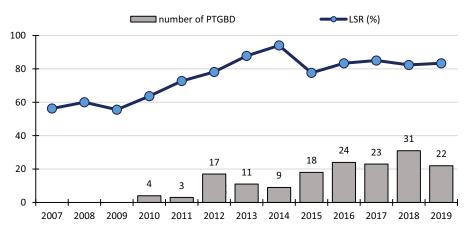


Figure 1. Number of percutaneous transhepatic gallbladder drainage (PTGBD) procedures per year and the annual LSR of the early/ urgent cholecystectomies for acute cholecystitis from 2007–2019. LSR, laparoscopic success rate (number of LCs/total number of operations).

The mean age of patients was 57.9 ± 17.2 years, and women accounted for 58.2% of the study population. In 82.1% of the cases, acute cholecystectomy was performed within 72 hours from the onset of symptoms, with the most common morphological diagnosis being ACC (73.5% of the cases). In most the cases, the severity of the inflammation was grade I or II, while only 2.88% of patients had grade III severity. BDI occurred in 2 cases out of the 465 acute cholecystectomies. Data pertaining to CR, LSR, and mortality are presented in **Tables 2** and **3**. In the overall study population, the CR was 16.89%, LSR was 78.28%, and the mortality rate was 1.62%.

The patients aged <65 years showed significantly higher LSR (87.25 vs 62.28%, P < .001) and lower CR (9.72 vs 30.67%, P < .001) than the older group.

More severe cholecystitis was associated with higher mortality rates (grade 1 vs II vs III: 1.17% vs 2.27% vs 8.33%, P = .183), a significantly higher CR (7.09% vs 32.93% vs 28.57%, P < .001), and a significantly lower LSR (91.11% vs 61.11% vs 38.46%, P < .001), respectively. If surgery was still inevitable for grade III severity, primary open cholecystectomy was performed in almost half (46.1%) of the cases.

The group with the highest CCI (at least 4 points) had a significantly higher mortality rate (6.19%, P = .001) and CR (39.53%, P < .001) than in the other groups, while LC was feasible in only half of these patients (50.4%, P < .001) (**Table 2**).

Regarding the ultrasound morphological diagnoses for early LC, mortality rates were the highest in the PC (4.08%) and AAC (3.85%) groups. The PC group also showed the worst CR and LSR (61.54%) and 29.41%, respectively).

A prior upper abdominal surgery was associated with higher CR and lower LSR (CR: 23.53% vs 17.04%; LSR: 59.09% vs 78.81%; P = .037) (**Table 2**).

Patients who underwent surgery within the 72-hour time frame had significantly lower CR (14.45% vs 25.71%, P = .008) and significantly higher LSR (81.69% vs 67.53%, P = .008) compared to those operated on beyond 72 hours (**Table 4**).

Following the introduction of PTGBD, the mortality rate showed a significant decrease (6.67% vs 1.21%, P = .04), and the decrease in CR (34% vs 15.11%) and the increase in LSR (56.25% vs 80.82%) were also significant compared to the previous period (P < .001) (**Table 5**).

On logistic regression, a history of upper abdominal surgery (odds ratio [OR]: 4.30; confidence interval [CI]: 1.47–12.60) and the severity of cholecystitis (OR: 3.77; CI: 2.23–6.37) showed the greatest influence on the chance of conversion during early LC (**Table 6**).

DISCUSSION

The 36 cases per year may seem low, but it should be noted that this is the number of early cholecystectomies for AC and it does not include successful conservative treatments for AC and PTGBDs. According to our previous publication, we have approximately 75 cases of ACC per year at our university.¹⁰

In the management of AC, the key surgical outcomes include the rate of operations that can be performed laparoscopically (CR and LSR), mortality, and the rate of BDI.

