

## Early Versus Delayed Laparoscopic Cholecystectomy for Acute Cholecystitis: A Single Center Experience

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### Rezumat

#### *Intervenție chirurgicală laparoscopică precoce versus întârziată pentru colecistită acută: experiența unui singur centru*

**Introducere:** Colecistita acută (AC) reprezintă o problemă de sănătate publică, crescând costurile de spitalizare, determinate, în special, de tratamentul chirurgical al acestor pacienți. Colecistectomia laparoscopică (LC) a devenit gold-standardul terapeutic, însă momentul intervenției: precoce (ELC) versus întârziată (DLC), rămâne încă de dezbatut. Obiectivul studiului vizează evaluarea rezultatelor postoperatorii între ELC și DLC. Subsidiar, au fost evaluate rezultatele din perioada prepandemică, comparativ cu cele din pandemia Covid-19.

**Material și Metodă:** Este prezentat un studiu observațional retrospectiv în care am inclus 266 de pacienți diagnosticați cu AC, internați în Clinica Chirurgie 1, SCJU Targu Mureș, din 2018 până în 2022. Aceștia au fost clasificați în grupul ELC (<72 ore de la debutul simptomelor) și DLC (>72 ore de la debutul simptomelor), fiind stratificați ulterior în 2 grupuri: pre-pandemic și pandemic. Au fost analizate: simptomatologia clinică, date paraclinice, detaliile chirurgicale și evoluția postoperatorie a pacienților.

**Discuții:** Rezultatele confirmă, mai puține conversii, spitalizare redusă în grupul ELC, pandemia Covid-19 nemodificând semnificativ datele din perioada prepandemică.

**Concluzii:** În concluzie, în prezentul studiu, ELC oferă avantaje semnificative, justificând preferința acestuia față de DLC. În ciuda scăderii incidenței internărilor pentru AC în timpul pandemiei,

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rezultatele postoperatorii sunt comparabile cu cele din perioada prepandemică. Studii multicentrice viitoare sunt necesare pentru evaluarea eficacității chirurgiei laparoscopice precoce.

Cuvinte cheie: colecistită acută, colecistectomie laparoscopică precoce, colecistectomie laparoscopică întârziată, COVID-19, CLP, CLI

## Abstract

*Introduction:* Acute cholecystitis (AC) represents a public health problem, increasing hospitalization costs, especially determined by the surgical treatment of these patients. Laparoscopic cholecystectomy (LC) has become the therapeutic gold standard, the timing of the intervention: early (ELC) versus late (DLC), is still debated, impacting the results. The primary objective of the study was to compare postoperative outcomes between ELC and DLC. Secondary objectives assessed surgical outcomes from the pre-pandemic period with those from the Covid-19 pandemic.

*Material and Methods:* A retrospective observational study is presented of 266 patients diagnosed with AC who were admitted to Clinic I of General Surgery, County Emergency Clinical Hospital of Târgu Mureș, from 2018 to 2022. They were classified into the ELC group (<72 hours from the onset of symptoms) and DLC (>72 hours from symptom onset) and were further stratified into pre-pandemic and pandemic cohorts. Data on clinical symptoms, paraclinical data, surgical details, and postoperative course were collected and analyzed.

*Discussion:* The results confirm fewer conversions to open surgery and reduced hospitalization in the ELC group. The pandemic did not significantly alter the timing of surgeries or patient demographics.

*Conclusion:* In conclusion, ELC for AC patients offers significant advantages, justifying its preference over DLC. Despite the decrease in the incidence of AC hospitalizations during the pandemic, postoperative outcomes are comparable to those in the pre-pandemic period. Future multicenter studies are recommended for a broader analysis of the efficacy of laparoscopic surgery in emergency settings.

Key words: acute cholecystitis, early laparoscopic cholecystectomy, delayed laparoscopic cholecystectomy, COVID-19, ELC, DLC

## Introduction

Acute cholecystitis (AC) is a leading cause of acute abdominal pain and often necessitates emergency surgical intervention (1,2). Laparoscopic cholecystectomy (LC) has become the preferred first-line surgical treatment due to its minimally invasive nature, resulting in shorter hospital stays, reduced surgical times, and expedited patient recovery compared to traditional cholecystectomy (3-5). The Tokyo Guidelines present a treatment continuum for AC that spans from early or immediate laparo-

scopic cholecystectomy (ELC) to delayed surgical intervention (DLC) following conservative management (6). It is recommended that ELC for AC patients be delayed until the acute phase has resolved, as early intervention has been associated with shorter postoperative stays and lower healthcare costs (7). The specific timing for ELC can vary from immediately to 10 days after symptom onset, depending on the chosen protocol (8).

