

Outcomes of Early versus Delayed Cholecystectomy in Patients of Acute Biliary Pancreatitis

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Abstract

INTRODUCTION: Gallstones cause acute pancreatitis (AP) in more than 75% of patients in developed countries. Pancreatitis affects 80% of patients with a mild onset (Atlanta classification). Acute biliary pancreatitis is responsible for 40% to 70% of all acute pancreatitis cases. The primary pathophysiological mechanism of gallstone pancreatitis is biliary obstruction, which leads to pancreatic inflammation. Cholecystectomy is the most effective treatment for preventing AP caused by gallstones from recurring. According to previous research, cholecystectomy recurrence can occur in up to 33% of cases.

OBJECTIVE: To determine the outcomes of early versus delayed cholecystectomy in patients of acute biliary pancreatitis caused by gallstones.

STUDY DESIGN: Descriptive Cross sectional Study.

SETTING: This study was conducted in the department of General Surgery, Bolan Medical Complex Hospital Quetta Pakistan.

DURATION: August 23, 2020 to August 24, 2021.

MATERIALS AND METHODS: After approval of synopsis, a total one hundred and sixteen (116) patients with diagnosis of mild to moderate acute biliary pancreatitis were included in this study. All patients were asked to sign a written informed consent by first briefing them about the outcomes of study and ensuring them the confidentiality of their data. For randomly dividing the patients into two each groups (early versus delayed) by using sealed-envelops method of randomization. Hospital stay between the groups was compared using independent sample t-test. Chi-square test was applied to compare qualitative (conversion rate, biliary leakage and mortality) variables between the groups. P-value ≤ 0.05 was taken as significant difference.

RESULTS: Age range in this study was from 20 to 65 years. The mean age in early group was 32.5 ± 11.47 years and in delayed group, the mean age was 32.5 ± 11.47 years. None of the patients underwent early cholecystectomy has biliary leakage 0 (0%). Thirteen patients 24 (41.33%) in the delayed group had biliary leakage, significant difference was observed (p-value < 0.05). 9 (15.5%) of the patients in early group had wound infection, whereas, in delayed group, 17 (29.3%) had wound infection; significant difference was observed (p-value < 0.05). None of them were converted to open cholecystectomy in both groups, no significant difference was observed. Both group had same mortality rate i.e. 1(1.7%), no significant difference was observed. The delayed group had higher length of hospital stay i.e. 8.87 ± 1.65 as compared to early group i.e. 8.87 ± 1.65 , significant difference was observed (p-value < 0.05)

CONCLUSION: In conclusion, postoperative complications are associated more with delayed laparoscopic cholecystectomy compared with early intervention, early laparoscopic cholecystectomy should be preferred by surgeons for treatment of acute cholecystitis with the advantage of shorter hospital stay and lower complication rate.

Keywords: Biliary pancreatitis, cholecystectomy, recurrent biliary events, ERCP

INTRODUCTION

Gallstones cause acute pancreatitis (AP) in more than 75% of patients in developed countries (1). Pancreatitis affects 80% of patients with a mild onset (Atlanta classification) (2). Acute biliary pancreatitis is responsible for 40% to 70% of all acute pancreatitis cases (3, 4). The primary pathophysiological mechanism of gallstone pancreatitis is biliary obstruction, which leads to pancreatic inflammation (5).

Cholecystectomy is the most effective treatment for preventing AP caused by gallstones from recurring. (6, 7). According to previous research, cholecystectomy recurrence can occur in up to 33% of cases (8).

One of the major concerns for general surgeons is the time it takes to operate on AP patients, which is still debatable (9-11). Patients with acute gallstone pancreatitis (AGP) should be treated as soon as they recover from the attack, according to the International Association of Pancreatology (IAP), and these patients should be operated on during the same hospital stay, according to the American College of Gastroenterology (ACG) (3). The British Society of Gastroenterology and the American Gastroenterological Association recommend that cholecystectomy be performed during the same hospital stay or within two weeks of the patient's discharge (12, 13).

