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Increase in Acute Cholecystitis and Laparoscopic Resection after COVID-19 Pandemic: A Japanese Single Center Experience

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Coronavirus disease 2019 (COVID-19) emerged as viral pandemic in the year 2019 and surgical intervention was forced to be restricted during the pandemic. This study aims to compare the perioperative outcomes of surgeries for acute cholecystitis in the period following the COVID-19 pandemic. A retrospective analysis was conducted on the demographic and perioperative data of 246 cholecystectomy cases performed between June 2017 and November 2022. This analysis focused on comparing patient background and perioperative outcomes before and after the COVID-19 pandemic. As a result, prior to the pandemic, 72 emergency surgeries for acute cholecystitis were performed, compared with 174 cases following the COVID-19 pandemic onset. This increase, particularly in mild and moderate acute cholecystitis cases, led to a significant rise in the proportion of laparoscopic resections and a concurrent decrease in postoperative hospital stays. Our findings suggest a potential increase in acute cholecystitis cases at our hospital coinciding with the COVID-19 pandemic. Early laparoscopic cholecystectomy, when feasible within the medical system's capacity, can be an effective treatment strategy during the pandemic.

Keywords: acute cholecystitis; cholecystectomy; COVID-19 pandemic; emergency surgery; laparoscopic resection
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Introduction

Acute cholecystitis, characterized by acute inflammation of the gallbladder, is primarily caused by obstruction of the cystic duct by gallstones (Gallaher and Charles 2022). The diagnosis and management of acute cholecystitis follow international guidelines (Yokoe et al. 2018). For patients without major complications, early laparoscopic cholecystectomy is the recommended intervention (Okamoto et al. 2018; Pisano et al. 2020). Alternatively, conservative management with antibiotics is used for cases of mild cholecystitis, and percutaneous gallbladder drainage is considered for patients for whom surgery is not a viable option (Yokoe et al. 2018).

Coronavirus disease 2019 (COVID-19), caused by infection with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged in 2019 (Rothan and Byrareddy 2020). Japan confirmed the first case of COVID-19 in January 2020, which subsequently led to widespread transmission (Amengual and Atsumi 2021). The global spread of COVID-19 led the World Health Organization (WHO) to declare the outbreak a public health emergency of international concern and subsequently a pandemic on March 11, 2020 (Cucinotta and Vanelli 2020). During the pandemic, surgical departments were forced to limit their activity to urgent procedures. Although some guidelines and evidence exist, the surgical management of patients during the COVID-19 pandemic was often left to the discretion of individual facilities, especially in contexts of limited medical resources (Moletta et al. 2020; Zheng et al. 2020). Decision-making regarding emergency surgery versus conservative treatment varies based on each facility's circumstances (CHOLECOVID Collaborative 2022). Reports suggest a decline in the need for surgical intervention for cholecystitis as a result of available alternative treatments (Koch et al. 2022).

This study aimed to investigate the impact of the pandemic on the management of acute cholecystitis at our hos-

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pital. Specifically, we analyzed changes in the frequency and nature of cholecystectomy procedures, focusing on emergency surgeries, operative techniques, and outcomes, and compared these to the corresponding metrics from the equivalent pre-pandemic period.

Materials and Methods

Patients and study design

This retrospective study included consecutive patients undergoing cholecystectomy at the Department of Surgery, Osaki Citizen Hospital between June 2017 and November 2022. In this period, 835 patients underwent cholecystectomy, primarily for cholelithiasis or cholecystitis (760 patients). Of these, 252 patients underwent emergent cholecystectomy, and 246 cases met the diagnostic criteria for acute cholecystitis according to the Tokyo Guidelines 2018 (Yokoe et al. 2018). The declaration of the COVID-19 pandemic by WHO in March 2020 led to the classification of patients into two groups: those who underwent cholecystectomy between June 2017 and February 2020 (pre-pandemic group) and those from March 2020 and November 2022 (pandemic group). We compared the differences in emergent cholecystectomies for acute cholecystitis before and after the onset of the COVID-19 pandemic.

The present study was performed in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of Osaki Citizen Hospital (20231214-38). Owing to its retrospective nature, the requirement for informed consent was waived.