| Table | 1. |
|------------------------------|---------------------------|
| Overall Data on Patients and | l Early Cholecystectomies |

| Overan Data on Fatients at | N | % |
|-------------------------------|-------|-----------------------|
| m . 1 | 465 | 100 |
| Total | 465 | 100 |
| Age | 57.07 | ı ± 1 7 20 |
| Mean ± SD | | ± 17.29 |
| Min–Max | |)–100 |
| 18–65 | 298 | 64.09 |
| 65+ | 167 | 35.91 |
| Sex | 271 | 50.20 |
| Female | 271 | 58.28 |
| Male | 194 | 41.72 |
| ASA score | 4=/ | 27.50 |
| 1 | 174 | 37.50 |
| 2 | 176 | 37.93 |
| 3 | 94 | 20.26 |
| 4 | 20 | 4.31 |
| NA | 1 | |
| CCI | | |
| CCI 0 | 143 | 30.75 |
| CCI 1–3 | 219 | 47.10 |
| CCI 4+ | 103 | 22.15 |
| Time frame* | | |
| 0–72 hours | 355 | 82.18 |
| Over 72 hours | 77 | 17.82 |
| NA | 33 | |
| US morphological diagnoses | | |
| AAC | 27 | 5.81 |
| ACC | 342 | 73.55 |
| EVF | 10 | 2.15 |
| HVF | 35 | 7.53 |
| PC | 51 | 10.97 |
| AC severity grade (TG18/TG13) | | |
| I | 259 | 57.30 |
| II | 180 | 39.82 |
| III | 13 | 2.88 |
| NA | 13 | |
| Period | | |
| Pre-PTGBD period | 48 | 10.32 |
| PTGBD period | 417 | 89.68 |
| BDI | 2 | 0.43 |

*Between onset of complaints and hospital admission. AAC, acute acalculous cholecystitis; AC, acute cholecystitis; ACC, acute calculous cholecystitis; ASA, American Society of Anesthesiologists score; CCI, Charlson comorbidity index; CR, conversion rate (number of converted LCs × 100/[total number of operations – number of primary open cholecystectomies]); EVF, empyema vesicae felleae; HVF, hydrops vesicae felleae; LSR, laparoscopic success rate (number of LCs/total number of operations); NA, no data; PC, covered perforated cholecyst; PTGBD, percutaneous transhepatic gallbladder drainage; TG13/18, Tokyo Guidelines 2013 and 2018; US, abdominal ultrasound.

Conversion to open surgery is required in many cases undergoing early laparoscopic surgery. In some cases, the procedure is started as open surgery due to various factors such as poor performance status of the patient, greater severity of inflammation, and history of prior surgery which can cause technical difficulties during LC. Therefore, we used LSR in addition to CR because it better reflects the success of the minimally invasive technique.

In this study, the CR, and LSR were 16.89% and 78.28%, respectively, and the mortality rate was 1.72%. Based on our data, several predictors of CR, LSR, and mortality during acute cholecystectomy can be identified. The most important factors influencing CR were age, CCI, severity of inflammation, and a history of upper abdominal surgery. A history of upper abdominal surgery is a well-known risk factor during both acute and elective cholecystectomies. ^{11,12} Any adhesions may have an unfavorable effect on LSR leading to increased CR.

In patients aged >65 years, AC is one of the most common acute surgical interventions. Based on our results, a particularly high CR should be expected in patients aged >65 years (30.67% vs 9.72%, P < .001). Previous studies have also identified higher age as a risk factor for conversion during early LCs performed for AC. He In their meta-analysis, Loozen et al studied 592 elderly patients (>70 years) and found a CR of 23% with a mortality rate of 3.5%. In patients aged >65 years, do Amaral et al found a higher CR but without a significant difference (CR: 10.3% vs 6.6%; P = .49). Di Martino et al (2022) also reported a higher CR in patients aged >85 years (10.3% vs 20%; P = .005).