Recent discourse has been active regarding the optimal timing for LC, with various studies from Europe, Japan, and the USA

contributing to the ongoing evaluation of ELC (9-11). The primary benefits of ELC include reduced hospitalization time, cost savings, and lower rates of rehospitalization (9). Conversely, many surgeons favor DLC for lower rate of biliary complications, shorter postoperative stay and lesser likelihood of conversions to open surgery, attributed to diminished inflammation and edema (12-14).

This study aims to rigorously evaluate the relative safety and efficacy of ELC versus DLC, considering procedural safety, operative duration, and both intraoperative and postoperative complications, including conversion rates to open cholecystectomy. Additionally, in light of the COVID-19 pandemic, which has impacted more than 700 million people, resulting in more than 6.9 million deaths globally as of December 31, 2023 (15), disrupting medical and societal activities, this study will also explore the implications of pandemic-era surgical protocols and lockdown measures in Romania on the timing and outcomes of surgical interventions for AC.

## Materials and Methods

### Study Design

This retrospective and observational study included all patients over the age of 18 with a diagnosis of acute cholecystitis (AC), confirmed through imaging, clinical assessment, intraoperative findings, and histopathological examination, admitted to the Surgery-I section of the County Emergency Clinical Hospital of Târgu Mureș, Romania.

Patients with simple biliary colic, choledocholithiasis, acute cholangitis, decompensated liver cirrhosis, massive ascites, intra-abdominal abscess, or free biliary perforation were excluded.

Initially, patients were categorized into two main groups based on the timing of their laparoscopic cholecystectomy (LC): the "Early Group" for surgeries performed within 72 hours of symptom onset, and the "Delayed Group" for those thereafter. Additionally, to consider the impact of the COVID-19 health

crisis on surgical management, patients were classified based on their admission date in relation to Romania's declaration of a state of emergency on March 16, 2020. Those admitted before this date were placed in the "Pre-Pandemic" group, while admissions after this date were assigned to the "Pandemic" group. RT-PCR positive COVID-19 patients were excluded from the study.

### Data Collection

Data recorded for each patient included age, gender, medical history, and clinical presentation, which encompassed symptoms such as pain in the right upper quadrant, nausea, vomiting, and the presence of Murphy's sign. Operative details were documented, including protocols followed, the frequency of conversion to open surgery, the number and types of complications, and the length of stay (LOS). Laboratory findings were quantified, including elevated white blood cell count, C-reactive protein, amylase, total bilirubin, aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), and gamma-glutamyl transferase (GGT).

Furthermore, to refine our understanding of the pathological underpinnings corresponding to clinical presentations, histopathological examination results of the cholecystectomy specimens were meticulously analyzed. Patients within the Early and Delayed Laparoscopic Cholecystectomy groups were further subclassified based on these findings into two subcategories: those with histologically confirmed acute cholecystitis and those with chronic cholecystitis. This subclassification was instrumental in elucidating the spectrum of cholecystitis managed surgically in our study cohort, providing insights into the correlation between preoperative clinical assessments and definitive histopathological diagnoses.

### Ultrasonography Findings

In relation to the ultrasonography findings, we recorded the presence of gallbladder stones,

pericholecystic fluid, dilatation of the intrahepatic and extrahepatic bile ducts, choledocholithiasis, and gallbladder wall thickening.

**Study Outcomes**

The primary endpoint of this study was to compare the incidence of postoperative complications between early and delayed laparoscopic cholecystectomy (LC). Secondary endpoints included an analysis of surgical complications and the risk of conversion from laparoscopic to open surgery during both the pre-pandemic and pandemic COVID-19 periods. Additionally, we assessed the length of hospitalization, duration of postoperative stay, and operation times.

**Statistical Analysis**

Data collection was carried out in MS Excel. Statistical, descriptive and inferential processing was performed with the EpiInfo version 3.5.4. Means or medians with confidence intervals were calculated for descriptive statistics. The mean was calculated for data with a normal distribution, and the median was calculated for those with a non-Gaussian distribution. To establish the differences in the mean, we used, depending on the Gaussian or non-Gaussian distribution, the two-tailed Student's t-test and Mann-Whitney test. For binary variables, we used the chi-square test or Fisher's exact test according to the values in the contingency table. All p values are two-tailed, with  $p < 0.05$  considered statistically significant.

