

Outcomes of early versus delayed cholecystectomy in patients with mild to moderate acute biliary pancreatitis: A randomised prospective study

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ABSTRACT

Aim: To study the outcomes of early versus delayed cholecystectomy in patients with mild to moderate acute biliary pancreatitis:

Methods: 80 patients were included in the study. They were divided into two groups with 40 patients in each group. Group A: (40) patients who underwent laparoscopic cholecystectomy after 48 hours from day of admission. Group B: (40) patients who discharged home after resolution of the acute phase and underwent laparoscopic cholecystectomy after 6 weeks. Both groups were compared as regard: operative time, intraoperative findings and complications, conversion to open surgery, use of abdominal drains, hospital stay, post operative complications, readmission after discharge.

Results: The mean age of patients in group A was 36.29 ± 10.33 years (range= 20-55 year) while in group B was 37.58 ± 10.22 y (range= 20- 53 y). The majority of the patients were female. 24 patients (60%) in group A and 32 patients (80%) in group B. In group A the operative time ranged from 46 minutes to 89 minutes with a mean of 67.5 ± 11.69 minutes, while in group B operative time ranged from 39 minutes to 76 minutes with a mean of 57.5 ± 9.98 minutes. P value was significant 0.014. In group A 5 patients (12.5%) have intraoperative finding of acute cholecystitis where as none of group B express acute cholecystitis intraoperatively, with no statistically difference (p value 0.069). There was no significant difference in intraoperative complications between both groups. The difference between the two groups is significant (0% vs. 40%, $p < 0.0001$). 7 patients (17.5%) required hospital readmission due to severity of the symptoms. 10 patients (25%) had biliary colic, 3 patients (7.5%) developed acute cholecystitis, and 4 patients (10%) had recurrent biliary pancreatitis.

Conclusion: We concluded that the early cholecystectomy in patients with mild acute biliary pancreatitis has no added risk of intra or post operative complications than delayed cholecystectomy. Also it significantly reduces the risk of recurrent biliary problems and length of hospital stay which has a great impact on the patients and health care resources.

Keywords: Cholecystectomy, Acute biliary pancreatitis, post operative complications

INTRODUCTION

Acute pancreatitis is a common disease in the emergency room with an annual incidence ranging from 4.9 to 35 per 100,000 population.¹ According to the Atlanta classification, 80% of patients with pancreatitis have mild acute pancreatitis.² Acute biliary pancreatitis is one of the most common types of acute pancreatitis, accounting for up to 40 to 70% of cases.³ After biliary pancreatitis, patients may experience a recurrent episode of biliary pancreatitis, common bile duct (CBD) obstruction, cholangitis, or biliary colics.^{4,5} Cholecystectomy and clearance of stones from the biliary tree remain the mainstay of treatment to prevent recurrent biliary events.⁶

Most cases of acute biliary pancreatitis (ABP) are mild and self limiting; however, 10e20% of patients develop severe pancreatitis, which is associated with high morbidity and mortality.⁶ The timing of cholecystectomy in patients with clinically severe pancreatitis, with local complications such as pancreatic necrosis and organ failure, is deliberately delayed until local complications have resolved, typically after approximately 6 weeks.⁷ For mild to moderate ABP, international guidelines recommend early cholecystectomy.^{8,9} However, the definition of “early” varies amongst the guidelines. The International Association of Pancreatology (IAP) recommends that all patients with gallstone pancreatitis should undergo cholecystectomy as soon as the patient has recovered from the at- tacks, whereas the British Society of Gastroenterology recommend cholecystectomy within the same hospital admission or up to 2 weeks after discharge.⁵ The American Gastroenterological Association guidelines suggest that cholecystectomy should be performed as soon as possible and in no case beyond 2e4 weeks after discharge,⁴ whereas the American College of Gastroenterology recommend cholecystectomy within index admission.⁹ The variation in the recommended timing of cholecystectomy between these guidelines arose from differing views and adopted practices, and more importantly, is due to the lack of evidence from prospective randomized controlled trials addressing the timing and safety of early operative intervention. The rationale for cholecystectomy during the same hospitalization, compared with interval cholecystectomy, is that it leads to a reduction in the frequency of recurrent biliary events (e.g., recurrent biliary pancreatitis, acute cholecystitis, symptomatic choledocholithiasis, and biliary colic) in these patients. Ito et al¹⁰ noted that there is an increased risk of recurrence within 2-4 weeks after discharge. In the group of patients who did not have cholecystectomy performed during the index admission, 13.4% developed recurrent ABP while awaiting cholecystectomy. A total of 12.5% of recurrences occurred within 1 week, 31.3% occurred within 2 weeks, and one-half of them within 4 weeks after discharge.¹⁰ This finding is crucial as recurrent at- tacks of biliary pancreatitis can be severe and life threatening.

