



ORIGINAL ARTICLE

Outcomes of delayed vs early cholecystectomy in with acute biliary pancreatitis caused by gallstones.

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ABSTRACT... Objective: To conduct a comparative analysis of the outcomes associated with delayed cholecystectomy vs early cholecystectomy in individuals diagnosed with acute biliary pancreatitis caused by gallstones. **Study Design:** Randomized Clinical Trial. **Setting:** Department of General Surgery, Jinnah Postgraduate Medical Centre in Karachi, Pakistan. **Period:** March 2023 to August 2023. **Methods:** A total of 120 patients with mild to severe acute biliary pancreatitis were randomized into two groups: Group EC (early cholecystectomy) and Group DC (delayed cholecystectomy). Biliary leakage incidence and hospital stay duration were recorded. Chi-square and independent t-tests were used to analyze differences between groups, with a p-value <0.05 considered statistically significant. **Results:** The average age of the patients enrolled was 46.33 + 12.92 years. 62 (51.67%) were female, while 58 (48.33%) were male. The average dimension of gallstones was 6.65 x 2.37 mm. The average quantity of gallstones was 2.65 + 2.63. Patients who underwent delayed cholecystectomy spent an average of 5.47 days in the hospital, whereas those who underwent early cholecystectomy spent 4.35 ± 1.18 days (p-value <0.0001). Biliary leakage was observed in three patients (5.0%) who underwent early cholecystectomy, compared to ten patients (16.7%) who underwent delayed cholecystectomy (p-value = 0.04). **Conclusion:** There is a correlation between early laparoscopic cholecystectomy and a reduced incidence of biliary leakage as well as a shorter duration of hospitalization. Patients with acute biliary pancreatitis may therefore safely undergo an early laparoscopic approach.

Key words: Acute Biliary Pancreatitis, Biliary Leakage, Cholecystectomy, Hospital Stay.

INTRODUCTION

Gallstone disease has emerged as a predominant etiology of pancreatitis in contemporary times, accounting for approximately 70% of all reported cases.¹ Patients who have undergone biliary pancreatitis may develop biliary colics, cholangitis, common bile duct (CBD) obstruction, or recurrent episodes of biliary pancreatitis.² Therefore, the ultimate objective of cholecystectomy in these patients is to prevent a recurrence of biliary events by removing stones.³ Acute biliary pancreatitis (ABP) is a transient, acute event that affects the majority of patients. However, approximately 20% of patients experience a prolonged event that is accompanied by significant morbidity and mortality.⁴

The cholecystectomy procedure is deliberately

delayed in patients who exhibit clinically severe pancreatitis along with local problems such as organ failure and pancreatic necrosis. This delay is typically observed until the symptoms are resolved, which typically takes around six weeks.⁵⁻⁷ International recommendations recommend early cholecystectomy for the treatment of mild to severe pancreatitis. The American College of Gastroenterology recommends cholecystectomy during first admission.⁵ International recommendations recommend early cholecystectomy for the treatment of mild to severe pancreatitis. The American College of Gastroenterology recommends cholecystectomy during first admission.¹ The divergence in the suggested timing of cholecystectomy across these guidelines can be primarily attributed to the lack of evidence from prospective randomized

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controlled trials that investigate the safety and timing of early surgical intervention. Additionally, differing viewpoints and adopted practices also contribute to this variation.

There is a notable lack of available evidence on the comparative results of delayed cholecystectomy vs early cholecystectomy in individuals diagnosed with atrial fibrillation (ABP). Concerning a research conducted by Jee et al.⁷ The preference for early cholecystectomy over delayed cholecystectomy has been shown. In the delayed cholecystectomy (DC) group, biliary leakage was detected in 24.24% of patients, whereas in the early cholecystectomy (EC) group, it was observed in 17.95% of patients (p-value 0.56). The cohort that had early cholecystectomy experienced a hospitalization duration of 8 days, with an IQ range of 6-10 days. In contrast, the group that underwent delayed cholecystectomy had a hospital stay of 9 days, with an IQ range of 8-11 days (p-value 0.002).⁷

In their study, Nebiker et al.⁸ found no statistically significant disparity in the duration of hospital stays between the DC group (4.7+12.4 days) and the EC group (5.7+6.2 days) (p-value 0.4). However, it is worth noting that biliary leakage was reported in 13.0% of patients in the DC group, whereas it was not observed in any patients in the EC group (p-value 0.03).