**Results**

**Overall Comparison of Early and Delayed Laparoscopic Cholecystectomy**

Our study evaluated 266 out of 467 patients diagnosed with acute cholecystitis, divided into Early (ELC,  $n=134$ , 50.37%) and Delayed (DLC,  $n=132$ , 49.63%) Laparoscopic Cholecystectomy groups. Gender distribution was similar across both groups (ELC: 47

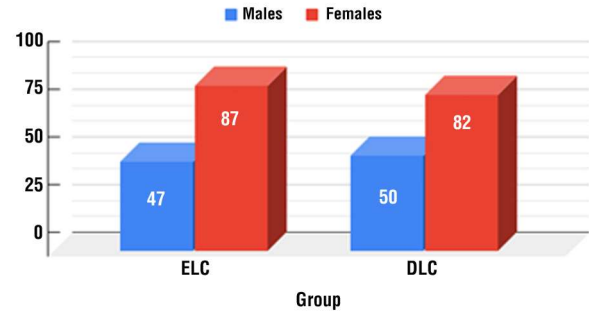


Figure 1. Gender Distribution in ELC and DLC groups

males, 87 females; DLC: 50 males, 82 females;  $p=0.318$ ), as shown in Fig. 1.

Age and previous abdominal surgeries showed no significant differences, with a slight, non-significant age disparity favoring the ELC group. Clinical symptoms were comparable, except DLC patients reported more pain irradiance ( $p=0.025$ ), and more ELC patients had fevers over  $38^{\circ}\text{C}$  ( $p=0.03$ ). Laboratory and ultrasound findings were mostly similar; notable were higher amylase levels and pericholecystic fluid in the DLC group ( $p=0.037$ ,  $p=0.048$ , respectively), as detailed in Table 1.

Surgical outcomes revealed comparable operating times and intraoperative blood loss. However, DLC had higher rates bile duct injuries (7 vs. 1 in ELC,  $p=0.039$ ), as shown in Fig. 2 and higher rates conversions to open surgery (14 vs. 6 in ELC,  $p=0.031$ ), as detailed in Fig. 3. Postoperative and total hospital stays were longer in the DLC group, with significant difference in total hospital stay

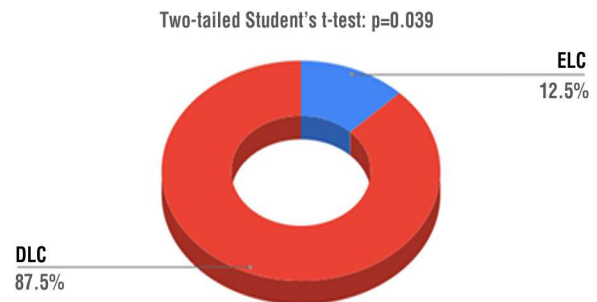


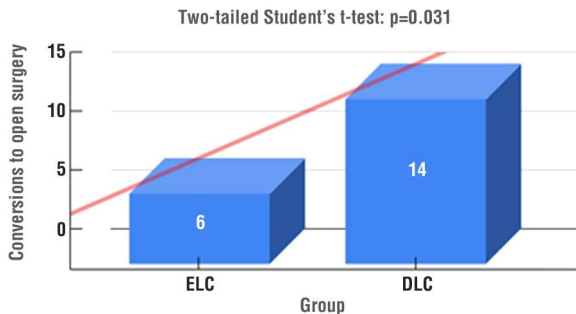
Figure 2. Rates of bile duct injuries in ELC and DLC groups

