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Early versus Delayed Laparoscopic Cholecystectomy for Acute Calcular Cholecystitis :A Prospective Randomized Study

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Abstract

Background: Laparoscopic cholecystectomy (LC) has become the gold standard in the treatment of symptomatic gallstones, while acute cholecystitis (AC)is a common surgical condition that may require hospital admission and subsequent surgical management. The aim of this work was to compare early versus delayed LC for acute calcular cholecystitis (ACC) regarding intraoperative findings, difficulties, possible complications and the postoperative outcomes.

Methods: This prospective randomized study was carried out on 70 patients aged > 18 years old, both sexes, diagnosed as ACC. Patients were divided into two equal groups: Group A: underwent early LC within 1 week from onset of symptoms and Group B: underwent delayed LC 6-8 weeks after the last attack of AC.

Results: Adhesions and increased GB wall thickness were significantly higher in group A than group B ($P<0.05$). Drain and adhesions were significantly higher in group A than group B ($P<0.05$). Analgesic requirement and hospital stay were significantly lower in group A than group B ($P <0.05$). Drain removal was significantly different between both groups ($P <0.001$). Intestinal injury and Jaundice didn't occur in any patients in both groups.Operative time, difficulty, bleeding, bile duct injury, conversion to open, bleeding and bile leakage were insignificantly different between both groups.

Conclusions: Early LC seems to offer a preferable approach for patients with ACC providing a more efficient treatment with less postoperative pain and shorter hospitalization, indicating a faster recovery.

Keywords:
Cholangiopancreatography, Laparoscopic Cholecystectomy, Acute Calcular Cholecystitis, Gallbladder
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Introduction:

Gallstones constitute a significant health problem affecting 10-15% of the adult population. Up to 35% of patients experience symptoms or complications such as acute cholecystitis (AC), cholangitis, or pancreatitis[1]. Laparoscopic cholecystectomy (LC) has become the gold standard in the treatment of symptomatic gallstones. The major advantages of LC include (less postoperative pain, less hospitalization time and recovery, and better cosmetic results[2, 3].

AC, an inflammatory condition of the gallbladder (GB), is a common surgical condition that may require hospital admission and subsequent surgical management[4]. Presentations vary from mild and self-limiting to a life-threatening disease with an approximate mortality rate of 0.6%[4, 5]. Associated complications include empyema, abscess formation, hemorrhagic transformation, or perforation of the GB with peritonitis. The 2018 Tokyo Guidelines provide clear guidance on the recommended management options[6].

The optimal timing of LC for cases of AC based on the onset of symptoms remains controversial. The general view in the treatment of AC is to be commenced firstly conservative therapy to prevent possible complications associated with inflammation, followed by LC after 6-8 weeks. Many literatures proposed a “golden 72 hour” period as the ideal timing for early LC, beyond which organized adhesions secondary to GB inflammation form within the Calot’s
triangle, rendering surgical dissection more difficult[7].

World Society of Emergency Surgery guidelines recommend early LC be performed as soon as possible within 7 days from hospital admission and within 10 days from the onset of symptoms.There’s an increasing preference for early LC over delayed LC because that early LC decreases overall hospital stay, eliminates the risks of gallstone-related morbidity and achieves similar conversion rate and outcomes[7, 8].

This work aimed tocompare early versus delayed LC for acute calcular cholecystitis (ACC) regarding intraoperative findings, difficulties, possible complications and the postoperative outcomes.

Patients and Methods:

This prospective randomized study was carried out on 70 patients aged > 18 years old, both sexes,diagnosed as ACC. The study was done from June 2023 to June 2024 after approval from the Ethical CommitteeKafr ElsheikhUniversity Hospitals, Kafr Elsheikh, Egypt. An informed written consent was obtained from the patients.

Exclusion criteria were patients with non-ACC, ACC complicated by common bile duct (CBD) stones or pancreatitis and previous hepatobiliary surgery.

Randomization

Patients were divided into two equal groups in a parallel manner by a computer-generated randomization list and their allocation code was kept in a closed opaque envelope: Group (A): underwent early LC within 1 week from onset of symptoms and Group (B): underwent delayed LC 6-8 weeks after the last attack of AC.

All patients were subjected tocomplete history taking, clinical examination, laboratory investigations [complete blood count (CBC),prothrombin time (PT) and activity, kidney and liver function tests, serum urea, creatinine, alanine aminotransferase (ALT), aspartate aminotransferase (AST), C- reactive protein (CRP), total and direct serum bilirubin, amylase, lipase, alkaline phosphatase enzyme, hepatitis C virus antibodies and hepatitis B surface antigen] and radiological investigations [pelvic-abdominal ultrasonography (US), abdominal computerized tomography (CT) andmagnetic resonance cholangiopancreatography (MRCP)].