Definitions

Operation time was defined as the duration from skin incision to abdominal wound closure. Complications were defined as any incidents that occurred in the hospital or within 90 days postoperatively, with major complications classified as grade IIIA or higher, as per the Clavian-Dindo classification (Clavien et al. 2009). Surgical site infection (SSI) identification followed the criteria set by the Center for Disease Control's National Nosocomial Infection Surveillance system (Mangram et al. 1999).

Patient management and operative procedure

Acute cholecystitis was diagnosed based on abdominal examination, blood count, biochemical tests, ultrasonography (US), and computed tomography (CT) imaging. In cases of acute cholecystitis with concurrent common bile duct stones, initial management involved endoscopic treatment. Emergency surgery was performed for patients suspected of having gangrenous cholecystitis based on US or CT findings, as well as for those with grade III cholecystitis deemed suitable for surgery. For patients with grade I or II cholecystitis who showed no improvement in symptoms or inflammatory response following conservative treatment, surgery was performed. The choice of surgical approach, either laparotomy or endoscopic surgery, was determined by the attending physician, considering factors such as abscess formation, perforation, and previous upper abdominal surgeries. Drains were placed in cases exhibiting severe intra-abdominal contamination, including bile leakage or abscess formation.

Statistical analysis

Statistical analyses were conducted using Fisher's exact test and the χ^2 test for categorical data. For continuous data, the Mann–Whitney *U* test was employed. Categorical variables are expressed as numbers and percentages, whereas continuous variables are expressed in terms of mean and interquartile range. A value of $P < 0.05$ was considered statistically significant. All statistical analyses were performed using JMP® Pro 17 software (SAS Institute, Cary, NC, USA).

Results

Patient overview and Tokyo severity assessment

Fig. 1 presents the patient data for those who underwent cholecystectomy between June 2017 and November 2022. In total, 835 cholecystectomies were performed, with 760 attributed to cholelithiasis or cholecystitis. When comparing the periods before and after the COVID-19 pandemic, 358 and 402 cholecystectomies were performed, respectively. Among these, 72 patients in the pre-pandemic period and 174 patients in the pandemic period underwent emergent surgery for acute cholecystitis. Notably, there was a significant increase in emergency surgeries for acute cholecystitis during the pandemic ($P < 0.001$). No surgeries were performed on patients with active COVID-19 infection. In terms of acute cholecystitis severity based on the Tokyo 2018 guidelines (Yokoe et al. 2018), 19% of patients were categorized as grade I, 58% as grade II, and 22% as grade III in the pre-pandemic period. In contrast, during the pandemic, these proportions were 23%, 67%, and 10%, respectively. A significant difference was observed in the incidence of grade III severity between the two periods ($P = 0.014$) (Table 1).

Patient characteristics

Table 2 presents a comparison of patient backgrounds. There was no difference in age, sex, body mass index (BMI), American Society of Anesthesiologists physical status (ASA-PS), Charlson comorbidity index (CCI), medical history, or physical examination findings upon admission. During the pandemic, the time from symptom onset to surgery did not differ significantly (63 hours vs. 53 hours, $P = 0.264$). All patients underwent a CT examination upon admission, and the incidence of abscess formation was lower in the pandemic group ($P = 0.034$). Blood biochemical tests indicative of cholecystitis severity, such as white blood cell count, platelet count, creatinine, total bilirubin, and albumin, showed no significant differences between the groups. However, a significant difference was observed in prothrombin time ($P = 0.010$).