**Table 1.** Early versus Delayed LC: Demographics, Lab Results, and Ultrasonography findings

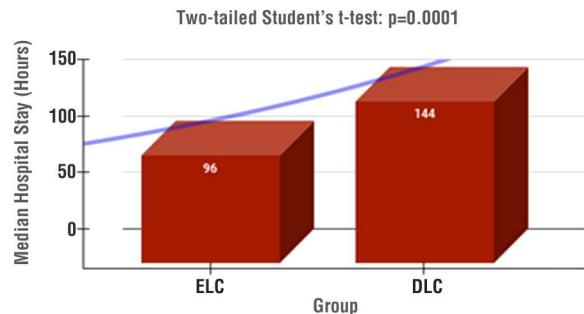
Patients' characteristics	Early Group (<72 h) (n=134)	Delayed Group (>72 h) (n=132)	p-value
Sex			0.318
Male	47	50	
Female	87	82	
Age (years)			-
Mean±SD	57.64±18.37	56.53±15.61	
Median (range)	60 (19-92)	57.5 (19-86)	
Surgical history			0.413
None	87 (64.91%)	84 (63.63%)	
Previous abdominal surgery	47 (35.07%)	48 (36.36%)	
Time from onset of acute symptoms to surgery (hours)			<0.0001
Mean±SD	51,04±19,39	153,6±66,43	
Median (range)	48 (24-72)	144 (96-504)	
Symptoms			
Pain in RUQ	133 (99.25%)	128 (96.96%)	0.180
Irradiance	32 (23.88%)	46 (34.85%)	0.025
Nausea/Vomiting	119 (88.80%)	123 (93.18%)	0.111
Temperature (>38°C)			0.03
Mean±SD	38.26 (±0.23)	38.09 (±0.18)	-
Median (Q1-Q3)	38.2 (37.8-38.8)	38 (37-38.5)	-
Murphy's sign			
Negative	64 (47.76%)	71 (53.78%)	-
Positive	70 (52.23%)	61 (46.21%)	0,164
Palpable gallbladder			
Absent	118 (88.06%)	110 (83.33%)	-
Present	16 (11.94%)	22 (16.67%)	0.138
Laboratory findings			
Elevated white blood cell count	76 (56.72%)	67 (50.75%)	0.166
Elevated CRP	2 (1.49%)	2 (1.52%)	0.494
Elevated ALT	39 (29.10%)	51 (38.64%)	0.051
Elevated AST	47 (35.07%)	53 (40.15%)	0.198
Elevated ALP	4 (2.99%)	4 (3.03%)	0.491
Elevated GGT	3 (2.24%)	6 (4.55%)	0.162
Elevated amylase	5 (3.73%)	17 (12.88%)	0.037
Elevated total bilirubin	15 (11.19%)	21 (15.91%)	0.134
Ultrasonography findings			
Gallbladder stones	88 (65.67%)	86 (66.67%)	0.464
Thick-walled gallbladder	67 (50%)	71 (53.79%)	0.230
Pericholecystic fluid	13 (9.70%)	22 (16.67%)	0.048
Intrahepatic bile duct dilatation	5 (3.73%)	5 (3.79%)	0.490
Extrahepatic bile duct dilatation	9 (6.72%)	4 (3.03%)	0.133
Choledocholithiasis	2 (1.49%)	0	-

( $p < 0.0001$ ), as illustrated in Fig. 4. Complications were rare and evenly distributed,

with one mortality in the DLC group. Detailed outcomes are presented in Table 2.



**Figure 3.** Rates of conversion to open surgery



**Figure 4.** Comparison of median hospital stay (Hours) between ELC and DLC groups

**Table 2.** Intraoperative findings and postoperative outcomes in all patients divided based on early versus delayed LC

Intraoperative findings	Early Group (<72 h) (n=134)	Delayed Group (>72 h) (n=132)	p-value
Operating time (min) Mean±SD	117.4 (±41.81)	118.3 (±41.67)	0.859
Blood loss (>200 ml)			0.315
Absent	130 (97.01%)	130 (98.48%)	
Present	4 (2.99%)	2 (1.51%)	
Bile duct injury			0.039
Absent	133 (99.25%)	125 (94.70%)	
Present	1 (0.75%)	7 (5.30%)	
Conversion to open surgery			0.031
Absent	128 (95.52%)	118 (89.39%)	
Present	6 (4.48%)	14 (10.61%)	
Postoperative Complication			
Surgical site (Wound) infection	-	2 (1.52%)	0.240
Bile leaks (>50-100 ml/24 h)	-	1 (0.76%)	0.497
Retained stones (in CBD)	1 (0.75)	0	0.503
Abscess	-	1 (0.76%)	0.491
Pancreatitis	1 (0.74%)	-	0.490
Bleeding	1 (2.98%)	1 (0.76%)	0.747
Degree of complications			-
Minor (Clavien <3)	134 (100%)	131 (99.24%)	
Major (Clavien ≥3)	0	1 (0.76%)	
Mortality	0	1 (0.76%)	-
Postoperative stay (hours)			0.713
Mean±SD	81.13 (±44.03)	83.64 (±65.21)	
Median (Q1-Q3)	72 (24-336)	72 (24-528)	
Length of hospital stay (hours)			<0.0001
Mean±SD	112 (±46.61)	156.4 (±84.89)	
Median (Q1-Q3)	96 (24-360)	144 (48-696)	