Operative assessment, the diagnosis of AC was based on the finding of acute upper abdominal pain, with acute right upper quadrant tenderness for more than 6 hours, associated nausea or vomiting, fever (>100oF), and ultrasonographic (USG) evidence of AC such as distended gall bladder, presence of gallstones with a thickened and edematous GB wall, positive Murphy's sign, and pericholecystic fluid collections. In addition, increased total leukocyte count (>10,000/mm^3).

Laparoscopic cholecystectomy

The surgery was done with the patient under general anesthesia using endotracheal intubation. Pneumoperitoneum was created by blind puncture with a Veress needle through a sub umbilical incision. Four laparoscopic ports were used: 10- mm umbilical for the optical instrument (0 degrees), 10-mm sub xiphoidal for working instruments, 5-mm right subcostal along the midclavicular line also for working instruments, and 5 mm on the right flank for retraction instruments. Adhesion release and exposure of the Calot triangle were undertaken first. If necessary, the GB was emptied through a laterally inserted Veress needle to allow better grasping. The cystic pedicle was detected to isolate the cystic duct and the artery separately. Both were then clipped and divided. The GB was dissected off its bed with a monopolar cautery hook. At completion of the surgery, the GB was placed in a retrieval bag and extracted through the sub xiphoidal incision, which was enlarged if necessary. Hemostasis was achieved in the GB bed, and after a through saline lavage, a suction drain was placed if clinically indicated and the incisions closed. Operative data was recorded (operative time, intra-operative difficulties, and complications: blood loss, intra-operative bleeding, intra-operative adhesions, Mirizzi's syndrome if present, bile duct injury, intestinal injury, and conversion to open surgery).

Postoperative follow up

Intravenous fluids, antibiotics, and analgesics were given to the patients as required. Feeding was resumed as soon as tolerated and such antibiotics were replaced by oral antibiotics. Postoperative complications were prospectively recorded within postoperative period after surgery including postoperative bleeding, the length of hospital stay, analgesic requirement, postoperative bile leakage, postoperative jaundice, postoperative day of the drain removal.

Follow-up post-discharge

Patients were followed in the outpatient clinic during the first week, second week, third month and sixth month.

Sample Size Calculation:

Using Open Epi software at power of study 80% and confidence level 95% [9, 10]. Sample size was calculated to be 70 patients divided as 35 in each group. Based on that need for analgesic doses>3 was 73.3% and 40% within early and delayed LC respectively [11].

Statistical analysis

Statistical analysis was done by SPSS v26 (IBM Inc., Chicago, IL, USA). Quantitative variables were presented as mean and standard deviation (SD) and compared between the two groups utilizing unpaired Student's t- test. Qualitative variables were presented as frequency and percentage (%) and were analyzed utilizing the Chi-square test or Fisher's exact test when appropriate. A two tailed P value < 0.05 was considered statistically significant.

Results:

Ninety- seven patients were assessed for eligibility, 19 patients did not meet the criteria, and eight patients refused to participate in the study. The remaining patients were randomly allocated into two equal groups (35 patients in each). All allocated patients were followed-up and analyzed statistically. **Figure 1**