MATERIAL AND METHODS

This randomized prospective study conducted after taking the approval of the protocol review committee and institutional ethics committee. 80 patients were included in the study. They were divided into two groups with 40 patients in each group.

Group A: (40) patients who underwent laparoscopic cholecystectomy after 48 hours from day of admission.

Group B: (40) patients who discharged home after resolution of the acute phase and underwent laparoscopic cholecystectomy after 6 weeks. patients with age < 18 and >60 years,

severe cardiopulmonary disease severe pancreatitis and obstructive jaundice or cholangitis were excluded from this study.

Acute pancreatitis was diagnosed when the patient has acute upper abdominal pain with elevated serum amylase/lipase more than 3 times of upper normal range. Severity was assessed according to Atlanta classification 2012. After detailed clinical examination, routine laboratory investigations were done. All patients had abdominal ultrasound to confirm presence of gall bladder stones. Conservative measures was started (IV fluid, proton pump inhibitors and paracetamol injection).

Both groups were compared as regard: operative time, intraoperative findings and complications, conversion to open surgery, use of abdominal drains, hospital stay, post operative complications, readmission after discharge.

Statistical analysis

Statistical analysis was conducted using SPSS 25.0 software and comparisons among the groups were analyzed by using Chi-square test.

RESULTS

80 consecutive patients with mild to moderate acute biliary pancreatitis were prospectively randomized into two groups:

Group A: early 48 h laparoscopic cholecystectomy

Group B: laparoscopic cholecystectomy after six weeks.

The mean age of patients in group A was 36.29 ± 10.33 years (range= 20-55 year) while in group B was 37.58 ± 10.22 y (range= 20- 53 y). The majority of the patients were female. 24 patients (60%) in group A and 32 patients (80%) in group B.

Table 1 Demographic profile of the patients

Demographic profile	Group A: early 48 h laparoscopic cholecystectomy	Group B: laparoscopic cholecystectomy after six weeks.
Gender		
Male	16(40%)	8(20%)
Female	24(60%)	32(80%)
Age in years	36.29 ± 10.33	37.58 ± 10.22

A significant differences in the operative time between both groups were shown in table.2. In group A the operative time ranged from 46 minutes to 89 minutes with a mean of 67.5 ± 11.69 minutes, while in group B operative time ranged from 39 minutes to 76 minutes with a mean of 57.5 ± 9.98 minutes . P value was significant 0.014.

Table 2 operative time in group A and group B

OperativeTime	Group A: early 48 h laparoscopic cholecystectomy	Group B: laparoscopic cholecystectomy after six weeks.	Test
Operative time (min)			Z = 2.78* P (0.014)*
- Minimum	46	39	
- Maximum	89	76	
- Mean±SD	67.5±11.69	57.5±9.98	

In group A 5 patients (12.5%) have intraoperative finding of acute cholecystitis where as none of group B express acute cholecystitis intraoperatively, with no statistically difference (p value 0.069) Table (2)

Table3. Intraoperative data in group A and group B

Intraoperative data	Group				χ ²	P
	A		B			
	No	%	No	%		
Acute cholecystitis						
No	35	87.5%	40	100%	3.44	0.069
Yes	5	12.5%	0	0%		

There were no major intraoperative complications like bowel injury, major blood vessels or major biliary injury. The main intraoperative unfavorable events that had occurred during surgery encompassed three main complications: gallbladder perforation, bleeding from the liver bed and port site bleeding. As shown in table 4. There was no significant difference in intraoperative complications between both groups.

Table4. Intraoperative complications in group A and group B

	Group A: early 48 h laparoscopic cholecystectomy		Group B: laparoscopic cholecystectomy after six weeks.		χ ²	P	
	No	%	No	%			
Intraoperative complications						5.31	0.17
No events	29	72.5%	29	72.5%			
Gall bladder perforation	7	17.5%	5	12.5%			
Bleeding from liver bed	3	7.5%	1	2.5%			
Bleeding from port site	0	0.0%	5	12.5%			
Use of drains	1	2.5%	0	0.0%			

Major events	0	0.0%	0	0.0%		
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All the cases were completed laparoscopically none of them were converted to open cholecystectomy in both groups.

None of the patients underwent early cholecystectomy has recurrent biliary issues (0%). 16 patients (40%) in the delayed group had gallstone-related problems during the interval between resolution of the acute pancreatitis and delayed cholecystectomy Table (5). The difference between the two groups is significant (0% vs. 40%, $p < 0.0001$). 7 patients (17.5%) required hospital readmission due to severity of the symptoms. 10 patients (25%) had biliary colic, 3 patients (7.5%) developed acute cholecystitis, and 4 patients (10%) had recurrent biliary pancreatitis.