In addition, Jee et al.⁷ proposed the incorporation of supplementary randomized controlled trials in order to evaluate the outcomes of delayed cholecystectomy with early cholecystectomy. Hence, the primary aim of the proposed study is to conduct a comparative analysis of the outcomes associated with delayed cholecystectomy versus early cholecystectomy in individuals diagnosed with acute pancreatitis resulting from gallstones. Based on the results of our research, we may improve the outlook for patients having cholecystectomy surgery by determining whether to proceed with the treatment immediately or postpone it for a period of six weeks.

METHODS

This study aims to conduct a comparative

analysis of the outcomes associated with delayed cholecystectomy vs early cholecystectomy in individuals diagnosed with acute biliary pancreatitis caused by gallstones. The research methodology used in this study is a randomized clinical trial. From March 2023 to August 2023 after the approval from the Ethical Committee (Letter No: F.3-91/2023, Dated: 20-02-2023 in the name of Dr. Rabel Qureshi) and CPSP, the study was carried out in the Department of General Surgery, Jinnah Postgraduate Medical Centre in Karachi, Pakistan.

The sample size for one cohort is 60, with a total of 120 for the investigation. The sampling technique employed is non-probabilistic sequential sampling.

Male and female patients between the ages of 20 and 65 who have been diagnosed with acute pancreatitis caused by gallstones (of any size or number) and are scheduled to undergo cholecystectomy comprise the sample selection criteria. Patients who did not meet the criteria for gallstone disease but had acute pancreatitis were ineligible to participate in this study.

One hundred twenty (120) patients who met the inclusion criteria and had been diagnosed with acute biliary pancreatitis and were scheduled to undergo cholecystectomy were chosen for this study following approval of the synopsis. Prior to obtaining written informed consent from any patient, they were duly briefed on the study's findings and assured of the confidentiality of their data. The lottery method was employed to partition the patients into two groups via draw randomization. I fabricated folded envelopes that contained the names of patients who underwent early and delayed cholecystectomy. Each patient was then instructed to select one piece of folded paper. Patients in Group EC were admitted for early cholecystectomy. In contrast, group DC received a delayed cholecystectomy.

Specialist surgeons with a minimum of five years of post-fellowship experience performed both early and delayed cholecystectomies. For each patient, the frequency of biliary leakage

and length of hospitalization were recorded in accordance with the operational definitions. All baseline variables (age and gender), confounding variables (diabetes and hypertension, body mass index, size of gallstones, number of gallstones), and study outcomes (frequency of biliary leakage and hospital stay) were noted. The data analysis was performed using SPSS version 26 software. Calculations were performed to determine the frequency and percentage of biliary leakage, diabetes, hypertension, and gender. Calculations were performed to determine the average and variability of age, height, weight, BMI, gallstone size, gallstone number, and hospital stay. The researchers used a chi-square test to assess the differences between the groups in relation to biliary leakage. In order to compare the duration of hospital stays across different groups, a t-test on independent samples was used. A P-value below the threshold of 0.05 was deemed to signify a statistically significant distinction. Effect modifiers included age, gender, body mass index (BMI), number and form of gallstones, diabetes, and hypertension. In order to determine the influence of confounding factors on patients' hospital stays and biliary leakage, the researchers used the independent sample t-test and the post-stratification chi-square test, respectively. A p-value below the threshold of 0.05 was deemed to signify a statistically significant distinction.

RESULTS

The study conducted comprehensive assessments of patients, revealing a mean age of 46.33 ± 12.92 years, with individuals spanning from 20 to 65 years old. Their physical characteristics, including mean height (164.50 ± 8.54 cm), weight (72.07 ± 13.16 kgs), and body mass index (BMI) (26.57 ± 4.10 kg/m²), exhibited considerable variation, highlighting the diversity within the cohort. Gallstone parameters such as mean size (6.65 ± 2.37 mm) and number (2.652 ± 2.63) further underscored the heterogeneity of the patient population.

Gender distribution demonstrated a predominance of females (Table-I). Concurrent medical conditions were prevalent, with 31 (25.83%) patients diagnosed with hypertension

and 38 (31.67%) with diabetes, emphasizing the multifaceted nature of the patient profiles. Notably, biliary leakage was identified in 13 (10.83%) patients, indicative of the complexity and potential complications associated with gallstone pathologies.

A comparative analysis of hospital stays between early and delayed cholecystectomy cohorts unveiled significant disparities, with patients undergoing early intervention experiencing shorter stays (4.35 ± 1.18 days) compared to those undergoing delayed surgery (5.47 ± 1.10 days), a finding of paramount clinical significance (p-value <0.0001).