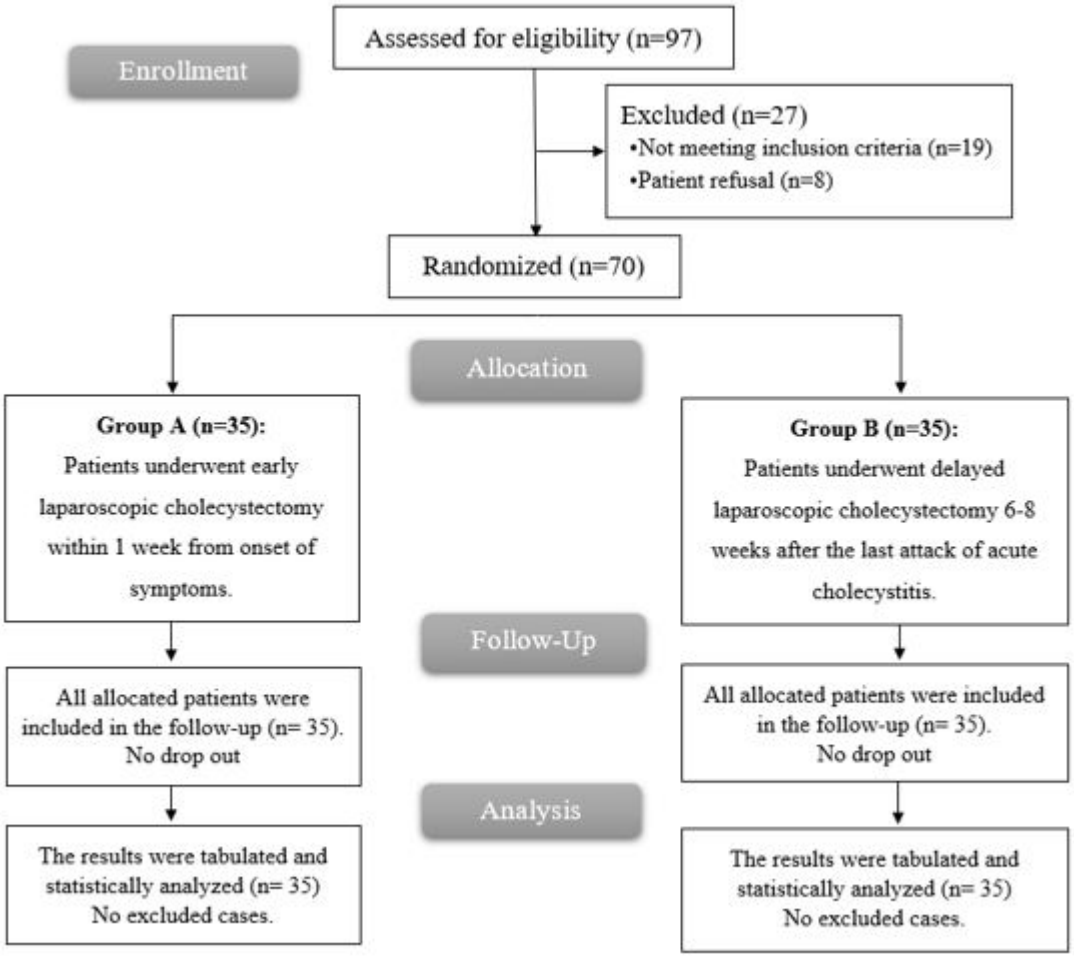


Figure 1: CONSORT flowchart of the enrolled patients

Table 1: Demographic data of the studied groups

		Group A (n=35)	Group B (n=35)	P value
Age (years)	**Mean ± SD**	46.06 ± 8.5	43.86 ± 6.78	0.235
	Range	22 - 57	19 - 53	
Sex	**Male**	16 (45.71%)	14 (40%)	0.629
	Female	19 (54.29%)	21 (60%)	

Clinical presentation

At initial presentation: all cases (70 cases, 100%) complained of pain symptoms,Pain was characterized most frequentlyas severepain, atright hypochondrial or epigastric regionsthateitherpersistsorescalatesover12to24hours.Althoughitmaybe ameliorated by administration of analgesia, it does not typically resolve entirely. Commonly, patients have a history of antecedent episodes of biliary colic. A positive Murphy sign which is (a palpation of the right upper quadrant during inspiration causes sudden cessation of breathing) was present in 70 cases (100%) at time of presentation. 64 cases (92%) had fever at time of presentation. Only one patient (1.4%) complained of jaundice to whom MRCPwas done to exclude biliaryobstruction and had revealed no obstructive stones nor lesions.

Table(2):Distribution of the studied cases according to Clinical Presentation

	No.	**%**
Righthypochondriapain	70	100
Murphy'ssign	70	100
Fever	64	92
Jaundice	1	1.4

Table (3): Distribution of the studied cases according to medical and surgical history

	No.	%
Medical history		
Free	42	60.0
Hypertension	15	21.4
Bronchial asthma	6	8.5
Diabetes mellitus	7	10
Surgical history		
Free	25	35.7
Previous abdominal operation	45	64.28

Laboratoryinvestigations

The most two important laboratory investigations that were observed in our study were: white blood cell count (WBCs) and c reactive protein (CRP). These two values were included in Tokyo classification of acute cholecystitis. They are important to confirm diagnosis of acute calcular cholecystitis. Table (6) illustrates the number of abnormal findings of these two variables among our patients. In all cases (WBC) counts were elevated (70 patients). In 39 cases (55.71%) ,(WBC) counts were elevated but less than 18000 cell\ml^3 while in the other 31 cases (44.82%)(WBC) counts were 18000 cell\ml^3 or more. In complicated acute calcular cholecystitis, (WBCs) count is 18000 cell\ml^3 or more. These complications included acute gangrenous cholecystitis and empyema of gallbladder. The mean value for (WBCs) count was 18.04 ± 3.87 range from 12.0 – 24.30 cell\ml^3. CRP was elevated in 53 cases (76%).The mean value for CRP was 10.0 ± 4.04 range from 3.0 – 16.0 U\L. Serum total bilirubin, serum alkaline phosphatase (ALP) and liver enzymes are of normal values.