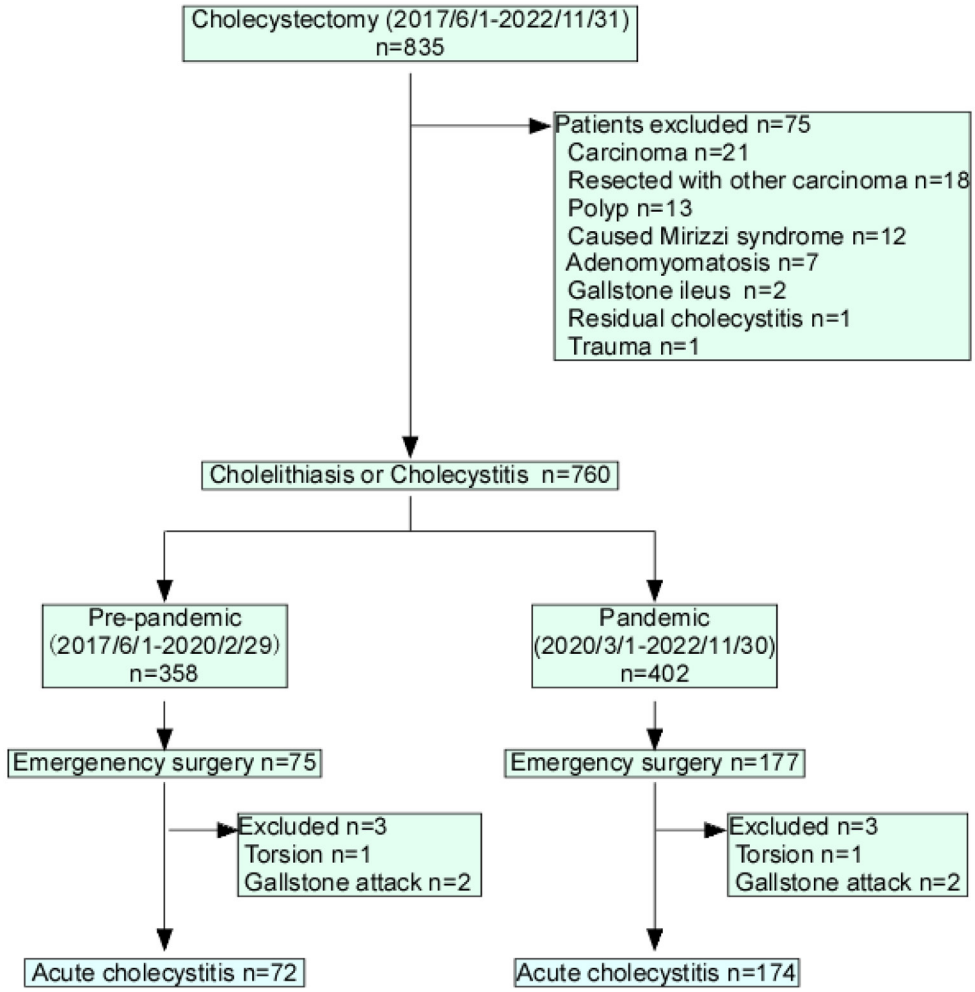

Fig. 1. Overview of the number of diagnoses and cholecystectomies.
This figure presents a flowchart illustrating the subjects selected for the analysis of acute cholecystitis, including the exclusion of certain cases.

Surgical procedure and outcomes

The intraoperative and postoperative outcomes are summarized in Table 3. Following the pandemic, there was a significant increase in the ratio of laparoscopic cholecystectomy ($P < 0.001$), while the frequency of drain placement declined ($P = 0.004$). No significant differences were observed in operative time, bleeding volume, or the surgical technique, including the bailout procedures. Postoperative complications occurred in 15 (21%) pre-pandemic and 22 (13%) post-pandemic cases ($P = 0.102$), predominantly bile leakage (3 [4.2%] vs. 5 [3.5%], $P = 0.603$) and surgical site infections (7 [9.7%] vs. 8 [4.6%], $P = 0.126$). Complications classified as Clavien–Dindo Grade IIIA or higher were observed in 6 (8.3%) pre-pandemic and 6 (3.5%) post-pandemic cases ($P = 0.106$). In the pre-pandemic period, 3 cases of intra-abdominal abscess required additional drainage, and 3 cases of bile leakage necessitated re-operation. Post-pandemic, there were 4 cases requiring drainage for intra-abdominal abscess, 1 case of pseudoaneurysm following percutaneous transhepatic gallbladder aspiration that required endovascular treatment, and 1 death due to sepsis. The postoperative hospital stay was significantly shorter in the pandemic group compared with the pre-pandemic group (8.0 days vs. 10.6 days, respectively; $P = 0.042$). No significant difference was observed in the rate of gangrenous cholecystitis in the postoperative pathological diagnosis (Table 4).

