

Original Research Article

Cholecystectomy in mild to moderate acute biliary pancreatitis when to intervene: early versus delayed

Kamran Hakeem Khan*, Waseem Yaar Khan, Zahid Khan, Muddasar Shahzad, Shahid Khan, Rashid Imran

Department of Surgery, Nowshera Medical College, Nowshera, Khyber Pakhtunkhwa, Pakistan

Received: 30 May 2020

Accepted: 07 July 2020

*Correspondence:

Dr. Kamran Hakeem Khan,

E-mail: kamranhakeemkhan@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Objective of the study was to compare the outcomes of early versus late cholecystectomy in mild to moderate acute biliary pancreatitis.

Methods: This comparative prospective study was conducted at Surgical Department of Qazi Hussain Ahmed Medical Complex, Nowshera from 1st January 2018 to 31st March 2020. Patients with mild to moderate acute biliary pancreatitis (ABP) were included in the study. Patients were divided into two groups. Group 1 having patients undergoing early (operated in 7 days) and Group 2 having patients with delayed (operated after 6 weeks) laparoscopic cholecystectomy. The outcomes like hospital stay, peri and post-operative complications, recurrent cholecystitis and pancreatitis were compared. $P < 0.05$ was considered significant.

Results: A total of 300 patients were included with 150 in each group. There were 70 (46.66%) males in group 1 while group 2 consisted of 68 (45.33%) males. The median time interval of operation to the laparoscopic surgery was 5 days in group 1 and 42 days in group 2. Peri operative outcomes were not significant between two groups ($p = 0.6$). About 14 (9.63%) patients were converted to open surgery in group 1 and 17 (10.53%) in group 2. Postoperative complications were also not significant between two groups ($p = 1.0$). Group 1 had small total length of stay as compared to group 2 ($p = 0.006$). Recurrent biliary events occurred in 63 (42.12%) patients in total with no event in group 1.

Conclusions: Patients with mild to moderate ABP having early laparoscopic cholecystectomy present with reduced recurrent biliary events and the total length of hospital.

Keywords: Acute biliary pancreatitis, Hospital stay, Laparoscopic cholecystectomy, Post-operative complications

INTRODUCTION

Treatment options and timings of cholecystectomy in patients with acute biliary pancreatitis (ABP) still remain controversial.^{1,2} Patients having multi organ failure secondary to severe acute biliary pancreatitis need to be treated conservatively before laparoscopic cholecystectomy can be done 6-8 weeks after the acute phase is settled. Gallstone is one of the most common cause of acute pancreatitis with rate of about 75%. In one of the retrospective study showed that about 45.1% of the

patients admitted for acute pancreatitis had biliary calculi as one of the cause.³

In case of mild acute biliary pancreatitis (ABP) treatment is seldom needed as most of them are self-limiting however about 10-20% of patients develop severe pancreatitis causing a high rate of mortality. For such type of patients having severe ABP the timings of cholecystectomy is always difficult decision as there are local complications like pancreatic necrosis which needs to be resolved before going for final procedure. It takes about approximately 6 weeks to settle such

complications. Early cholecystectomy is recommended for mild to moderate ABP.^{4,7}

There are differences between guidelines. The International Association of Pancreatology (IAP) recommends early cholecystectomy for gallstone pancreatitis as soon as the patient has recovered from the attack, whereas the British Society of Gastroenterology recommends cholecystectomy after about 2 weeks of acute attack.⁵ However American Gastroenterological Association guidelines recommend cholecystectomy as soon as possible and not beyond 2-4 weeks after discharge.³ All these variations in guidelines for timing of cholecystectomy might be because of lack of evidence from prospective randomized controlled trials.

The early cholecystectomy during same hospitalization is recommended due to reduced frequency of recurrent biliary events like recurrent biliary pancreatitis, acute cholecystitis, symptomatic choledocholithiasis, and biliary colic. Ito et al wrote an increased risk of recurrence within 2-4 weeks post discharge. In his study 13.4% developed recurrent ABP while awaiting cholecystectomy. Similarly 12.5% of recurrences occurred within 1 week, while 31.3% occurred within 2 weeks of discharge.⁸ Another study from Netherlands demonstrated about three-quarters of the patients of mild biliary pancreatitis underwent cholecystectomy within 6 weeks post discharge.⁹ As a matter of fact majority of surgeons prefers interval cholecystectomy due to its safety profile. Some studies preferred early intervention but the patients in these studies had mild acute ABP, without multi organ dysfunction.^{2,10} This approach also reduce the recurrence of acute pancreatitis, which came to be in about 30-50% of the patients waiting period for cholecystectomy.¹¹

Therefore the main aim of this study was to find out a comparison between early and delayed approach for ABP requiring laparoscopic cholecystectomy. These results will add to the pool of study conducted on Pakistani population.