Table 5. Recurrent Rate

	Groups				P
	A		B		
	No	%	No	%	
Recurrent Rate	No		16	40%	< 0.0001
Biliary colic	0	0%	10	25%	
Acute cholecystitis	0	0%	3	7.5 %	
Recurrent biliary pancreatitis	0	0%	4	10%	

The total length of stay (LOS) (which includes the index admission plus admission for precholecystectomy recurrences plus admission for cholecystectomy) is longer in group B compared with group A. In the B group, median total LOS is 9.5 days whereas it is 8.5 days in the A group ($p 0.003$).

DISCUSSION

Worldwide gallstones are the most common cause of acute pancreatitis accounting for approximately 45% of cases. The migration of biliary calculi or impaction of a stone at the ampulla of vater is the probable cause of gallstone pancreatitis. The diagnosis of acute pancreatitis relies on combination of clinical evaluation and the use of supportive laboratory and radiological investigations.¹¹

For several decades surgeons believed that laparoscopic cholecystectomy in acute biliary pancreatitis during index of admission is a risky procedure and associated with high risk of morbidities and complications. This is well established now in severe episodes of acute pancreatitis because of extensive edema and local complications.¹² Sanjay et al¹³ concluded that delayed interval cholecystectomy is more safe and associated with less morbidities and readmission.

In mild to moderate pancreatitis however many studies were published about optimal timing for cholecystectomy, limited randomized clinical trials were available. Till now despite of some guidelines and recommendations, there no consensus it is safe or not to discharge patients with mild to moderate pancreatitis before doing cholecystectomy.^{6, 9,14,15}

Recent studies and meta analyses concluded that delayed cholecystectomy had no advantages over the early intervention as regard intra and post operative complications. In our current study early cholecystectomy did not add any complications or morbidities to the patients compared with delayed ones.¹⁶⁻¹⁸

Although duration of surgery in delayed group was less than the early group in our study, there was no significant differences in intraoperative complications and the conversion rate was the same in both groups.

Dacosta et al., Noel et al., and Omar et al, found no significant difference in intraoperative complications in between early and delayed cholecystectomy.¹⁹⁻²¹

In delayed cholecystectomy the patients had high risk of biliary symptoms that in some circumstances necessitate inpatient admission as acute cholecystitis or recurrent pancreatitis.

Van Baal et al,¹⁶ Bakker et al²² and Ito et al.¹⁰ have suggested that there is a substantial risk of recurrent biliary events after discharge from hospital following an episode of acute biliary pancreatitis and before interval cholecystectomy

Johnstone et al,¹⁸ Randial et al,¹⁷ Wilson et al²³ and Alimoglu et al,²⁴ reported high incidence of recurrent biliary events 9-60% in delayed cholecystectomy patients. Shir Li Jee et al²⁵ reported recurrent biliary issues in 44% in delayed group.

In our study, 40% of the patients in delayed group developed recurrent biliary problems prior to delayed cholecystectomy, 17.5% required hospital admission.

Ito et al¹⁰ have suggested that two weeks interval prior to cholecystectomy is considered too long because nearly 30% of recurrence occurs in the first 2 weeks after discharge, Shir li Jee et al²⁵ also reported 27% of recurrence in the first 2 weeks.

In our study, Patients who underwent early cholecystectomy had short hospital stay when compared to the other delayed group. This significant difference may be attributed to recurrent hospital admission in delayed group (16.6%) which has also a great economic impact.

Shir li Jee et al,²⁵ (3) found that early cholecystectomy was associated with a significantly shorter length of hospital stay when compared with the delayed group (p Z 0.0016). With no increase in complications or mortality.

CONCLUSION

We concluded that the early cholecystectomy in patients with mild acute biliary pancreatitis has no added risk of intra or post operative complications than delayed cholecystectomy. Also it significantly reduces the risk of recurrent biliary problems and length of hospital stay which has a great impact on the patients and health care resources.

REFERENCES

1. Peery AF, Crockett SD, Barritt AS, Dellon ES, Eluri S, Gangarosa LM, Jensen ET, Lund JL, Pasricha S, Runge T, et al. Burden of gastrointestinal, liver, and pancreatic diseases in the United States. *Gastroenterology*. 2015;149(7):1731–41.
2. Nadesan S, Qureshi A, Daud A, Ahmad H. Characteristics of acute pancreatitis in University Kebangsaan Malaysia. *Med J Malaysia*. 1999;54(2):235e241.
3. Tenner S, Baillie J, DeWitt J, Vege SS. American College of Gastroenterology guideline: management of acute pancreatitis. *Am J Gastroenterol*. 2013; 108(9):1400–15 1416.