Discussion

Following WHO's declaration of the COVID-19 pandemic on March 11, 2020, numerous modifications were required in the management of emergent cases necessitating potential surgical interventions (De Simone et al. 2020). A scoping review by Karlafti et al. (2022) observed an overall decline in the number of cases performed for emergency surgery. Surek et al. reported a reduction in emergency surgeries for appendicitis and acute cholecystitis, whereas instances related to trauma, gastrointestinal bleeding, perforation, and mesenteric ischemia remained unaffected by the pandemic (Surek et al. 2021). Emergency surgeries contin-

Table 1. Number of surgeries and Tokyo severity.

		Pre-pandemic	Pandemic	P value
Cholecystectomy		358	402	NA
Elective surgery		283	225	
after cholecystitis		152	103	0.084
cholelithiasis		131	122	0.035
Emergency surgery		75	177	< 0.001
Acute cholecystitis		72	174	< 0.001
Tokyo severity	Grade I	14 (19.4%)	40 (22.9%)	0.541
	Grade II	42 (58.3%)	116 (66.7%)	0.215
	Grade III	16 (22.2%)	18 (10.3%)	0.014

Table 2. Baseline characteristics of patients with acute cholecystitis.

	Pre-pandemic	Pandemic	P value
Total number of patients	72	174	
Age (years) *	69.0 (32-95)	70.5 (31-100)	0.596
Sex (male/female)	47/25	95/79	0.122
BMI (Kg/m^2) **	23.8 ± 3.60	24.4 ± 4.12	0.508
ASA (1/2/3/4)	4/39/28/1	9/111/52/1	0.565
CCI (0-5/ ≧ 6)	55/17	136/38	0.762
Comorbidity			
Hypertension	43 (59.7%)	104 (59.8%)	0.994
Hyperlipidemia	28 (38.9%)	49 (28.2%)	0.099
Diabetes mellitus	19 (26.4%)	57 (32.3%)	0.325
Cardiovascular disease	15 (20.8%)	38 (21.8%)	0.861
Cerebrovascular disease	9 (12.5%)	18 (10.3%)	0.623
Condition at time of hospitalization			
Fever **	37.5 (± 0.45)	37.0 (± 0.29)	0.279
Murphy's sign	47 (65.3%)	109 (62.6%)	0.696
Conscious disorder	3 (4.2%)	4 (2.3%)	0.423
Abscess formation	10 (13.9%)	10 (5.6%)	0.034
Hours onset to surgery *	62.6 (13-336)	53.4 (5-288)	0.264
Preoperative laboratory data *			
White cell count 10^3/l	15.2 (5.8-34.5)	14.2 (4.1-30.0)	0.301
Platelet cell count 10^4/l	22.3 (4.3-39.4)	22.3 (4.9-96.2)	0.397
C-reactive peptide mg/dl	17.4 (0.06-50.1)	16.1 (0.06-40.9)	0.573
Prothrombin time%	75.0 (31-118)	84.0 (10-136)	0.010
Total bilirubin mg/dl	1.82 (0.4-7.5)	1.51 (0.2-7.4)	0.092
AST U/l	66.1 (14-435)	2.2 (11-528)	0.246
ALT U/l	51.8 (10-281)	59.7 (7-673)	0.704
Alkaline Phosphatase U/l	343 (25-1768)	208 (4-1175)	< 0.001
γ-GTP U/l	103 (8-474)	97 (8-846)	0.885
Creatinine mg/dl	0.96 (0.44-2.70)	0.98 (0.16-9.43)	0.092
Albumin g/dl	3.4 (1.7-5.2)	3.4 (1.5-6.9)	0.597

BMI, body mass index; ASA-PS, American Society of Anesthesiologists physical status; CCI, Charlson comorbidity index; AST, aspartate aminotransferase (GOT); ALT, alanine aminotransferase (GPT); ɤ-GTP, γ-glutamyl transpeptidase. *Data expressed as the median (interquartile range). **Data expressed as the mean ± standard deviation.