METHODS

This comparative prospective study was carried out in Qazi Hussain Ahmed Medical Complex, Nowshera, over a period of 2 years from 1st January 2018 to 31st March 2020. All those patients who were diagnosed with mild to moderate acute biliary pancreatitis meeting the inclusion criteria were included, after asking informed consent. These patients were then divided into two groups on the basis of operation timings. Group 1 consists of patients undergoing early and Group 2 having patients undergoing delayed laparoscopic cholecystectomy. Patients aged more than 25 years admitted to surgical department were included.

The diagnosis of acute pancreatitis was made on the basis of following three features: (1) clinical signs of

pancreatitis, like upper abdominal pain, nausea, vomiting, and epigastric tenderness; (2) Elevated serum amylase level of at least thrice the upper limit of normal; and (3) Characteristic findings of acute pancreatitis on abdominal imaging. Biliary pancreatitis was diagnosed on the basis of confirmatory diagnosis of gallstones and/or sludge on radiological imaging.

The severity of pancreatitis as mild and moderate was defined by the presence of the following: (1) no pancreatic necrosis and/or peri pancreatic collections; (2) no persistent (>48 hours) organ failure; (3) clinical stability with hospital admission not requiring intensive care unit (ICU) or high dependency unit (HDU) care; and (4) absence of concomitant acute cholangitis. Patients with severe pancreatitis (as defined by the presence of 3 or more of Ranson's or Imrie criteria on admission), admitted to ICU or HDU or with suspected acute cholangitis, patients with multiple medical co-morbidities and pregnancy were also excluded.

Patients in Group 1 were operated within 7 days of admission for acute pancreatic attack while patients in Group 2 were subjected to surgery electively after six weeks of acute attack. Patients in both groups were subjected to laparoscopic cholecystectomy. Open cholecystectomy was performed if there was contraindication to laparoscopy.

All patients received appropriate peri-operative antibiotic prophylaxis. Laparoscopic procedure was carried out in the standard way with three ports: 10 mm infra-umbilical camera port, 10 mm epigastric port and 5 mm right sub costal port. Dissection was done with the harmonic scalpel. Drain was used whenever needed. In this study time interval from onset of pain to operation, operative time, difficult dissection, conversion rate, complications and discharge time was studied. The results of both group 1 and group 2 were then compared. Patients were followed up for a minimum of three months.

Data was analyzed using the SPSS version 16.0 (Chicago, IL, United States of America). Means and medians were used with inter-quartile ranges (IQRs) for continuous variables and Manne Whitney U test was performed for level of significance. Categorical variables were presented in frequencies and Chi-square test was used.

RESULTS

A total of 300 patients were included with 150 in each group. There were 70 (46.66%) males and 80 (53.33%) females in group 1 while group 2 consisted of 68 (45.33%) males and 82 (54.66%) females. Mean age was 45.5±2.5 years in Group 1 while in Group 2 the mean age was 43.5±3.0 years. The range of age was 25-65 years. Statically no significant difference between the two groups in case of age and gender was found (p>0.05) (Table 1).

Table 1: Demographic variables of study population (n=300).

Variables	Group 1 (n=150)	Group 2 (n=150)	P value
Age mean	45.5±2.5	43.5±3.0	0.85
Ranges	(25-65)	(25-65)	
Gender	N (%)	N (%)	0.56
Male	70 (46.66)	68 (45.33)	
Female	80 (53.33)	82 (54.66)	
Time			Not
Mean (range)	5 (1-7)	42 (24-56)	calculated

The median time interval of intervention from time of diagnosis to the laparoscopic surgery was 5 days in group 1 and 42 days in group 2 (Table 1). Peri-operative outcomes are shown in Table 2.

Table 2: Comparison of peri operative outcomes and hospital stay in study population (n=300).