Table(4): Statistical analysis of the studied cases according to Laboratory investigations

	No.	**%**
Whitebloodcellscount (WBCs)		
<18	39	55.71 %
≥18	31	44.82 %
Min.– Max.	12.0 – 24.30	
Mean±SD.	18.04 ± 3.87	
Median	17.80	
elevated C-Reactiveprotein (CRP)	53	76 %
Min.– Max.	3.0 – 16.0	
Mean±SD.	10.0 ± 4.04	
Median	10.0	

Table 5: Laboratory investigation of the studied groups

			Group A (n=35)	Group B (n=35)	P value
Liver function tests	**ALT (U/L)**	**Mean ± SD**	78.74 ± 16.7	80.26±21.38	0.742
		Range	33 – 98	31 - 107	
	AST (U/L)	**Mean ± SD**	72.14±22.99	69.34 ± 18.65	0.578
		Range	31 – 108	36 - 95	
	Direct bilirubin (mg/dL)	**Mean ± SD**	0.27 ± 0.08	0.24 ± 0.09	0.161
		Range	0.15 - 0.4	0.1 - 0.4	
	Total bilirubin (mg/dL)	**Mean ± SD**	0.88 ± 0.39	1.02 ± 0.26	0.070
		Range	0.2 - 1.7	0.6 - 1.4	
	Alkaline phosphatase (IU/L)	**Mean ± SD**	89.57 ±24.16	96.91 ±27.61	0.241
		Range	51 – 126	47 - 138	

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase.

ALT, AST, direct bilirubin, total bilirubin and alkaline phosphatase were insignificantly different between both groups

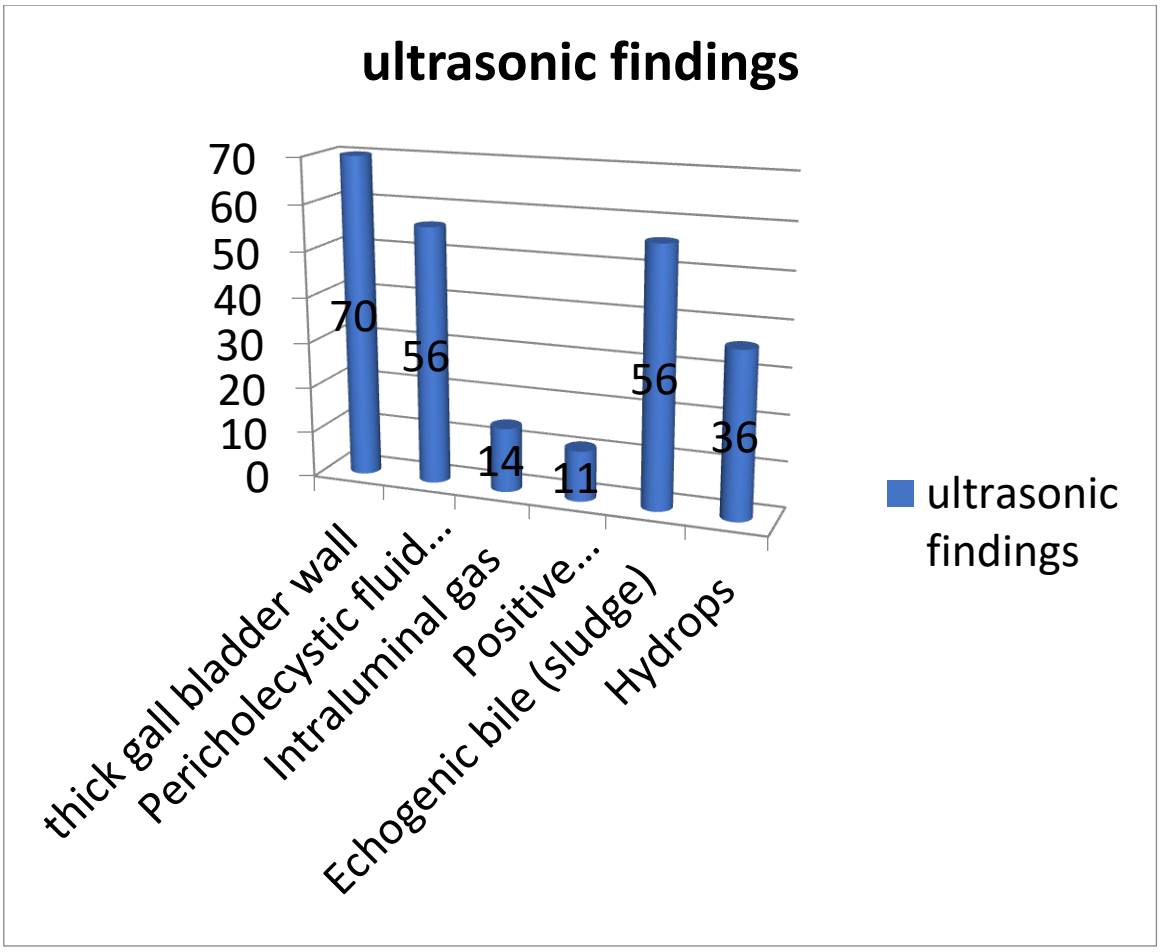
Ultrasonographicfindings

Preoperative ultrasound studies were available for all patients and were interpretedby the radiologist, as suggestive of acute calcular cholecystitis by the presence of gallbladder stones in all cases (70 patients).