The performance status of the patient is an important determinant of the choice of treatment for AC, and this is reflected in the Tokyo Guidelines 2018 flowchart.² ASA score and CCI are the 2 most commonly used scoring systems to determine performance status. ASA assesses the risk of general anesthesia, while CCI is a predictor of 10year survival. In our study, both an increase in the ASA score and an increase in CCI were associated with greater risk and poorer surgery-related outcomes. Patients with higher ASA scores had significantly lower LSR. The CR increased with an increase in ASA from 1-3, but patients with ASA 4 performance status had slightly lower CR. This was attributable to the fact that a higher percentage of patients with ASA 4 status underwent primary open surgery because of their lower cardiac capacity and the higher risk (unfavorable cardiopulmonary effect of abdominal insufflation). The rate of operations with excessive risk may be reduced with proper



| | Table 2. Characteristics of Cholecystectomies (CCY) Performed Indicated by Acute Cholecystitis (AC) | | | | | | | |
|--------------|---------------------------------------------------------------------------------------------------------------|---------------|------------------|----------|--------|-----------------------|-------|--|
| | Converted LC | LC LC | Primary Open CCY | Total | CR (%) | LSR (%) | P* | |
| Total | 74 | 364 | 27 | 465 | 16.89 | 78.28 | | |
| Age (years) | , - | 301 | _, | 209 | 1000) | , o. _ | | |
| 18–65 | 28 | 260 | 10 | 298 | 9.72 | 87.25 | | |
| 65+ | 46 | 104 | 17 | 167 | 30.67 | 62.28 | >.001 | |
| Sex | • | 101 | -7 | 107 | 30107 | 02.20 | | |
| Female | 37 | 217 | 17 | 271 | 14.57 | 80.07 | | |
| Male | 37 | 147 | 10 | 194 | 20.11 | 75 . 77 | .305 | |
| ASA score | 37 | 11/ | | 1/1 | 20.11 | 7 3•77 | | |
| 1 | 13 | 156 | 5 | 174 | 7.69 | 89.66 | | |
| 2 | 30 | 136 | 10 | 176 | 18.07 | 77.27 | | |
| 3 | 27 | 60 | 7 | 94 | 31.03 | 63.83 | >.001 | |
| 4 | 4 | 11 | 5 | 20 | 26.67 | 55.00 | | |
| NA | • | 1 | | 1 | 20.07 | <i>J</i> J. 00 | | |
| CCI | | 1 | | <u>.</u> | | | | |
| CCI 0 | 6 | 137 | | 143 | 4.20 | 95.80 | | |
| CCI 1–3 | 34 | 175 | 10 | 219 | 16.27 | 79.91 | >.001 | |
| CCI 4 + | 34 | 52 | 17 | 103 | 39.53 | 50.49 | ×.001 | |
| US morpholog | | <i>></i> - | -7 | 100 | 37.33 | 3002) | | |
| AAC | 4 | 21 | 2 | 27 | 16.00 | 77.78 | | |
| ACC | 39 | 290 | 13 | 342 | 11.85 | 84.80 | | |
| EVF | 3 | 7 | 13 | 10 | 30.00 | 70.00 | | |
| HVF | 4 | 31 | | 35 | 11.43 | 88.57 | | |
| PC | 24 | 15 | 12 | 51 | 61.54 | 29.41 | | |
| | ade (TG18/TG13) | | | 7- | 02.72 | | | |
| Ι | 18 | 236 | 5 | 259 | 7.09 | 91.12 | | |
| II | 54 | 110 | 16 | 180 | 32.93 | 61.11 | >.001 | |
| III | 2 | 5 | 6 | 13 | 28.57 | 38.46 | >.001 | |
| NA | | 13 | | 13 | | 00000 | | |
| Upper abdomi | inal surgery | -3 | | -5 | | | | |
| No | 68 | 331 | 21 | 420 | 17.04 | 78.81 | | |
| Yes | 4 | 13 | 5 | 22 | 23.53 | 59.09 | .037 | |
| NA | 2 | 20 | 1 | 23 | -0.70 | 27-47 | | |
| Lower abdomi | | | - | | | | | |
| No | 51 | 255 | 19 | 325 | 16.67 | 78.46 | | |
| Yes | 21 | 89 | 7 | 117 | 19.09 | 76.07 | .605 | |
| NA | 2 | 20 | 1 | 23 | -21-2 | | | |