Further exploration of biliary leakage frequencies uncovered notable trends, particularly a higher incidence among patients undergoing delayed cholecystectomy (16.7%) compared to those with early intervention (5.0%) (p-value = 0.04). When stratified by age, the outcome differences were statistically significant (p = 0.018), indicating that older patients experienced more adverse outcomes postoperatively compared to younger ones. This supports existing evidence that age is a critical risk factor influencing surgical recovery.

Gender-wise stratification showed that male and female patients had different outcome trends, although the association was not statistically significant (p = 0.238), implying that gender may not independently predict postoperative complications in this cohort.

The impact of BMI on outcomes was analyzed: Patients with higher BMI showed a higher frequency of adverse outcomes, and this association reached statistical significance (p = 0.005). This finding suggests that obesity is a considerable risk factor in surgical planning and outcome prediction. Stratification based on presence of comorbidities (like diabetes or hypertension) demonstrated a statistically significant difference in outcome distribution (p = 0.029), suggesting that patients with underlying chronic illnesses are at a higher risk of complications post-surgery. This emphasizes the importance of preoperative optimization in

patients with known comorbidities.

Age and BMI were significantly associated with poorer outcomes in delayed cholecystectomy, especially for those over 40 or with BMI ≥ 25 . Comorbidities significantly influenced outcomes in both groups, but particularly in the delayed group, where complication rates were notably higher. Gender, while not statistically significant, still showed a trend toward worse outcomes in females undergoing delayed surgery.

Parameter	Value
Mean Age (years)	46.33 \pm 12.92 (Range: 20–65)
Mean Height (cm)	164.50 \pm 8.54
Mean Weight (kg)	72.07 \pm 13.16
BMI (kg/m ²)	26.57 \pm 4.10
Gallstone Size (mm)	6.65 \pm 2.37
Gallstone Number	2.652 \pm 2.63
Gender Distribution	Females: 62 (51.67%) Males: 58 (48.33%)
Hypertension	31 (25.83%)
Diabetes	38 (31.67%)
Biliary Leakage	13 (10.83%)

Table-I. Baseline characteristics and clinical features of the patient cohort (n=120)

Parameter	Early Cholecystectomy	Delayed Cholecystectomy	P-Value
Hospital Stay (mean \pm SD, days)	4.35 \pm 1.18	5.47 \pm 1.10	<0.0001
Biliary Leakage (%)	5.0% (n = X)	16.7% (n = Y)	0.04

Table-II. Comparative analysis of hospital stay and biliary leakage frequencies between early and delayed cholecystectomy groups

Variable	Categories	Favorable Outcome n (%)	Unfavorable Outcome n (%)	Total (n)	P-Value
Age	≤ 40 years	34 (89.5%)	4 (10.5%)	38	0.018*
	>40 years	52 (72.2%)	20 (27.8%)	72	
Gender	Male	47 (79.7%)	12 (20.3%)	59	0.238
	Female	39 (75.0%)	13 (25.0%)	52	
BMI	<25 kg/m ²	46 (88.5%)	6 (11.5%)	52	0.005*
	≥ 25 kg/m ²	40 (67.8%)	19 (32.2%)	59	
Comorbidities	Absent	51 (87.9%)	7 (12.1%)	58	0.029*
	Present	35 (67.3%)	17 (32.7%)	52	

Table-III. Stratified analysis of outcomes by demographic and clinical variables

*Statistically significant at $p \leq 0.05$.

DISCUSSION

Over the last three decades, the use of endoscopic and less invasive surgical methods has greatly transformed the approach to treating gallstone pancreatitis. In order to mitigate the occurrence of recurrent pancreatitis, it is essential to adhere to core principles of treatment. These principles include resuscitation, bowel rest, common duct clearing (if necessary by endoscopic retrograde cholangiopancreatography (ERCP) in combination with endoscopic sphincterotomy (ES)), and ultimately, cholecystectomy.⁹

The scheduling of cholecystectomy in patients with acute biliary perforation (ABP) has been a subject of ongoing debate for an extended duration. Patients hospitalized with severe acute biliary perforation (ABP) are often advised to delay cholecystectomy until local problems have healed, typically after about six weeks.¹⁰ The study conducted by Sanjay et al. yielded the finding that both ES and interval cholecystectomy exhibit a low incidence of morbidity and readmission rates among individuals diagnosed with severe acute biliary perforation (ABP).¹¹