Cholecystectomy is still not widely performed in index hospital stays, despite recent guidelines and published literature. Because of the risk of complications from early surgery in these patients, many hospitals delay cholecystectomy until all vital laboratory parameters have returned to normal and abdominal pain has subsided (14, 15).

Only 14.7% of ABP patients are operated within the same hospital admission, according to a study conducted in England with 25,000 patients (16).

According to a study from the United States, only 50% of ABP patients who are admitted are operated in the same hospital admission. Many of the admitted patients in these centers are not operated in the same hospital admission, especially in centers where cholecystectomy is not performed on a large scale (17).

According to Jee et al research's early cholecystectomy is preferable to delayed cholecystectomy. Biliary complications occurred 44.12 percent of the time in the delayed cholecystectomy (DC) group and 0.0 percent of the time in the early cholecystectomy (EC) group, with an average hospital stay of 8 days in the early cholecystectomy group and 9 days in the delayed cholecystectomy group (p-value 0.002). (18). While Nebiker et al. found no significant difference in hospital stay between the DC and EC groups (4.7 days in DC and 5.7 days in EC), biliary leakage occurred in 13.0 percent of DC patients versus 0.0 percent in the EC group (19).

According to our best literature review, studies on the outcomes of EC and DC in patients with acute biliary pancreatitis caused by cholelithiasis have produced mixed results. Jee et al. also suggested that more randomized controlled trials be conducted to compare the outcomes of early and delayed cholecystectomy (18). The proposed study's goal was to compare the outcomes of early cholecystectomy versus delayed cholecystectomy in patients with acute pancreatitis due to gallstones.

1. Acute Biliary Pancreatitis:

A patient was labelled as having AGP if they fulfilled the following criteria: a history of acute upper abdominal pain, nausea, vomiting and tenderness in the epigastrium, an increase in the levels of serum amylase more than three times the upper limit of normal, an increase in the levels of serum lipase and detection of gallstones on ultrasonography. The classification of mild to moderate pancreatitis was based on the following criteria: A Ranson's score (RS) of <3 was labelled as mild and 3-6 was considered moderate pancreatitis, no evidence of pancreatic necrosis on abdominal imaging and no evidence of organ failure.

2. Early Cholecystectomy:

Cholecystectomy that was done within the same hospital admission of patient due to pancreatitis caused by gallstones will be labelled as early cholecystectomy (EC).

3. Delayed Cholecystectomy:

Cholecystectomy that was done within 2 to 4 weeks after discharge of acute pancreatitis patient from the hospital was labelled as delayed cholecystectomy.

4. Study Outcomes:

Outcomes of study were measured in terms of hospital stay and biliary leakage

A. Hospital Stay:

The time from the day of surgery to the day of discharge of patients from the hospital was taken as hospital stay time. Post-operative hospital stay was calculated at the time of discharge of patient from the hospital following departmental protocols.

B. Biliary Leakage:

Appearance of bile in the abdominal drains was labelled as biliary leakage.

C. Surgical Site Infections:

The development of purulent discharge at the surgical incision site (detected on routine post-operative examination) either from the superficial incisional or deep incisional surgical site after surgery within the hospital stay period or within seven days after surgery was considered as surgical wound infection.

Sample Size: The sample size for this study was calculated using the following formula;

$$n = (Z_{\alpha/2} + Z_{\beta})^2 * (p_1(1-p_1) + p_2(1-p_2)) / (p_1 - p_2)^2,$$

Frequency of biliary leakage after DC : 13.0%⁸

Frequency of biliary leakage after EC : 0.0%⁸

Sample Size for one group : 58

Total Sample size of the study : 116

SAMPLING TECHNIQUE: Non probability, Consecutive sampling

Inclusion criteria:

- ✓ All diagnosed patients of acute pancreatitis caused by gallstones and planned for cholecystectomy.
- ✓ Patients having age 20-65 years
- ✓ Both genders including male and female

Exclusion Criteria:

Patients were excluded if they had any of the following:

- Severe pancreatitis (defined using Ranson's or Imrie criteria at the time admission).
- Requiring admission to ICU or HDU.
- Having major co-morbidities.
- Pregnant females.