The gallbladder wall was thick 3.5-4 mm or more in all cases 100% (70 patients). Pericholecystic fluid collection was present in 56 cases (80%). In 56 cases (80%),there were echogenic bile (sludge), where in 11 cases (16%) there were positive ultrasonographic Murphy's sign. Intramural gas was present in 14 cases (20%) with suspected acute gangrenous cholecystitis. Further abdominal CT scan was done to verify the presence of complications. Gallbladder hydrops: distension of the gall bladder greater than 8 cm longitudinally or 5 cm transversely was found in 36 cases (52%).

Table(6):Distributionof thestudiedcasesaccordingtoUltrasoundfindings

	No.	**%**
3.5-4mm(ormore)thick gallbladderwall	70	100.0
Pericholecysticfluidcollection	56	80.0
Intraluminalgas	14	20.0
PositiveultrasonographicMurphy'ssign	11	16.0
Echogenicbile(sludge)	56	80.0
Hydrops: distension of the gall bladder greater than 8 cm longitudinally or5 cm transversely	36	52.0


ultrasonic findings
70
60
50
40
30
20
10
0
70
56
14
11
56
36
thick gall bladder wall
Pericholecystic fluid...
Intraluminal gas
Positive...
Echogenic bile (sludge)
Hydrops
ultrasonic findings

Computed tomography (CT) and magnetic resonant cholangiopancreatography (MRCP) (table VII)

Abdominal CT was indicated in 31 cases (44%) in whom complications were suspected. In all of these cases WBCs count was elevated 18000 cell\ml or more. There were clinical doubt of complications as high grade fever, tachycardia and exaggerated abdominal pain.Also, they had ultrasonographic findings that suggest complications as intramural gases.

MRCP was done only in one case who had jaundice to exclude biliary obstruction. MRCP was negative for biliary stones or lesions. Total serum bilirubin may be elevated without definite pathological lesions in particular cases with acute calcular cholecystitis.

Table(7):Distribution of the studied cases according to Abdominal computed tomography (CT) and Magnetic resenonantcholangio-pancreatography (MRCP)

	No.	**%**
Abdominalcomputedtomography(CT)		
Yes	11	44.0
No	14	56.0
Magneticresenonantcholangio-pancreatography (MRCP)		
Yes	1	1.43
No	69	98.57

Table 8: Intraoperative data of the studied groups

		Group A (n=35)	Group B (n=35)	P value
Operative time (min)	Mean ± SD	64.29 ±15.15	73.29 ± 22.19	0.052
	Range	35 – 110	40 – 90	
Difficulty	Simple	9 (25.71%)	13 (37.14%)	0.361
	Medium	21 (60%)	20 (57.14%)	
	Difficult	5 (14.29%)	2 (5.71%)	
Drain		35 (100%)	35 (100%)	---
Adhesions		26 (74.28%)	35 (100%)	0.008*
Complications	Bleeding	6 (17.14%)	5 (14.29%)	0.743
	Bile duct injury	0 (0%)	0 (0%)	---
	Intestinal injury	0(0%)	0 (0%)	---
	Conversion to open	0 (0%)	0 (0%)	---

Operative time, difficulty and bleeding were insignificantly different between both groups. Drain significantly higher in group A than group B while adhesions are higher in group B than group A.Intestinal injury and conversion to open didn't occur in any patients in both groups.

Table 9: Postoperative data of the studied groups

		Group A (n=35)	Group B (n=35)	P value
Analgesic requirement	<3 doses	10 (28.57%)	22 (62.86%)	0.004*
	>3 doses	25 (71.43%)	13 (37.14%)	
Complications	Bleeding	2 (5.71%)	1 (2.86%)	1
	Bile leakage from the drain	1 (2.86%)	0 (0%)	1
	Jaundice	0 (0%)	0 (0%)	---

Drain removal after operation	24 h after surgery	9 (25.71%)	25 (71.42%)
	>24 h after surgery	26 (74.28%)	10(28.57%)

	Group A	Group B	P value
Hospital stay in days	2.18 ± 0.38 d	2.68 ± 1.04	0.009

Auscultation of peristalsis and the start of oral fluid intake

Peristalsis was audible and oral fluid intake started in the same day of surgery in 53 cases (76%), oral fluid intake commenced on the first postoperative day in 17 patients (24%).

Postoperative complications

No cases of common bile duct (CBD) injuryor post-operative jaundice that indicates missed CBD stones were noted.

In one case (1.4%) bile leak was noted from the drain, it was 100 ml in day one postoperatively, 50 ml in second day and stopped in day three and the patient was discharged without fever nor jaundice.

Inonecase(1.4%)portsiteinfectionthatwas managedconservatively.

Postoperative follow uptable(XI)

The postoperative ultrasound controls at one month from discharge in all cases showed normal size of the main biliary tract with no suspicion of missed stones. There were minimal fluid collection in surgical bed of gallbladder in five patients (20%) without any clinical manifestations. They needed no further surgical nor radiological interventions with evidence of significant progressive regression in fluid amount during regular ultrasonographic follow up.