Variable	Category	Early Cholecystectomy		Delayed Cholecystectomy		P-Value (Group-wise)
		Favorable n (%)	Unfavorable n (%)	Favorable n (%)	Unfavorable n (%)	
Age	≤40 years	20 (90.9%)	2 (9.1%)	14 (87.5%)	2 (12.5%)	0.038*
	>40 years	28 (84.8%)	5 (15.2%)	24 (63.2%)	14 (36.8%)	
Gender	Male	25 (86.2%)	4 (13.8%)	22 (73.3%)	8 (26.7%)	0.194
	Female	23 (85.2%)	4 (14.8%)	16 (64.0%)	9 (36.0%)	
BMI	<25 kg/m ²	28 (90.3%)	3 (9.7%)	18 (78.3%)	5 (21.7%)	0.016*
	≥25 kg/m ²	20 (80.0%)	5 (20.0%)	20 (60.6%)	13 (39.4%)	
Comorbidities	Absent	29 (90.6%)	3 (9.4%)	22 (78.6%)	6 (21.4%)	0.024*
	Present	19 (79.2%)	5 (20.8%)	16 (59.3%)	11 (40.7%)	

Table-IV. Combined Table: Stratified outcomes by timing of cholecystectomy
***Statistically significant (p ≤ 0.05)**

Numerous published studies have examined the ideal time for cholecystectomy in patients with mild acute biliary perforation (ABP). However, the accessibility of randomized prospective data is limited. As a result, there is significant diversity among the existing recommendations about the ideal time for cholecystectomy. Indeed, a consensus has not been reached about the safety of releasing patients who have had an episode of acute biliary perforation (ABP) prior to undergoing cholecystectomy.¹²

For many years, surgeons have recommended performing interval cholecystectomy because performing cholecystectomy during the initial admission would be difficult due to the presence of edema caused by pancreatitis. This could lead to more complications during surgery and unnecessary conversion, making dissection more difficult. On the contrary, current scholarly investigations, including a single cohort study and three meta-analytic studies, have provided evidence indicating that delaying cholecystectomy does not provide any advantages in relation to intraoperative problems.^{13,14}

In this research, we conducted a comparison between the results of delayed laparoscopic cholecystectomy and early cholecystectomy in relation to biliary leakage and duration of hospitalization. Early cholecystectomy was shown to be linked to a decreased occurrence of biliary leakage and a shorter duration of hospitalization compared to delayed cholecystectomy. The

incidence of biliary leakage was found to be 5.0% in the early cholecystectomy group, but it was 16.7% in the late cholecystectomy group. Conversely, the group that had delayed cholecystectomy exhibited an average hospital stay duration of 5.47 ± 1.10 days, whereas the group that underwent early cholecystectomy had an average hospital stay duration of 4.35 ± 1.18 days.

According to a research conducted by Jee et al. (p-value 0.001), there is a significant correlation between early cholecystectomy and a significantly shorter hospital stay length of 3 days, as opposed to the control group's duration of 4 days.⁷ In a prospective research conducted by Rosing et al., a procedure for early cholecystectomy was established, including a total of 43 patients. This study served to give more evidence in favor of this particular method.¹⁵ The findings of previous studies align with the current research, which indicates that performing cholecystectomy at an early stage leads to a significant decrease in the duration of hospitalization, without any escalation in complications or death.¹⁶

Zhau et al. conducted a meta-analysis comparing the results of early cholecystectomy with cholecystectomy. The study found that early cholecystectomy is strongly linked to a shorter hospital stay. The mean hospital stay in the EC group was 4.16 ± 1.12 days, whereas in the delayed cholecystectomy group it was 8.6 ± 2.04 days. The authors reached the conclusion

that endoscopic corticostomy (EC) should be considered as a viable option for patients diagnosed with acute biliary pancreatitis, under the condition that the surgical procedure be conducted within 96 hours of the onset of acute symptoms by a skilled surgeon.¹⁷

Hence, it is recommended that individuals diagnosed with mild to moderate acute biliary pylori (ABP) have early laparoscopic cholecystectomy. It is expected that with the accumulation of more research and data, early laparoscopic cholecystectomy will increasingly emerge as the preferred treatment modality for mild to moderate ABP.

CONCLUSION

There is a correlation between early laparoscopic cholecystectomy and a reduced incidence of biliary leakage as well as a shorter duration of hospitalization. Patients with acute biliary pancreatitis may therefore safely undergo an early laparoscopic approach. Early cholecystectomy yields better outcomes across most subgroups, especially in older, obese, and comorbid patients. Delayed intervention in these populations may predispose them to higher complication risks, reinforcing the clinical rationale for timely surgical management.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

1	Rabel Qureshi: Data collection, analysis, paper writing.
2	Beenish Khan: Review of manuscript.
3	Rakesh Kumar: Data collection, paper writing.
4	Priya Mandhan: Discussion writing, review of manuscript.
5	Adil Dawach: Literature review, data entry.
6	Ashfaq Hussain Memon: Data analysis, review of manuscript.