Data Collection Procedure:

After approval of synopsis, a total one hundred and sixteen (116) patients with diagnosis of mild to moderate acute biliary pancreatitis were included in this study. All patients were asked to sign a written informed consent by first briefing them about the outcomes of study and ensuring them the confidentiality of their data (**Annexure II**). For randomly dividing the patients into two each groups by using sealed-envelops method of randomization.

In patients randomized to the early group; these patients were underwent LC within the same hospital admission when the patient not need any opioid for pain relief, and was able to take normal diet and CRP levels was reduced i.e. <100 mg/L.

In the delayed group; in these patients LC was done in same hospital admission, the patients were discharge after medical management but within 6 weeks after discharge from hospital.

Data of patients pre-surgery history, operative variable and post-operative outcomes were collected in a prospective manner for each patient.

Data Analysis Procedure:

Data analysis was carried out using SPSS version 23 Software. Hospital stay between the groups was compared using independent sample t-test. Chi-square test was applied to compare qualitative variables between the groups. P-value ≤ 0.05 was taken as significant difference.

RESULTS

Age range in this study was from 20 to 65 years. The mean age in early group was 32.5 ± 11.47 years with mean height was 181.9 ± 11.8 m, mean weight was 73 ± 21.8 kg and mean BMI was 34.31 ± 3.47 kg/m² and in delayed group, the mean age was 32.5 ± 11.47 years with mean height was 182.7 ± 12.3 , mean weight was 69 ± 22.3 kg and mean BMI was 35.066 ± 2.83 kg/m², **as shown in table 1.**

The early group included 13 (23%) male and 45 (67%) female, whereas, delayed group included 17 (29.3%) male and 41 (70.6%) female, **as shown in table 2.**

In early group, 23 (39.6%) were diabetic, 27 (46.5%) were hypertensive and 11 (19%) were smokers, whereas, in delayed group, 19 (33%) were diabetic, 23 (39.6%) were hypertensive and 13 (22.4%) were smokers, **as shown in table #3.**

None of the patients underwent early cholecystectomy has biliary leakage 0 (0%). Thirteen patients 24 (41.33%) in the delayed group had biliary leakage, significant difference was observed (p-value < 0.05). 9 (15.5%) of the patients in early group had wound infection, whereas, in delayed group, 17 (29.3%) had wound infection, significant difference was observed (p-value < 0.05). None of them were converted to open cholecystectomy in both groups, no significant difference was observed. Both group had same mortality rate i.e. 1(1.7%), no significant difference was observed. The delayed group had higher length of hospital stay i.e. 8.87 ± 1.65 as compared to early

group i.e. 8.87 ± 1.65 , significant difference was observed (p -value < 0.05), as shown in table #9.

The outcomes of both groups were also stratified with respect to age, gender, BMI, hypertension, diabetes and smoking status, as shown in table 4.

Table I: Mean Age of the Patients (Months), Mean Weight of the Patients (kg), Mean Height of the Patients (meter), Mean BMI of the Patients (kg/m²)

Age of the Patients	Mean \pm SD
Group-A	32.5 ± 11.47
Group-B	34.59 ± 10.02
Weight	
Group-A	73 ± 21.8 kg
Group-B	69 ± 22.3 kg
Height	
Group-A	181.9 ± 11.8
Group-B	182.7 ± 12.3
BMI	
Group-A	34.31 ± 3.47
Group-B	35.066 ± 2.83

Table 2: Gender Distribution of the Patients

Gender	Group-A n (%)	Group-B n (%)
Male	13 (23%)	17 (29.3%)
Female	45 (67%)	41 (70.6%)