Variables	Group 1	Group 2	P value
	N=150 (%)	N=150 (%)	
	N (%)	N (%)	
Conversion to open	14 (09.63)	17 (10.53)	1.6
Duration of surgery (min), median (range)	75 (60-120)	80 (60-120)	0.86
Overall complications	20 (13.33)	18 (12.0)	0.9
Peri-operative complication	5 (3.33)	7 (4.66)	0.6
Postoperative complication	15 (10.0)	11 (7.33)	1.0
Mortality	0	0	0
Total LOS (days), median (range)	7 (6-10)	10 (8-14)	0.006

Patients in both groups underwent laparoscopic cholecystectomy. About 14 (9.63%) patients were converted to open surgery in group 1 and 17 (10.53%) in group 2. Out of these converted patients in both groups, 10 patients were found to have severe adhesions causing difficulty in dissection of the Calot's triangle.

The median duration of surgery in group 1 was 75 minutes while it was 80 minutes in group 2 with p=0.86. Peri-operative complications rate between two groups was not significant with p=0.6. The operative mortality was found to be 0%. Postoperative complications were also not significant between two groups (p=1.0). In group 1, about 15 patients developed post-operative complications while in group 2, 11 patients had post op complications. About 5 out of 15 patients in group 1 developed surgical site infections.

When it comes to total length of stay (LOS), it was significantly higher in group 2 as compared to group 1 (p=0.006). Recurrent biliary events occurred in 63 (42.12%) patients in total with no event in group 1. About 45 (30.21%) patients in total had biliary colic with 15 patients in early group. About 10 (06.82%) patients developed acute cholecystitis, and 6 (4.65%) patients had recurrent biliary pancreatitis. Most of the re admissions occurred within 4 weeks of operation for both the groups. All these events and admission rates are presented in Table 3.

Table 3: Follow up complications in study population (n=300).

Variable	Patients N (%)	Admissions N (%)
No. of recurrent biliary events	63 (42.12)	31 (50.33)
Biliary colic	45 (30.21)	10 (22.00)
Acute cholecystitis	10 (06.82)	2 (18.00)
Recurrent biliary pancreatitis	6 (4.65)	1 (13.33)
Time of onset of recurrent biliary events after discharge		
Within 2 weeks	44 (29.67)	
Within 4 weeks	105 (70.33)	
After 4 weeks	40 (26.67)	
Time after discharge (days), median (range)	18 (12-25)	

DISCUSSION

One of the most commonly encountered complications of gall stones is acute biliary pancreatitis. Mild cases respond well to medical treatment. Cholecystectomy is indicated to prevent gall stones related complications and laparoscopic cholecystectomy is the procedure of choice.¹² For treating patients of ABP surgeons still don't want to take risk and prefer to wait for the symptoms to get settled, however in our study when we compared the early versus late approach, there was not much difference between the two arms of the study in respect to peri and post-operative complications.² For patients with ABP, timing of cholecystectomy has been always debated. Sanjay et al. study was in favour of early intervention as compared to delayed intervention in severe ABP, which is associated with minimal morbidity and readmission rates.¹³ There is always confusion regarding the discharge of ABP patients prior to undergoing cholecystectomy. In our study, there was no significant difference between early versus late cholecystectomy regarding overall complication rate, overall conversion rate, duration of surgery, and mortality rate. Some retrospective studies suggested substantial risk for recurrent biliary events after discharge from hospital after an episode of ABP without undergoing cholecystectomy with reported rate between 9% and 60%.¹⁴⁻¹⁷ In our study recurrent biliary events was 42% for the late group which is comparable to

literatures. Some studies have supported early intervention in mild cases of ABP.^{1,10}

Surgeons not in favour of early laparoscopic cholecystectomy argue that one should wait for at least 6-8 weeks because there is an increase in anesthesia and procedure related morbidity and mortality in ABP patients. One thing which resulted in such assumptions was the criteria for selection as there study included sever APB also which resulted in biased results. Another reason for not supporting early laparoscopic cholecystectomy is the dissection issue due to adhesions although in our study only 2 patients were found to have difficulty in dissecting the tissue.