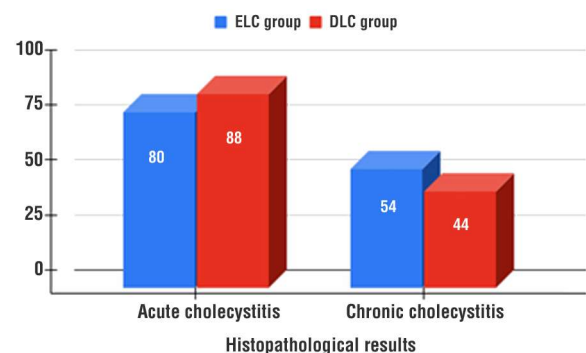
### Histopathological Outcomes

The histopathological analysis of LC specimens introduced an additional dimension to our understanding of surgical outcomes. Results from each specimen were carefully recorded to categorize patients based on their postoperative histopathological diagnosis, distinguishing between acute and chronic cholecystitis within the Early (ELC) and Delayed (DLC) Laparoscopic Cholecystectomy groups, as shown in *Fig. 5*. This subclassification enabled a more nuanced comparison between the two groups.

#### Early Laparoscopic Cholecystectomy (ELC) group

Among the 134 patients undergoing ELC, histopathological results identified 80 as acute cholecystitis and 54 as chronic cholecystitis. Patients with acute cholecystitis had significantly longer surgeries (mean  $125.6 \pm 4.944$  minutes) than those with chronic (mean  $105.2 \pm 4.755$  minutes,

$p=0.005$ ). Both groups experienced minimal blood loss, with no significant difference ( $p=0.355$ ), and similar low complication rates, including negligible instances of surgical site infections or bile leaks. Acute cholecystitis patients had a higher, yet non-significant, number of conversions to open surgery (5 versus 1 for chronic,  $p=0.132$ ). No mortalities were reported. The median postoperative stay



**Figure 5.** Distribution of acute and chronic cholecystitis in the ELC and DLC groups based on postoperative histopathological diagnosis

was significantly different (acute: 3 days, chronic: 2 days;  $p=0.029$ ). The median length of the total hospital stay was the same in both acute and chronic cholecystitis subsets at 3 days, but the range of stay in chronic cholecystitis was narrower (1-10 days), with a significant  $p$ -value ( $p=0.017$ ). Detailed data on these findings can be found in *Table 3.1*.

#### *Delayed Laparoscopic Cholecystectomy (DLC) group*

In the Delayed Laparoscopic Cholecystectomy (DLC) cohort of 132 patients, histopathological evaluation identified 88 as having acute cholecystitis while 44 were classified with chronic cholecystitis.

The duration of surgery differed significantly, with chronic cholecystitis requiring less time (mean  $105.2 \pm 4.755$  minutes) than acute (mean  $125.6 \pm 4.944$  minutes,  $p=0.0035$ ). Blood loss was minimal and comparable between subsets ( $p=0.355$ ). Acute cholecystitis subset had a slightly higher incidence of bile duct injuries ( $p=0.298$ ) and more frequent conversions to open surgery (12 vs. 2 in chronic), nearing statistical significance ( $p=0.057$ ). Complication rates were low, with one surgical site infection in each subset and no bile leaks, abscesses, pancreatitis, or significant bleeding differences.

Acute cholecystitis subset had one mortality. Postoperative hospital stays were slightly longer for acute cholecystitis (median 3 days) than chronic (median 2.5 days,  $p=0.007$ ), with no significant difference in the median total hospital stay (acute: 6 days, chronic: 5 days,  $p=0.366$ ). Detailed data on these findings can be found in *Table 3.2*.

#### *Pandemic vs. Pre-Pandemic Comparison*

During the pre-pandemic period, 165 patients underwent LC, split between 79 ELC and 86 DLC. Gender distribution, age, leukocytosis, and ultrasound findings showed no significant differences. Intraoperative incidents and postoperative complications were also similar, with a significant difference in conversion to open surgery ( $p=0.0389$ ) and postoperative complications ( $p=0.018$ ). The length of hospital stay was significantly different ( $p<0.0001$ ).

In the pandemic period, out of 101 patients, 55 underwent ELC and 46 DLC. Again, gender distribution, age, leukocytosis, and ultrasound findings did not differ significantly. While intraoperative incidents and postoperative complications were comparable, a significant difference was observed in the length of hospital stay ( $p=0.0035$ ).