Table 3: Frequency of Diabetes Mellitus in Patients with Acute Biliary Pancreatitis Underwent for Cholecystectomy, Hypertension in Patients with Acute Biliary Pancreatitis Underwent for Cholecystectomy, Smokers in Patients with Acute Biliary Pancreatitis Underwent for Cholecystectomy

Diabetes Mellitus	Group-A	Group-B
Yes	23 (39.6%)	19 (33%)
No	35 (60.4%)	39 (67)
Hypertension		
Yes	27 (46.5%)	23 (39.6%)
No	31 (53.4%)	35 (60.4%)
Smoker		
Yes	11 (19%)	13 (22.4%)
No	47 (81%)	45 (77.58%)

Table 4: Comparison of Outcomes of Early Versus Delayed Cholecystectomy in Patients of Acute Biliary Pancreatitis Caused by Gallstones, Age between 20 to 40 Years, Age > 40 to 65 Years, in Male Patients of Acute Biliary Pancreatitis Caused by Gallstones., BMI ≤ 29 kg/m², BMI >29 kg/m², Diabetic Patients of Acute Biliary Pancreatitis Caused by Gallstones, Non-Diabetic Patients of Acute Biliary Pancreatitis Caused by Gallstones.

Outcomes	Group-A n (%)	Group-B n (%)	P-value
Biliary Leakage			
Yes	0(0%)	24 (41.3%)	0.00
No	58 (100%)	34 (58.7%)	
Wound Infections			
Yes	9 (15.5%)	17 (29.3%)	0.118
No	49 (84.4%)	41 (70.6%)	
Conversion to open cholecystectomy			
Yes	0(0%)	0(0%)	NA
No	58 (100%)	58 (100%)	
Mortality			

Yes	1(1.7%)	1(1.7%)	
No	57(98.27%)	57 (98.27%)	1.00
Mean Hospital Stay	6.2 ± 2.90	8.87± 1.65	<0.000
Outcomes			
Biliary Leakage			
Yes	0	09	0.000
No	23	18	
Wound Infections			
Yes	03	06	0.467
No	23	21	
Conversion to open cholecystectomy			
Yes	0	0	NA
No	23	27	
Mortality			
Yes	0	0	NA
No	23	27	
Mean Hospital Stay	6.09 ± 2.7	8.85± 1.59	<0.000
Biliary Leakage			
Yes	0	15	
No	35	16	0.000
Wound Infections			
Yes	06	11	0.467
No	29	20	
Conversion to open cholecystectomy			
Yes	0	0	NA
No	35	31	
Mortality			
Yes	01	01	NA
No	34	30	
Mean Hospital Stay	6.2 ± 2.8	8.84± 1.60	<0.000
Outcomes	Group-A (n=13)	Group-B (n=17)	P-value
Biliary Leakage			
Yes	0	06	0.000
No	13	11	
Wound Infections			
Yes	02	05	0.427
No	11	12	
Conversion to open cholecystectomy			
Yes	0	0	NA
No	13	17	
Mortality			
Yes	0	0	NA
No	13	17	
Mean Hospital Stay	6.2 ± 2.7	8.9± 1.5	<0.000
Outcomes	Group-A (n =45)	Group-B (n =41)	P-value
Biliary Leakage			
Yes	0	18	0.000
No	45	23	
Wound Infections			
Yes	07	12	0.193
No	38	29	
Conversion to open cholecystectomy			
Yes	0	0	NA
No	45	41	
Mortality			
Yes	01	01	1.000
No	44	40	