^{*}Fisher's exact test and χ^2 test. AAC, acute acalculous cholecystitis; ACC, acute calculous cholecystitis; ASA, American Society of Anesthesiologists score; CCI, Charlson comorbidity index; CR, conversion rate (number of converted LCs × 100/[total number of operations – number of primary open cholecystectomies]); EVF, empyema vesicae felleae; HVF, hydrops vesicae felleae; LSR, laparoscopic success rate (number of LCs/total number of operations); NA, no data; PC, covered perforated cholecyst; TG13/18, Tokyo Guidelines 2013 and 2018; US, abdominal ultrasound.

Table 3.Overall Mortality by Patient and Intervention Characteristics

| | | Ove | Overall Mortality | | |
|----------------|--------------|-------|-------------------|-------|--|
| | N | N | % | P^* | |
| Total | 465 | 8 | 1.72 | - | |
| Age (years) | | | | | |
| 18–65 | 298 | 4 | 1.36 | .466 | |
| 65+ | 167 | 4 | 2.45 | | |
| Sex | | | | | |
| Female | 271 | 5 | 1.88 | .554 | |
| Male | 194 | 3 | 1.57 | | |
| ASA score | | | | | |
| 1 | 174 | | 0 | .002 | |
| 2 | 176 | 2 | 1.15 | | |
| 3 | 94 | 4 | 4.44 | | |
| 4 | 20 | 2 | 11.11 | | |
| NA | 1 | | | | |
| CCI | | | | | |
| CCI 0 | 143 | | 0 | .001 | |
| CCI 1–3 | 219 | 2 | 0.92 | | |
| CCI 4+ | 103 | 6 | 6.19 | | |
| US morpholo | gical diagno | oses | | | |
| AAC | 27 | 1 | 3.85 | - | |
| ACC | 342 | 4 | 1.18 | | |
| EVF | 10 | | 0 | | |
| HVF | 35 | 1 | 2.94 | | |
| PC | 51 | 2 | 4.08 | | |
| AC severity gr | rade (TG18/ | TG13) | | | |
| I | 259 | 3 | 1.17 | .183 | |
| II | 180 | 4 | 2.27 | | |
| III | 13 | 1 | 8.33 | | |
| NA | 13 | | | | |

*Fisher's exact test and Pearson's χ^2 test. AAC, acute acalculous cholecystitis; ACC, acute calculous cholecystitis; ASA score, American Society of Anesthesiologists score; CCI, Charlson comorbidity index; EVF, empyema vesicae felleae; HVF, hydrops vesicae felleae; NA, no data; PC, covered perforated cholecyst; TG13/18, Tokyo Guidelines 2013 and 2018; US, abdominal ultrasound.

patient selection and conservative treatment in "difficult" cases.

The most recent Tokyo Guidelines 2018 recommend that the treatment strategy should be guided by the severity of inflammation.² Consistent with the guidelines, the severity

of cholecystitis was one of the most important determinants of CR (OR: 3.77; CI: 2.23-6.37). The significant differences found in LSR also demonstrate the direct effect of the severity of inflammation on the outcomes. The 91.12% LSR observed in grade I cases dropped to 38.46% in grade III cases. CR was higher in grade II cases than in grade III cases, which is likely attributable to the higher rate of primary open surgery in grade III cases. The expected difficulty of the surgery also increases with the severity of inflammation. Severe inflammation hampers the identification of anatomic structures, resulting in an increased risk of conversion and BDI. Because of the relatively low number of cases, no meaningful conclusions can be drawn from the BDI-related results (n = 2, 0.43%), but the circumstances of the cases may provide useful information. A patient (41 years old male, CCI 0, grade II) with BDI (Strasberg D, Hannover D4)^{18,19} detected during laparoscopic surgery underwent immediate laparoscopic direct suture without ERCP. In the other case (76 years old female, CCI 7, Grade III), a BDI (Strasberg E3, Hannover D3) was confirmed on postoperative day 6 after LC, which led to ERCP followed by reconstruction with Roux-Y hepatico-jejunostomy. Two previous studies have also reported similar incidence rates of BDI (0.26-0.53%).^{20,21} A study of 781 patients by Törnqvist (2016) also found that acute cholecystectomy in itself is a risk factor for BDI (OR: 1.97); in grade I cases, there was no increase in the risk of BDIs (OR: 0.96), but grades II and III cases showed a considerably higher risk of BDI (OR: 2.41 and 8.43, respectively).²²