**Table 3.1.** Surgical outcomes in early laparoscopic cholecystectomy (ELC) group based on the histopathological findings

Intraoperative findings	All patients (n=134)	Acute Cholecystitis (n=80)	Chronic Cholecystitis (n=54)	p-value
Operating time (min) Mean±SD		125.6 (±4.944)	105.2 (±4.755)	0.005
Blood loss (>200 ml)	4	2	2	0.355
Bile duct injury	1	-	1	0.201
Conversion to open surgery	6	5	1	0.132
<b>Postoperative Complication</b>				
Surgical site (Wound) infection	-	-	-	-
Bile leaks (>50-100 ml/24 h)	-	-	-	-
Retained stones (in CBD)	1	-	1	-
Abscess	-	-	-	-
Pancreatitis	-	-	-	-
Bleeding	1	1	-	-
Mortality	-	-	-	-
<b>Postoperative stay (days)</b>				
Median (Q1-Q3)		3 (1-14)	2 (1-5)	0,029
<b>Length of hospital stays (days)</b>				
Median (Q1-Q3)		3 (1-14)	3 (1-10)	0,017

**Table 3.2.** Surgical outcomes in delayed laparoscopic cholecystectomy (DLC) group based on the histopathological findings

Intraoperative findings	All patients (n=132)	Acute Cholecystitis (n=88)	Chronic Cholecystitis (n=44)	p value
Operating time (min) Mean ± SD		125.6 (±4.944)	105.2 (±4.755)	0.0035
Blood loss (>200 ml)	2	2	0	0.221
Bile duct injury	7	4	3	0.298
Conversion to open surgery	14	12	2	0.057
<b>Postoperative Complication</b>				
Surgical site (Wound) infection	2	1	1	0.3333
Bile leaks (>50-100 ml/24 h)	1	1	-	-
Retained stones (in CBD)	-	-	-	-
Abscess	1	1	-	0.3333
Pancreatitis	1	-	1	0.1666
Bleeding	1	1	-	-
Mortality	1	1	-	-
<b>Postoperative stay (days)</b>				
Median (Q1-Q3)		3 (1-14)	2.5 (1-22)	0,007
<b>Length of hospital stays (days)</b>				
Median (Q1-Q3)		6 (3-20)	5 (2-29)	0,366

The total comparison between pre-pandemic and pandemic periods showed no significant differences in demographic data, clinical findings, or operative outcomes, indicating that the pandemic had minimal impact on these variables in the context of LC, as detailed in *Table 4*.

**Discussion**

The management of acute cholecystitis (AC)

remains a significant concern in surgical practice, with the timing of laparoscopic cholecystectomy (LC) playing a pivotal role in patient outcomes. In our study, a prompt approach to ELC within 72 hours of symptom onset was associated with improved surgical and recovery outcomes, including lower conversion to open surgery and shorter hospital stays.

Gutt et al. (16) have previously shown that ELC minimizes mortality and hospital stays, a

**Table 4.** Comparative analysis of laparoscopic cholecystectomy outcomes: pre-pandemic versus pandemic

Characteristics	Pre-Pandemic COVID-19 Period (n=165)				Pandemic COVID-19 Period (n=101)				Total p value
	Total	ELC	DLC	p-value	Total	ELC	DLC	p-value	
	165 patients	79	86		101 patients	55	46		
Age (years) Mean ± SD	57.48 (±17.59)	55.99 (±1.814)	58.86 (±2.030)	0.2961	56.42 (±16.08)	57.31 (±2.016)	55.35 (±2.571)	0.5442	0.619
Female	101 (61.21)	50	51	0.3022	68 (67.33)	37	31	0.4959	0.159
Male	64 (38.79)	29	35		33 (32.67)	18	15		
Leukocytosis	91 (55.15)	44	47	0.4471	52 (51.48)	32	20	0.0742	0.281
Ultrasound findings	112 (67.88)	57	55	0.1331	64 (63.37)	32	32	0.1233	0.226
Intraoperative Incidents	87 (52.72)	41	46	0.4200	46 (45.54)	26	20	0.3545	0.129
Conversion to open surgery	10 (6.06)	2	8	0.0389	10 (9.90)	4	6	0.1797	0.131
Postoperative complications	5	0	5	0.0181	3	2	1	0.3623	0.499
<b>Operating time (min)</b>									
Median (Q1-Q3)	120 (30-270)	120 (30-270)	120 (60-240)	0.318	120 (60-240)	120 (60-210)	95 (60-240)	0.148	0.475
<b>Postoperative stay</b>									
Median (Q1-Q3)	3 (1-22)	3 (1-10)	3 (1-22)	0.802	3 (1-14)	3 (1-14)	2.5 (1-10)	0.180	0.639
<b>Length of hospital stays</b>									
Median (Q1-Q3)	5 (1-29)	4 (1-10)	6 (3-20)	<0.0001	5 (2-15)	4 (2-15)	5.5 (2-13)	0.0035	0.361