Mean Hospital Stay	6.3 ± 2.7	8.80± 1.69	<0.000
Outcomes	Group-A (n =32)	Group-B (n=31)	P-value
Biliary Leakage			0.000
Yes	0	11	
No	32	20	
Wound Infections			0.365
Yes	05	08	
No	27	23	
Conversion to open cholecystectomy			NA
Yes	00	00	
No	32	31	
Mortality			1.000
Yes	01	01	
No	31	30	
Mean Hospital Stay	6.2 ± 2.7	8.85± 1.63	<0.000
Outcomes	Group-A (n= 26)	Group-B (n=27)	P-value
Biliary Leakage			0.000
Yes	00	13	
No	26	14	
Wound Infections			0.202
Yes	04	09	
No	22	18	
Conversion to open cholecystectomy			NA
Yes	00	00	
No	26	27	
Mortality			NA
Yes	00	00	
No	26	27	
Mean Hospital Stay	6.2 ± 2.90	8.87± 1.65	<0.000
Outcomes	Group-A (n=23)	Group-B (n=19)	P-value
Biliary Leakage			0.000
Yes	00	05	
No	23	14	
Wound Infections			1.000
Yes	04	04	
No	19	15	
Conversion to open cholecystectomy			NA
Yes	00	00	
No	23	19	
Mortality			NA
Yes	01	00	
No	22	19	
Mean Hospital Stay	6.3 ± 2.70	8.79± 1.63	<0.000
Outcomes	Group-A (n=35)	Group-B (n=39)	P-value
Biliary Leakage			0.000
Yes	00	19	
No	35	20	
Wound Infections			0.065
Yes	05	13	
No	30	26	
Conversion to open cholecystectomy			NA
Yes	00	00	
No	35	39	

Mortality			1.000
Yes	00	01	
No	35	38	
Mean Hospital Stay	6.2 ± 2.70	8.87± 1.55	<0.000
Outcomes	Group-A (n=27)	Group-B (n=23)	P-value
Biliary Leakage			0.000
Yes	00	09	
No	27	14	
Wound Infections			0.183
Yes	04	08	
No	23	15	
Conversion to open cholecystectomy			NA
Yes	00	00	
No	27	23	
Mortality			1.000
Yes	00	01	
No	27	23	
Mean Hospital Stay	6.19 ± 2.70	8.85± 1.59	<0.000
Outcomes	Group-A (n=31)	Group-B (n=35)	P-value
Biliary Leakage			0.000
Yes	00	15	
No	31	20	
Wound Infections			0.382
Yes	05	09	
No	26	26	
Conversion to open cholecystectomy			NA
Yes	00	00	
No	31	35	
Mortality			1.000
Yes	01	00	
No	30	35	
Mean Hospital Stay	6.2 ± 2.70	8.87± 1.64	<0.000
Outcomes	Group-A (n=11)	Group-B (n=13)	P-value
Biliary Leakage			0.000
Yes	00	04	
No	11	09	
Wound Infections			1.000
Yes	02	03	
No	09	10	
Conversion to open cholecystectomy			NA
Yes	00	00	
No	11	13	
Mortality			NA
Yes	00	00	
No	11	13	
Mean Hospital Stay	6.2 ± 2.7	8.87± 1.63	<0.000
Outcomes	Group-A (n=47)	Group-B (n=45)	P-value
Biliary Leakage			0.000
Yes	00	20	
No	47	25	
Wound Infections			0.083
Yes	07	14	
No	40	31	
Conversion to open cholecystectomy			NA
Yes	00	00	
No	47	45	

Mortality			1.000
Yes	01	01	
No	46	45	
Mean Hospital Stay	6.2 ± 2.80	8.85± 1.63	<0.000

DISCUSSION

For decades, surgeons believed that laparoscopic cholecystectomy in patients with acute biliary pancreatitis at the time of admission was a risky procedure with a high risk of morbidity and complications. Because of extensive edema and local complications, this is now well established in severe episodes of acute pancreatitis (11).

According to Sanjay et al (20); delayed interval cholecystectomy is safer and is associated with fewer morbidities and readmissions. Despite the fact that many studies about the best time for cholecystectomy have been published in mild pancreatitis, there are few randomized clinical trials available. Despite some guidelines and recommendations, there is no consensus on whether or not it is safe to discharge patients with mild pancreatitis prior to cholecystectomy (21-24).