Although trend-level changes can be seen and conclusions can be drawn from mortality data, statistical claims cannot be established because of the low number of deaths. A larger study is required to obtain more robust data in this regard.

ACC was the most common morphological diagnosis determined by US. Mortality rates were the highest in the PC (4.08%) and AAC (3.85%) groups. Perforation poses an increased risk and is a more difficult surgical situation, as demonstrated by the high CR (61.54%) and low LSR (29.41%). In a prospective study by Eldar (1997), besides hydrops, and empyema, gangrenous cholecystitis was the most common cause of conversion.²³ A study of 373 patients by Terho (2016) yielded a similar result. They reported a CR of 22.5% and identified the following risk factors: elevated CRP levels, diabetes, age >65 years, and gangrenous gallbladder.²⁴ The high mortality rate associated with AAC is likely attributable to the fact that acalculous cholecystitis is a part of the septic condition in many cases, not the cause of it, but with a different background



Table 4.
Characteristics and Overall Mortality of Early/Urgent Cholecystectomies (CCY) for Acute Cholecystitis Based on Time between Onset of Complaints and Hospital Admission

| A | LC | Converted LC | Primary Open CCY | Total | P^* | LSR (%) | CR (%) |
|--------------------|-------------------|-------------------|-------------------|-------------------|-------|---------|--------|
| Time frame (hours) |) | | | | , | , | |
| Mean ± SD | 37.94 ± 39.65 | 47.33 ± 45.57 | 63.35 ± 63.83 | 40.75 ± 42.54 | | | |
| Min–Max | 2-288 | 5-168 | 7–264 | 2-288 | | | |
| Total | 364 | 74 | 27 | 465 | - | 78.28 | 16.89 |
| Time frame# | | | | | | | |
| 0–72 hours | 290 | 49 | 16 | 355 | .008 | 81.69 | 14.45 |
| Over 72 hours | 52 | 18 | 7 | 77 | | 67.53 | 25.71 |
| NA | 22 | 7 | 4 | 33 | | | |
| | | | Ov | rerall mortality | | | |

| В | | Overa | | |
|---------------|-----|-------|------|-------|
| | N | N | % | P^* |
| Total | 465 | 8 | 1.72 | - |
| Time frame# | | | | |
| 0–72 hours | 355 | 5 | 1.41 | .613 |
| Over 72 hours | 77 | 2 | 2.60 | |
| NA | 33 | 1 | | |

[#]Time between onset of complaints and hospital admission; *Fisher's exact test and χ^2 test. LSR, laparoscopic success rate (number of LCs/total number of operations); CR, conversion rate (number of converted LCs $\times 100$ /[total number of operations – number of primary open cholecystectomies], NA, no data.

cause.^{25,26} Aledo et al (2017) may have been referring to this when they suggested percutaneous drainage instead of cholecystectomy for AAC, but also recommended cholecystectomy in the case of low surgical risk.²⁷ This is contradicted by our previous results that an exceptionally high in-hospital mortality of 55.56% can be expected following PTGBD performed for AAC²⁴ and that primary early cholecystectomy should perhaps be considered in such cases.