finding our study corroborates in part through observing a shorter total hospital stay for ELC patients ( $p < 0.0001$ ). Yet, our lack of mortality in the ELC group and a singular occurrence in the DLC group diverges from their reported mortality benefit, which may be due to demographic differences or our study's scope. Roulin et al. (17) also reported diminished morbidity and costs with ELC, which is consistent with our findings of decreased bile duct injury rates ( $p = 0.039$ ), fewer conversions to open surgery ( $p = 0.031$ ), and shorter hospital stays ( $p < 0.0001$ ), indicating potential economic and morbidity advantages.

The meta-analyses by Dai et al. (18), Siddiqui et al. (9), Moody et al. (19), and Cao et al. (20) resonate with our study, especially regarding the similarity in conversion rates and postoperative complications between ELC and DLC. Acar et al. (21) found no significant differences in surgical durations between ELC and DLC, aligning with our findings of comparable operation times ( $p = 0.859$ ). Nonetheless, we observed marked differences in total hospital stays ( $p < 0.0001$ ), this aligns with Goh et al.'s (22) findings, suggesting that ELC may offer a recovery advantage in specific contexts. Ozkardeş et al. (23) did not note differences in operation time and conversion rates, paralleling our results. However, they reported longer hospital stays and increased costs for DLC, reflecting our findings of prolonged hospitalization for DLC patients ( $p < 0.0001$ ), which supports ELC's economic and efficiency benefits.

Arafa et al. (24) contrasted our findings by reporting prolonged operation times and increased blood loss for ELC, as we observed no significant differences in these metrics ( $p = 0.859$  for operation time and  $p = 0.315$  for blood loss). This could result from varying surgical techniques, patient demographics, or the severity of clinical presentations.

In our study, ELC patients benefited from lower rates of bile duct injury ( $p = 0.039$ ) and a reduced need for conversion to open surgery ( $p = 0.031$ ), validating the technical ease and lower complication likelihood associated with early intervention. Conversely, the increased

operation times posited by Arafa et al. (24) were not evidenced in our data, bolstering the argument for ELC within a well-orchestrated clinical framework, as advocated by current research favoring prompt AC management.

Furthermore, our study's histopathological analysis post-surgery revealed an intriguing distribution of cholecystitis pathology. Despite clinical indications of AC supported by para-clinical evidence, a portion of patients were histopathologically diagnosed as chronic cholecystitis - 40.2% in the ELC group and 33.3% in the DLC group. This unexpected subclassification into acute and chronic cholecystitis may reflect a certain proportion of patients presenting with clinical signs indicative of an acute episode, yet ultimately possessing chronic pathological changes. Notably, within the ELC cohort, the median postoperative stay for patients with chronic cholecystitis was shorter at 2 days compared to 3 days for acute cholecystitis ( $p = 0.029$ ). The total hospital stay trend was similar, being longer for acute cholecystitis in both groups but statistically significant only in the ELC group ( $p = 0.017$ ). These findings align with Damani et al. (25), who noted a marginally extended total hospital stay for acute cholecystitis, suggesting the more pronounced inflammatory response in acute cases may necessitate longer hospitalization. Moreover, the ELC group showed a trend towards fewer conversions to open surgery in chronic cases (6 vs. 1,  $p = 0.132$ ). Damani et al. (25) observed a similar pattern, indicating the less inflamed tissue in chronic cases might be easier to manage laparoscopically. In the DLC group, with a slightly higher incidence of acute pathology, the number of conversions in acute cholecystitis was notably higher (12 vs. 2), verging on statistical significance ( $p = 0.057$ ), which may suggest the advantages of ELC over DLC in managing acute conditions.

This subclassification based on histopathological results does not change the consensus that ELC is beneficial overall; however, it adds depth to our discussion by suggesting that for certain patient subsets, specifically those with chronic changes, ELC may offer even greater

advantages. Moreover, considering that the overall rates of conversion to open surgery are lower in ELC, especially in cases of acute pathology, this distinction becomes crucial in the ongoing debate regarding the optimal timing for cholecystectomy in the context of acute cholecystitis.