In terms of intra- and post-operative complications, recent studies and meta-analyses concluded that delayed cholecystectomy had no advantages over early intervention.

For patients with acute cholecystitis, the optimal timing for laparoscopic cholecystectomy was previously considered to be 6 to 8 weeks after the acute phase to allow for resolution of the acute gallbladder inflammation (8). Several clinical trials, though mostly small and retrospective, have shown that early laparoscopic cholecystectomy is safe and reduces hospital stay, with morbidity and mortality rates comparable to those of elective delayed cholecystectomy (25-30). Ohta et al (31); compared four timing groups of laparoscopic cholecystectomy (72 hours, 4–14 days, 3–6 weeks, and >6 weeks after onset of symptoms) in a retrospective study of 100 patients that the best timing for laparoscopic cholecystectomy for acute cholecystitis is within 72 hours, which results in the shortest total stay in the hospital compared to operations performed later. Faloret al (29); performed early laparoscopic cholecystectomy (within 48 hours of admission) in 117 of 303 patients with mild gallstone pancreatitis; the procedure was delayed until test values returned to normal. They concluded that early laparoscopic cholecystectomy is safe, with a shorter hospital stay and lower morbidity and death.

We found that early laparoscopic cholecystectomy has a shorter hospital stay, lower morbidity, and mortality rate than delayed laparoscopic cholecystectomy for the treatment of acute cholecystitis owing to gallstones in this prospective, randomized research. The findings of our investigation are consistent with those of studies done by Aziz M, et al. and zkardeş AB, et al (32,33).

According to Van Baal and colleagues (34); Bakker et al (35); and Ito et al (36); there is a significant risk of recurring biliary events after discharge from the hospital after an incident of acute biliary pancreatitis and before interval cholecystectomy, Johnstone et al (37); Randial et al (38); Wilson et al (39); and Alimoglu et al (40); observed a significant rate of recurrent biliary events in delayed cholecystectomy patients (9-60%). Recurrent biliary problems were found in 44% of the delayed group in the study conducted by Shir Li Jee et al (41); in our study, 41.3% of participants in the delayed group developed biliary complication and none of the patient developed re biliary complication in the early group.

According to Chang et al (37), early laparoscopic cholecystectomy is associated with a higher rate of wound infections than delayed intervention, whereas wound infection rates are higher in the early group than in the delayed group in our study.

All of the cases in our study were completed laparoscopically, and none of them were converted to open cholecystectomy in either group, the finding is similar to that of Aziz M, et al ();

In a randomized, controlled trial including 75 patients, early laparoscopic cholecystectomy (<24 hours) was found to decrease the morbidity during the waiting period for elective laparoscopic cholecystectomy, the rate of conversion to open cholecystectomy, and hospital stay. Siddiqui et al(42); examined four clinical studies including 375 patients and showed that early laparoscopic cholecystectomy resulted in a shorter hospital stay and longer operation time, but no significant difference was observed in conversion rates between early and delayed laparoscopic cholecystectomy. In addition, the death rate is comparable between groups. Early laparoscopic cholecystectomy for acute cholecystitis is beneficial in terms of the length of hospital stay without increases in morbidity or mortality, according to a best-evidence topic that analyzed 92 papers (meta-analyses, randomized control trials, prospective controlled studies, and retrospective cohort studies) Skouras C et al(43).

Limitations:

- The number of people that took part in the study was quite limited.
- Because a non-probability consecutive sampling technique was utilized, the results may not be generalizable to the entire population.
- Because it was a single hospital-based study, the findings may not be applicable to the entire Pakistani population.

CONCLUSION

In conclusion, postoperative complications are associated more with delayed laparoscopic cholecystectomy compared with early intervention; early laparoscopic cholecystectomy should be preferred by surgeons for treatment of acute cholecystitis with the advantage of shorter hospital stay and lower complication rate. However, more studies with larger sample size may be done in order to firm up the conclusion.

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