Table 3. Surgical procedure and outcome of emergent cholecystectomy.

	Pre-pandemic	Pandemic	P value
Intraoperative outcomes			
Operative time (min)	109 (48-239)	113 (41-276)	0.510
Bleeding (mg)	232 (0-2674)	228 (0-5250)	0.341
Laparoscopic resection	43 (60%)	144 (83%)	< 0.001
Conversion (laparoscopic to open)	2 (2.8%)	14 (8.1%)	0.127
Bailout procedure	23 (32%)	51 (29%)	0.682
Reconstituting	17 (24%)	36 (21%)	0.612
Fenestrating	6 (10%)	11 (11%)	0.826
Drain placement	56 (78%)	101 (58%)	0.004
Postoperative course			
Morbidity			
Complication	15 (21%)	22 (13%)	0.102
Major complication	6 (8.3%)	6 (3.5%)	0.106
Bile leakage	3 (4.2%)	5 (2.9%)	0.603
SSI Deep incisional	5 (6.9%)	4 (2.3%)	0.077
SSI Superficial incisional	2 (2.8%)	4 (2.3%)	0.825
Pneumonia	1 (1.4%)	0 (0%)	0.119
Postoperative hospital stay (day) *	10.6 (2-60)	8.0 (2-38)	0.042
In-hospital death	0 (0%)	1 (0.6%)	0.519
Re-admission	0 (0%)	1 (0.6%)	0.519

SSI, surgical site infection. *Data expressed as the median (interquartile range).

Table 4. Pathological diagnosis.

	Pre-pandemic	Pandemic	P value
acute cholecystitis	11 (15.3%)	33 (19.0%)	0.340
acute on chronic cholecystitis	23 (31.9%)	63 (36.2%)	0.668
gangrenous cholecystitis	38 (52.8%)	78 (44.8%)	0.256

ued for cases with high mortality risks when delayed surgical intervention could be detrimental. The management of acute cholecystitis offers various options, ranging from medical treatments to percutaneous or tube cholecystostomy, tailored to factors such as patient age, comorbidities, medication use, and admission time (Lee and Yim 2018). Early laparoscopic cholecystectomy, traditionally a standard treatment for acute cholecystitis, is known for its benefits in reducing hospital stay duration, lessening comorbidity, and enhancing cost-effectiveness (Mayumi et al. 2018; Pisano et al. 2020). However, during the COVID-19 pandemic, a shift toward conservative treatment was observed, deemed safer and more preferred (Vallès et al. 2021; Stavridis et al. 2022; Tóth et al. 2023). The CHOCOLATE trial, a multicenter randomized study, compared laparoscopic cholecystectomy with percutaneous catheter drainage in high-risk patients with acute cholecystitis. This trial found a significantly higher rate of major complications in the percutaneous drainage group (65% vs. 12%) (Loozen et al. 2018). Although emergency surgery might be necessary in certain cases, non-surgical treatments, including percutaneous catheter drainage, were increasingly considered and often favored during the pandemic (Lapsekili et al. 2021; Martinez Caballero et al. 2021; Koch et al. 2022).

Conversely, our hospital observed a steady rise in emergency cholecystectomies during the pandemic (Fig. 2). Specifically, there was an approximate 2.5-fold increase following the onset of the COVID-19 pandemic. Our hospital serves as an acute medical care provider in a regional core hospital. Because there were no other medical institutions in our area that closed or merged surgical departments, it is unlikely that the rise in cholecystitis patients at our hospital was due to changes of medical system after the pandemic. While elective surgeries post-conservative treatment have declined (154 cases vs. 102 cases), overall surgical interventions for acute cholecystitis have increased (72 cases vs. 174 cases) (Table 1). Despite some cases not proceeding to surgical intervention post-conservative treatment, these trends suggest an increase in acute cholecystitis after the COVID-19 pandemic. Similar patterns were