### *Impact of Covid-19 Pandemic on Laparoscopic Cholecystectomy Outcomes*

The Covid-19 pandemic presented unprecedented challenges to healthcare delivery, including in the practice of LC. While the CHOLECOVID study (26) observed a shift towards CT imaging and more conservative management of grade II/III cholecystitis, our findings did not reflect a significant change in diagnostic or management approaches. Similarly, we did not observe a delay from presentation to ultrasound, suggesting that diagnostic processes for cholecystitis were not compromised during the pandemic.

Contrary to increased mortality rates associated with LC during the pandemic reported by Vuu et al. (27) and Koch et al. (28), our study showed no significant change in inpatient mortality ( $p=0.499$ ), hinting at an effective patient selection during this period. Consistent with Demetriou et al. (29), we found no significant differences in intraoperative times, indicating maintained surgical efficiency despite pandemic pressures. Furthermore, our surgical quality and perioperative protocols remained robust, as evidenced by the sustained rate of complete cholecystectomies and no significant increase in conversion to open surgery ( $p=0.1797$ ).

In light of the Joint Romanian Society of digestive endoscopy (SRED) and Romanian Association of Endoscopic Surgery (ARCE) recommendations (30), our decision to exclude COVID-19 positive patients from the study was influenced by two key factors. Firstly, the recommendations underscore the heightened risk of aerosol generation during laparoscopic procedures, which could increase the potential for virus transmission to healthcare personnel. Due to this fact, laparoscopic procedures were

mostly, if not completely, avoided in COVID-19 positive cases. Secondly, the systemic impact of COVID-19 on patients could distort the outcomes of laparoscopic cholecystectomy, introducing variables that are not directly related to the surgical process itself but rather to the systemic effects of the virus, such as increased inflammatory responses or potential coagulopathies (31). Our focus was to assess the intrinsic factors influencing laparoscopic cholecystectomy outcomes, independent of the systemic and procedural complications that a COVID-19 positive status could introduce.

Finally, echoing Karlafti et al. (32), our findings confirm that the pandemic did not significantly alter the number of cases or the incidence of complications. Furthermore, an analysis of the median length of hospital stays during both the pre-pandemic and pandemic periods did not reveal a significant overall difference ( $p=0.361$ ), indicating that the duration of hospitalization remained consistent, in line with our institutional protocols that prioritized patient care and safety without compromising surgical efficiency and quality. Notably, within each respective period, a statistically significant difference in the length of hospital stays was observed between ELC and DLC patients (pre-pandemic  $p<0.0001$ , pandemic  $p=0.0035$ ), underscoring the efficacy of early laparoscopic cholecystectomy over delayed procedures.

### **Limitations**

Our study's insights must be contextualized within the constraints of its retrospective design, primarily sourced from a single institution, which may limit the generalizability of the findings. Exclusions applied to the patient selection could also restrict the applicability to a broader clinical context. The study is further limited by the lack of long-term follow-up data, which could impact the robustness of the conclusions drawn. To extend the applicability of these findings and validate them across varied clinical environments, future multi-center studies with a more extensive follow-up period are recommended, particularly to

analyze the efficacy of laparoscopic surgery in emergency settings.

## Conclusions

Our investigation into the optimal timing for laparoscopic cholecystectomy (LC) in the management of acute cholecystitis (AC) underscores the distinct advantages of early laparoscopic cholecystectomy (ELC), such as reduced hospitalization periods and lower conversion rates to open surgery, confirming the effectiveness of early intervention. This efficacy is further bolstered by the lack of significant differences in postoperative complications between the Early and Delayed Groups. The histopathological insights from our study also highlight ELC to be particularly advantageous when considering the lower rates of conversion to open surgery observed in acute cases. In the context of the COVID-19 pandemic, our study suggests that despite the unprecedented global healthcare challenges, the timing of surgical interventions for acute cholecystitis and the associated outcomes were not detrimentally impacted. Our analysis indicates that there was no significant difference in the length of hospital stays between the pre-pandemic and pandemic periods ( $p=0.361$ ), signifying that our institutional protocols successfully navigated the pandemic's constraints while maintaining the quality and efficiency of care. Furthermore, our data show that the pandemic did not notably affect the demographic distribution of patients nor the incidence of postoperative complications, affirming the resilience of our healthcare delivery during a period of substantial systemic stress.

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## Competing interests

The authors declare no conflicts of interest.

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## Ethics Approval and Consent to Participate

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Targu Mures Emergency County Hospital, Romania (protocol code 31586, on 5 December 2022).

Informed consent was obtained from all the subjects involved in the study.

## Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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