Table (10): Distribution of the studied cases according to One month postoperative abdominal ultrasonography follow up

	No.	**%**
Free	69	98.58
Smallsubhepaticpartiallyloculatedfluid collection	1	1.42

Discussion

Acute cholecystitis is the most common acute disease in hepatobiliary surgery and one of the most common diseases in digestive tract surgery in general. With aging, the incidence increases from 4% in the third decade to 27% in the seventh decade of life **(Janjic et al., 2020)**.

Laparoscopic cholecystectomy (LC) has now replaced open cholecystectomy (OC) as the first choice in the treatment of AC unless contraindications to LC are found. In clinical practice in many countries, LC is not usually performed during the acute episode of AC for many reasons **(Arafa et al., 2019)**.

Early laparoscopic cholecystectomy (ELC) is defined as an operation performed within 72 hours of the onset of symptoms of acute calcular cholecystitis, while delayed laparoscopic cholecystectomy (DLC) is performed after a period of conservative treatment to allow the inflammation to subside, typically after 6 weeks or more **(Rian, 2020)**.

However, many previous studies have shown early LC (ELC) to be beneficial with regard to lower hospital costs and a shorter length of stay compared with delayed LC (DLC) **(Janjic et al., 2020)**.

A laparoscopic cholecystectomy is usually delayed because of fears that early surgery may be associated with a higher rate of morbidity including post operative bile leakage, and a higher rate of conversion to open surgery. The updated Tokyo Guidelines suggest that an early laparoscopic cholecystectomy (ELC) is mandatory for patients with mild cholecystitis, whereas

delayed laparoscopic cholecystectomy (DLC) can be performed in patients with moderate or severe cholecystitis**(Gomi et al., 2018)**.

Although the laparoscopic cholecystectomy is currently the gold standard treatment for symptomatic gallstone disease, the optimal timing of a cholecystectomy in patients with acute cholecystitis remains controversial **(Yuksekdag et al., 2021)**.

Therefore, the aim of this work was to compare early versus delayed Laparoscopic cholecystectomy for acute calcular cholecystitis regarding intraoperative findings, difficulties, possible complications and the postoperative outcomes.

This prospective randomized study was conducted on 70 patients diagnosed with acute calcular cholecystitis who were categorized into two groups; Group (A) who underwent early laparoscopic cholecystectomy within 1 week from onset of symptoms, and Group (B) who underwent delayed laparoscopic cholecystectomy at 6-8 weeks after the last attack of acute cholecystitis.

In our study ,The mean age of patients was 46.06 ± 8.5 years , range 22 – 57 years in group A .,while in group B , The mean age of patients was 43.86 ± 6.78 years , range 19 – 53 years .The median age of patients in this study is similar to that of other studies.

All patients in this study presented with right hypochondrial pain , 92% of patients suffered from fever, positive Murphy's sign was elicited in 100% of patients and only one patient had jaundice (4%).

In the study **Chau, Tang et al**, 21 patients (67.7%) had fever.

In the study **Ozkardes, Tokac et al**, all patients had tenderness and pain in the upper abdominal area and 90% had Murphy sign positive.

The most important laboratory investigations that were observed in our study were white blood cell count (WBC) and C-reactive protein (CRP). WBC count was elevated in all cases ranged from 12000 to 24300 c\ml^3. The mean WBCs count was 18.04 ± 3.87 c\ml^3.It was 18000 c\ml^3 or more in 44% of cases. CRP ranged from 3.0 to 16.0 U\L with median 10.0 ± 4.04 U\L. The WBC counts and serum CRP levels at admission significantly predicted the severity of acute cholecystitis.

In the study **Merriam, Kanaan et al** , all patients had elevated WBC count, patients with gangrenous cholecystitis exhibited a significantly higher degree of leukocytosis compared to patients with non gangrenous cholecystitis (17,000 ± 600 vs 11,000 ± 300 WBC/mL^3). In **Stevens, Chi et al** , 151 patients (60%) had leukocytosis more than 10,400 c\ml^3.

In the study **Yacoub, Petrosyan et al**, the mean WBC count in patients with acute calcular cholecystitis was 13500 c\ml^3.

In the study **Yetkin, Uludag et al**, 60 cases (55.55%) had leukocytosis.

In the study **Tang and Cuschieri** , elevated C-creative protein and white blood cell count reflect the severity of the inflammation of cholecystitis and have been identified as risk factors for conversion. However, elevated C-creative protein level appears to be the most powerful predictor for conversion, followed WBC count.

In the current study, ALT, AST, direct bilirubin, total bilirubin and alkaline phosphatase were insignificantly different between both groups.