4. Forsmark CE, Baillie J. AGA Institute technical review on acute pancreatitis. *Gastroenterology*. 2007;132(5):2022-2044.
5. UK guidelines for the management of acute pancreatitis. *Gut*. 2005;54(Suppl 3:iii):1e9.
6. Banks PA, Freeman ML. Practice guidelines in acute pancreatitis. *Am J Gastroenterol*. 2006;101(10):2379-2400.
7. Nealon WH, Bawduniak J, Walser EM. Appropriate timing of cholecystectomy in patients who present with moderate to severe gallstone-associated acute pancreatitis with peri-pancreatic fluid collections. *Ann Surg*. 2004;239(6):741-749. discussion 49-51.
8. Toouli J, Brooke-Smith M, Bassi C, et al. Guidelines for the management of acute pancreatitis. *J Gastroenterol Hepatol*. 2002;17. Suppl:S15-39.
9. Tennet S, Bailie J, DeWitt J, Vege SS. American College of Gastroenterology Guideline : management of acute pancreatitis. *Am J Gastroenterol*. 2013. <http://dx.doi.org/10.1038/ajg.2013.218>.
10. Ito K, Ito H, Whang EE. Timing of cholecystectomy for biliary pancreatitis: do the data support current guidelines? *J Gastrointest Surg*. 2008;12(12):2164-2170.
11. Parans H, Mayo A, Paran D. Octreotide treatment in patients with severe acute pancreatitis. *Dig Dis Sci*. 2000; 45: 2247- 2251.
12. Nealon WH, Bawduniak J and Walser EM. Appropriate timing of cholecystectomy in patients who present with moderate to severe gallstone-associated acute pancreatitis with peripancreatic fluid collections. *Ann Surg*. 2004;239(6):741-749. discussion 49-51.
13. Sanjay P, Yeeting S, Whigham C, et al. Endoscopic sphincterotomy and interval cholecystectomy are reasonable alternatives to index cholecystectomy in severe acute gallstone pancreatitis (GSP). *Surg Endosc*. 2008; 22(8):1832-1837.
14. I W, Warshaw A, Imrie C, et al. IAP Guidelines for the Surgical Management of Acute
15. Forsmark CE and Baillie J. AGA Institute technical review on acute pancreatitis. *Gastroenterology*. 2007;132(5):2022-2044.
16. Van Baal MC, Besselink MG, Bakker OJ, et al. Timing of cholecystectomy after mild biliary pancreatitis: a systematic review. *Ann Surg*. 2012;255(5):860-866.
17. Randal Perez LJ, Fernando Parra J, Aldana Dimas G. The safety of early laparoscopic cholecystectomy (<48 hours) for patients with mild gallstone pancreatitis: a systematic review of the literature and meta-analysis. *Cir Esp*. 2014;92(2):107-113.
18. Johnstone M, Marriott P, Royle TJ, et al. The impact of timing of cholecystectomy following gallstone pancreatitis. *Surgeon*. 2014;12(3):134-140.
19. Da Costa DW, Bouwense SA, Schepers NJ, et al. Dutch Pancreatitis Study Group. Same-admission versus interval cholecystectomy for mild gallstone pancreatitis (PONCHO): a multicentre randomized controlled trial. *Lancet* 2015; 386: 1261–1268.
20. Noel R, Arnelo U, Lundell L, et al. Index versus delayed cholecystectomy in mild gallstone pancreatitis: results of a randomized controlled trial. *HPB (Oxford)* 2018; 20: 932– 938.
21. Omar MA and Marwa N. Acute biliary pancreatitis – optimal time for cholecystectomy: a prospective randomized study. *Clin Surg* 2018; 3: 2151.
22. Bakker OJ, van Santvoort HC, Hagens JC, et al. Timing of cholecystectomy after mild biliary pancreatitis. *Br J Surg*. 2011;98(10):1446-1454.

23. Wilson CT and de Moya MA. Cholecystectomy for acute gallstone pancreatitis: early vs delayed approach. *Scand J Surg.* 2010 85(2):81-99.
24. Alimoglu O, Ozkan OV, Sahin M, et al. Timing of cholecystectomy for acute biliary pancreatitis: outcomes of cholecystectomy on first admission and after recurrent biliary pancreatitis. *World J Surg.* 2003;27(3):256-259
25. Shir Li Jee, RazmanJarminB , Kin Foong Lim A, et al. Outcomes of early versus delayed cholecystectomy in patients with mild to moderate acute biliary pancreatitis: A randomized prospective study. *Asian journal of surgery*(2018) 41, 47-54.