The optimal timing for early LC is one of the most contested issues in the management of AC. In our department, we endeavor to perform LC as early as possible within 72 hours, and preferably within 48 hours. During our study, surgical outcomes were better for operations performed within 72 hours than for those carried out beyond 72 hours. The <72-hour group showed a lower mortality rate (1.41% vs 2.6%) and CR (14.45% vs 25.71%) and higher LSR (81.69% vs 67.53%; P = .008).

Numerous studies have sought to determine the ideal time frame. In the study by Hadad et al (2007), the CR increased proportionately with the time elapsed from the onset of symptoms to surgery, with a CR of 9.5% for operations performed within 2 days and a CR of >38% for operations performed beyond 5 days.²⁸ Alore et al (2019) recommended 2 days for the timing of surgery, although their recommendation was for the period after the date of hospitalization.²⁹ Also based on the time of hospitalization, a prospective, randomized, multicenter study, the "ACDC study," published in 2013, recommended surgery within 24 hours according to several criteria (morbidity, hospital stay, hospital cost).³⁰ Mora-Guzmán et al (2020) studied CR, surgery time, BDIs, other complications, reoperations, hospital stay, rehospitalizations, and care costs in 381 patients.31 Interestingly, they found no significant difference between those subjected to surgery within 7 days and those beyond 7 days. In their 2019 and 2020 publications, Wiggins et al and Altieri et al obtained more favorable results regarding CR, BDI, and hospital day in those operated on within 72 hours. 32,33 In 2021 Ohya evaluated 327 cases of acute cholecystectomy and concluded that surgery performed beyond 72 hours are expected to be more difficult and associated with

Table 5.Characteristics and Overall Mortality of Early/Urgent Cholecystectomies (CCY) for Acute Cholecystitis Based on the Pre-Percutaneous Transhepatic Gallbladder Drainage (PTGBD) Period and the PTGBD Period

| A | LC | Converted LC | Primary Open CCY | Total | P^* | LSR (%) | CR (%) |
|------------------|-----|--------------|------------------|-------|-------|---------|--------|
| Total | 364 | 74 | 27 | 465 | - | 78.28 | 16.89 |
| Period | | | | | | | |
| Pre-PTGBD period | 27 | 14 | 7 | 48 | >.001 | 56.25 | 34.15 |
| PTGBD period | 337 | 60 | 20 | 417 | | 80.82 | 15.11 |

| | | Overa | Overall mortality | | |
|------------------|-----|-------|-------------------|-------|--|
| В | N | N | % | P^* | |
| Total | 465 | 8 | 1.72 | - | |
| Period | | | | | |
| Pre-PTGBD period | 48 | 3 | 6.67 | .04 | |
| PTGBD period | 417 | 5 | 1.21 | | |

^{*}Fisher's exact test and χ^2 test. LSR, laparoscopic success rate (number of LCs/total number of operations); CR, conversion rate (number of converted LCs × 100/[total number of operations – number of primary open cholecystectomies].

Table 6.
Impact of Patient/Physician-Related Characteristics on Conversion Analysed with Logistic Regression

| | | | 95% CI for OR | | |
|-------------------------|------|------|---------------|-------|--|
| | P | OR | Lower | Upper | |
| CCI | .000 | 1.56 | 1.28 | 1.89 | |
| ASA score | .328 | 0.81 | 0.53 | 1.23 | |
| AC severity grade | .000 | 3.77 | 2.23 | 6.37 | |
| Upper abdominal surgery | .008 | 4.30 | 1.47 | 12.60 | |
| PTGBD period | .117 | 0.53 | 0.24 | 1.17 | |
| Time frame (hours) | .251 | 1.00 | 1.00 | 1.01 | |
| Constant | .000 | 0.02 | | | |

Overall model fit, Nagelkerke $R^2 = 0.315$; goodness-of-fit, Hosmer–Lemeshow test P = .053; classification table, correct predictions = 82.06%. CI, confidence interval; OR, odds ratio.