In our study ultrasonography was the first radiological investigation required which revealed gallstones and 3.5 - 4 mm or more thick gall bladder wall in all cases, pericholecystic fluid collection in 56 (80%) cases, echogenic bile (sludge) also in 56 (80%) cases, distension of the gall bladder greater than 8 cm longitudinally or 5 cm transversely was detected in 36 (52%) cases, Intraluminal gas in 14 (20%) cases and positive ultrasonographic Murphy's sign was found in 11 (16%) cases.

In the study **Pinto, Reginelli et al** , ultrasound is the preferred imaging examination for the diagnosis of acute cholecystitis and is the first method used when the clinical presentation is suggestive of biliary pathology. Ultrasound has the best sensitivity and specificity for evaluating patients with suspected gallstones. An increased gallbladder wall thickness of > 3.5 mm is a reliable and independent predictor of acute cholecystitis and has a positive predictive value of 95% for the diagnosis of acute cholecystitis.

In the study **Peng, Sheikh et al** , abdominal ultrasonogrphy revealed gallbladder wall thickened more than 3 mm in 37 (70%) patients, pericholecystitic fluid in 5 (9%) patients, positive sonographic Murphy's sign in 3(6%) patients, sludge within gallbladder in 2(4%) patients and distended gallbladder in 0ne (2%) patient.

In the study **Kolla, Aggarwal et al** , among 20 patients who underwent early laparoscopic cholecystectomy within the first day of admission, abdominal ultrasound revealed the presence of gallstones in 20 (100%) patients, thickened edematous gallbladder wall in 12 (60%) patients, distended gallbladder in 17 (85%) patients, U/S Murphy's sign positive in 11 (55%) patients and pericholecystic fluid in 3 (15%) patients.

In our study abdominal CT scan was done for 31 cases(44%) to confirm the diagnosis as sonography was inconclusive and to exclude complications, such as gangrenous, emphysematous cholecystitis or gallbladder perforation. Presenting findings that favor abdominal CT scan for such patients were WBCs count 18000 cell\ml or more, male gender, high grade fever, tachycardia and exaggerated abdominal pain with rigidity. Also, ultrasonographic findings that suggest complications as intramural gases, presence of heterogeneous or striated thickening of the gallbladder wall and pericholecystic fluid collections. The presence of intraluminal membranes representing desquamative gallbladder mucosa is a specific finding of gangrenous

cholecystitis but is less common. MRCP is a safe and sensitive imaging technique for common bile duct pathology, when used to exclude CBD stones. It was done for one patient who suffered from jaundice and was negative for biliary stones or lesions. Total serum bilirubin may be elevated without definite pathological lesions in particular cases with acute calcular cholecystitis.

In the study **Bennett et al** , CT achieved a high specificity for the diagnosis of acute gangrenous cholecystitis (96%) with a low sensitivity (29.3%). The CT findings with the highest specificity for gangrenous cholecystitis were gas in the wall or lumen, intraluminal membranes, irregular or absent wall and pericholecystic abscess.

In our study, the mean operative time was 64.29 ±15.15 minutes for group A and 73.29 ± 22.19 minutes for group B .

In the study **Zhu, Zhang et al** , the average duration of surgery was 44.1 minutes (SD 5.32) for early surgery, and 66.4 minutes (SD 3.05) for late surgery, this difference was statistically significant.

In the study **Tzovaras, Zacharoulis et al** , the mean operative time was 55 minutes (ranged from 35 to 90 min) in the first group who underwent laparoscopic cholecystectomy within the first three days from onset of symptoms , it was 62.5 min (25-120 min) in the second group who underwent surgery between 4^{th} to 7^{th} days from onset of complain and it was 72.5 min (35-120 min) in the 3^{rd} group who were operated after the first week.

In the present study, postoperative pain severity assessment was achieved according to visual analog scale within 24 hours postoperatively. It ranged from 1 to 7 with a mean of 2.48. The median was 2.0.

In the study **Rouf Gul et al** , the mean visual analog score of postoperative pain within the first 24 hours after surgery was 2.83±0.834 in the early group who underwent surgery within 1 week of complain and it was 2.50±0.861 in the delayed surgery group after 6-8 weeks with no statistically difference.

Laparoscopic cholecystectomy in acute setting is definitely more difficult due to adhesions and bleeding. As a result for the purpose of ease , a number of modifications can be adapted like using a 5th port, emptying the gall bladder before grasping, subtotal cholecystectomy etc. Also subhepatic drain can be placed for controlling bile leak which is expected more in acute setting **(Ibrarullah et al., 2023)**.

In our study, controlled Intra-operative bleeding is reported in 6 cases (17.14%) of group A and in 5 cases (14.29%) of group B. Bleeding occurred during dissection on bed or callot triangle or vascular injury. Drain is reported in all cases of both groups

In our study there were no cases of common bile duct (CBD) injury or intestinal injuries or conversion to open cholecystectomy or even post-operative jaundice that indicates missed CBD stones. Also, there were no deaths in our study.