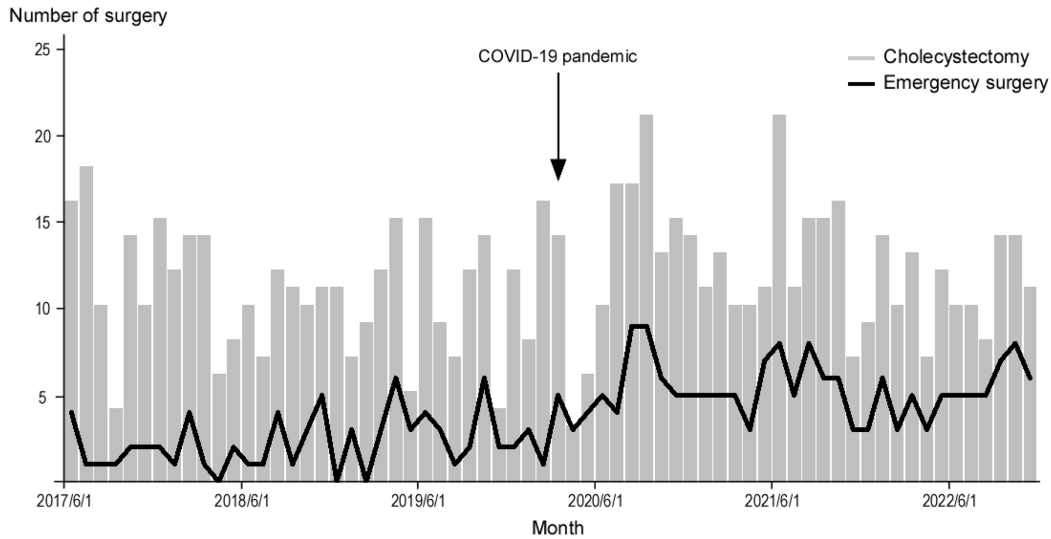

Fig. 2. Monthly elective and emergency surgeries.
This figure displays the monthly counts of surgeries performed for cholecystitis or cholelithiasis, comparing the periods before and after the onset of the pandemic.

observed in a tertiary medical center during the pandemic (Rahimli et al. 2022; Tóth et al. 2023). This increase can be attributed to patients delaying medical consultation until symptoms worsened, often resulting in advanced stages of inflammation (Cano-Valderrama et al. 2020; Westgard et al. 2020). Moreover, there have been reports of an increase in the incidence of gangrenous cholecystitis (Asti et al. 2020; De Simone et al. 2022).

In Japan, the spread of infection progressed at a relatively slow pace (Kokudo and Sugiyama 2021). Our hospital had the advantage of continuing emergency surgeries even during the pandemic, although elective surgeries such as cholecystectomy were sometimes postponed as a result of staff infections and bed shortages. The reverse transcription polymerase chain reaction test has been used as a screening tool for COVID-19 infections since April 2021. There were no cases of cholecystitis requiring surgery in patients with COVID-19. The time from symptom onset to surgery remained consistent pre- and post-pandemic (62.6 hours vs. 53.4 hours, respectively, $P = 0.264$), suggesting that patients did not delay hospital visits, potentially facilitating early diagnosis and treatment. Most cases of cholecystitis requiring emergency surgery were of mild to moderate severity, and the surgical technique appeared straightforward. A significant increase in laparoscopic resections was noted ($P < 0.001$), contributing to a reduction in hospital stays (10.6 days vs. 8.0 days, respectively, $P = 0.042$). Moreover, no significant difference in postoperative complications was observed pre- and post-pandemic ($P = 0.102$). Similar observations have been reported by other hospitals (Karlafti et al. 2022; CHOLECOVID Collaborative 2022). A limitation of this study is the exclusion of surgeries in patients with COVID-19. Previous research has shown that performing emergency surgeries on patients with COVID-19 can increase complications and the duration of hospital stays (Ohta et al. 2023). Therefore, conservative treatment is generally recommended for these patients. Given its advantages in terms of complications and hospital stay duration, cholecystectomy is preferable when feasible, particularly during the COVID-19 pandemic.

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Author Contributions

M.O. and R.K. were involved in the conception and design, data acquisition, analysis, and interpretation of data, drafting of the manuscript, and final approval. H.N. and A.M. contributed to acquisition data and analysis. M.K. and K.N. were involved in critical revision and final approval.

Conflict of Interest

The authors declare no conflict of interest.

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