greater blood loss and higher CR, as well as longer surgery time and hospital stay.¹¹ In a prospective multicentric observational study published in 2023, Fugazzola et al examined data from 1,117 patients who underwent early cholecystectomy for ACC and found fewer intraoperative complications and subtotal cholecystectomies for operations performed within 72 hours of the onset of symptoms, but no significant difference in conversion

and mortality.³⁴ In a retrospective study of 569 patients who underwent urgent cholecystectomy (within 72 hours of hospital admission), Kirkendoll et al (2022) concluded that surgery performed within 24 hours was associated with shorter hospital stays, less cost, fewer BDI and lower CR.³⁵ In addition to surgical outcomes, hospital costs have been an important consideration in many studies. This was investigated by Sutton et al in their prospective study, which also found more favourable outcomes in terms of cost for early, urgent cholecystectomies.³⁶ Based on the above, the time frame remains uncertain, but based on our results and the literature, acute CCY is recommended as soon as possible, but within 72 hours from the onset of complaints.

Ultrasound-guided transhepatic biliary drainage has been used since the 1980s.^{37–39} Patients beyond the time frame or those with high risk can be treated temporarily or even definitively with drainage. At first sight, the introduction of PTGBD in our department improved the surgical outcomes of early cholecystectomies with regard to LSR (**Figure 1**), CR, and mortality²⁶; however, these results should be treated with a certain skepticism, as detailed below. After the introduction of drainage in 2010, fewer high-risk acute cholecystectomies were required, leading to an improvement over the results from before the introduction of drainage (pre-PTGBD and PTGBD periods: CR, 34.15% vs 15.11%; LSR, 56.25% vs 80.82%), with most high-risk cases subjected to drainage. As shown in our previous



publication, an in-hospital mortality rate of 11.72% should be expected following PTGBD. Considering all the patients who underwent early LC and/or PTGBD for AC, the reduction in mortality only decreased from 6.67% (early cholecystectomy only) to 4.6% (cholecystectomy ± PTGBD) after the introduction of PTGBD. In addition, the rate of successful laparoscopic procedures cannot be improved considerably. An extraordinarily difficult procedure must thus be expected even after PTGBD. For delayed (52/61) and emergency (9/61) surgery following PTGBD, the CR, and LSR were 17.57% and 71.76%, respectively.²⁶

It should be noted that surgery was not needed afterward in many cases and that, therefore, drainage may be a definitive solution in managing elderly patients in poor condition and with high risk. ^{26,40,41}

CONCLUSION

In most centers, the management of AC is based on the 2018 Tokyo Guidelines, but it is important to adopt a multidisciplinary approach to individualize the treatment strategy. The measures of the efficacy of surgical treatment may include mortality, BDI, CR, and LSR. In this study, the patient's performance status (ASA score and CCI), history of upper abdominal surgery, and the severity (grade) of cholecystitis had the greatest impact on CR and LSR. Increased severity of inflammation is liable to lead to more complications and a higher CR. The question of the time frame is still debatable. However, to achieve the best CR and LSR and a low BDI rate, cholecystectomy as early as possible, but certainly within 72 hours of the onset of symptoms, is recommended, in line with previous studies. In elderly patients with numerous comorbidities, PTGBD may be a bridging or even a definitive solution. But it is also important to underline that older, comorbid patients are definitely associated with higher mortality, which cannot be significantly improved by the use of PTGBD as bridging therapy.

Although there have been many studies on AC, the investigation and refinement of risk factors for CR and mortality, the role of PTGBD, and the time frame still warrant further investigation with larger number of cases using prospective multicentre studies or meta-analysises.

Limitations

Some notable limitations of this study should be acknowledged. The retrospective study design may have introduced an element of bias. Moreover, data pertaining to

body mass index and detailed ultrasound findings (eg, gallbladder wall thickness) could not be obtained during data collection. Lack of precise distinction between mortality during and after hospital stay was also a limitation. Because of the low mortality and low incidence of BDI, the relevant risk factors could not be identified. Larger multicenter studies can provide more definitive evidence in this regard.

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