Concerning adhesions , All cases of group B have intra-operative adhesions. Only 25% of cases of group A have no adhesions if presented and operated early during the acute attack

In one case , bile leak was noted from the drain and stopped in day three postoperatively with no need for further investigations or surgical intervention, the patient was discharged without fever nor jaundice.

In one case , port site infection that was managed conservatively.

In the study **Casillas et al** , in the late laparoscopic cholecystectomy group, there was one case with minor bile duct injury, resulting in cystic duct stump leak and biloma that was treated by percutaneous drainage and endoscopic retrograde cholangiography with stenting, while in early group there were no significant complications noted.

In the study **Melloul et al**, in the early cholecystectomy group, minor complications included two cases of paralytic ileus, two abdominal wall abscesses, and one cholangitis. Major complications occurred in 21% after early cholecystectomy. Severe bleeding from the gallbladder bed and high-output biliary leak in two patients each required open reoperation at postoperative day one

In the study **Peng et al**, there was a higher rate of postoperative bile leakage in early operations after 48 hours of onset of symptoms (4 cases _ 7.6%_) than for surgery within 48 hours (no cases), but the difference was not significant (P value = 0 · 400).

In the study **Tzovaras et al**, no major bile duct injuries occurred. Four cases had bile leak, two in the intermediate group who underwent surgery from 4^{th} to 7^{th} day of onset of symptoms and two in the "delayed" group who underwent surgery beyond the 8^{th} day. The first was attributed to the gallbladder fossa, the second from an avulsed cystic duct and the remaining two from a friable cystic stump. The first case eased spontaneously after 48 h, the other three cases with bile leak were treated successfully with ERCP, sphincterotomy and stenting of the common bile duct. There was only one case complicated with wound infection and treated with surgical debridement.

In the study **Chau, Tang et al** , Two patients in the laparoscopic cholecystectomy group had surgery complicated by cystic stump leakage, which was confirmed at postoperative ERCP and one patient complicated with wound infection and managed conservatively. There was no major bile duct injury for patients in this study.

(El-Kordy et al., 2019) showed that the Intra-operative bleeding occurred once in group (A) and didn't occur in group (B) and it was due to avulsion of the cystic artery due to its difficult dissection with no significant difference between groups. Conversion to open cholecystectomy with ligation of the bleeding vessel was done after a

failed trial of controlling the artery during laparoscopy.

The pathophysiological basis for these results lies in understanding the progression of the acute inflammatory process. Early in the course of acute cholecystitis, the inflamed, edematous tissues are often helpful in delineating tissue planes. As inflammatory process continues these normal tissue planes are replaced by fibrotic adhesions that make dissection difficult **(Salem et al., 2018)**.

In the present study, the mean hospital stay was 2.18 ± 0.38 days for group A and 2.68 ± 1.04 days for group B and this is one of the main advantages of early cholecystectomy in shortening the hospital stay and preventing recurrent attacks of biliary pancreatitis that require readmission to the hospital. This mean postoperative hospital stay showed a little difference from that of other studies.

In the study **Osman, Ebru et al**, the mean postoperative hospital stay was 1.5 days. In the study **Yetkin, Uludag et al**, the mean hospital stay was 1.48 days.

In the study **Asif Saeed et al**, the mean hospital stay was 2 days.

In the study **Tzovaras, Zacharoulis et al**, the mean hospital stay postoperatively was 2 days in group I of patients who underwent laparoscopic cholecystectomy in the first three days of onset of complain, it was also two days for group II who underwent surgery between 4^{th} to 7^{th} day of complain and the same for group III of patients who were operated beyond the day eight of onset of symptoms. There were no significant differences in postoperative hospital stay between the early and delayed groups.

The drain was removed 24 h after laparoscopic cholecystectomy, unless there was bile (any amount) or 100 mL of blood in the drain bag. In case the drain had to stay in place for bile leak, it was not removed, unless the leak had completely ceased. In case the drain had to stay in place for bleeding, it was removed when the amount was 100 mL/24 h and the patient was hemodynamically stable with stable hemoglobin (no decrease >1 g/dL). Intra-abdominal fluid collections >50 mL were followed up with serial ultrasonographic examinations, and patients were discharged if no increase was detected.

In our study , Drain was removed 24 h after operation at 9 (25.71%) of cases of group A and 25 (71.42%) of cases of group B. Drain was left for > 24 h after operation at 26 (74.28%) of cases of group A and 10 (28.57%) of cases of group B. It depended on the drain bag output respective to color and amount of the discharge.

Conclusions:

Early LC seems to offer a preferable approach for patients with ACC providing a more efficient treatment with less postoperative pain and shorter hospitalization, indicating a faster recovery.

There are no significant differences in the preoperative clinical presentations (symptoms and laboratory findings) or most intraoperative challenges (operative time, difficulty, bleeding, bile duct injury, and conversion to open surgery) between early and delayed LC for ACC. However, significant differences were observed in the presence of adhesions and increased GB wall thickness, favoring early LC.

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