In our study adhesions were more found in late group about 8 as compared to early group and dissection was more difficult in these patients when they were operated after 6-8 weeks. Some of the studies favour our results.^{10,19}

Another study by Schachter showed difficulty in laparoscopic dissection in ABP by the presence of adhesions to gall bladder area, accompanied with intra-operative bleeding and the need of a drain resulted in conversion to open approach in about 10.5% of their patients. However, they also concluded that late intervention in ABP is not advantageous.²⁰

A study by Tang et al showed a conversion rate of 67% when operated within the first week and 18% when operated after the first week of the attack. Other parameters like time to discharge was less in early group as compared to late.¹⁰ Although study by Tang et al reported against our findings where he reported hospital stay of 5.4 days for early and 2.8 days when operated after the first week.¹⁰ A study by Papi et al in a meta-analysis, reported a longer hospital stay for patients for late ABP group.¹ The development of postoperative pseudocyst or pancreatic necrosis acts as a factor for deferring surgery until 6-8 weeks after the attack as suggested by study of Nealon et al.²¹ But we did not encounter such complications.

In our study recurrent biliary events resulted in >50% severe symptoms requiring admission to hospital. In a study by Ito et al reported recurrence rate of 31% for the patients who waited for 2 weeks or more.⁸ In our study, patients in delayed cholecystectomy group had longer length of stay (LOS) than patients who underwent cholecystectomy during admission. A study by Rosing et al supported early cholecystectomy which is comparable to our results; having reduced length of stay.²² Recurrent pancreatitis has been shown to occur after cholecystectomy. The cause might be retained CBD stones or sludge. In our study we also encountered some cases but retained stones were not found.

CONCLUSION

In conclusion of our study it is found that patients with mild to moderate ABP having early laparoscopic cholecystectomy within the admission period reduces recurrent biliary events and decreases the total length of hospital. Moreover there is no difference related to complications peri and post operatively and also conversion rate to open surgery between the 2 groups. Therefore, early laparoscopic cholecystectomy in patients with mild to moderate ABP can be performed safely.

ACKNOWLEDGEMENTS

We would like to acknowledge all the studied patients for their cooperation. We wish to pay special gratitude to Prof Dr. Mohammad Jehangir Khan, Dean Nowshera Medical College and Dr. Arif Khan, Hospital Director, Qazi Hussain Ahmed Medical Complex, Nowshera for their support and encouragement throughout the project. We also acknowledge our families and friends for their continuous support and motivation.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Papi C, Catarci M, D'Ambrosio L, Gilli L, Koch M, Grassi GB, et al. Early surgery for acute calculous cholecystitis is better than delayed. *Am J Gastroenterol.* 2004;99:147-55.
2. Ranson JHC. The timing of biliary surgery in acute pancreatitis. *Ann Surg.* 1979;189:654-63.
3. Nadesan S, Qureshi A, Daud A, Ahmad H. Characteristics of acute pancreatitis in University Kebangsaan Malaysia. *Med J Malaysia.* 1999;54(2):235-41.
4. Forsmark CE, Baillie J. AGA Institute technical review on acute pancreatitis. *Gastroenterology.* 2007;132(5):2022-44.
5. Working Party of the British Society of Gastroenterology. UK guidelines for the management of acute pancreatitis. *Gut.* 2005;54(3:iii):1e9.
6. Banks PA, Freeman ML. Practice guidelines in acute pancreatitis. *Am J Gastroenterol.* 2006;101(10):2379-400.
7. 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.
8. Ito K, Ito H, Whang EE. Timing of cholecystectomy for biliary pancreatitis: do the data support current guidelines? *J Gastrointest Surg.* 2008;12(12):2164-70
9. Bakker OJ, van Santvoort HC, Hagens JC. Timing of cholecystectomy after mild biliary pancreatitis. *Br J Surg.* 2011;98(10):1446-54.

10. Tang SC, Stain G, Tang EF, Berne TV. Management of acute pancreatitis: from surgery to interventional intensive care. *Gut.* 2005;54:426-36.
11. Tong S, Altkorn D. Acute gallstone pancreatitis: how and when to intervene. *Gut.* 2005;54:426-36.
12. Soper NJ, Brunt LM, Callery MP, Steven AE, Giuseppe A. Role of laparoscopic cholecystectomy in the management of acute gallstone pancreatitis. *Am J Surg.* 1994;167:42-51.
13. Sanjay P, Yeeting S, Whigham C, Judson H, Polignano FM, Tait IS. Endoscopic sphincterotomy and interval cholecystectomy are reasonable alternatives to index cholecystectomy in severe acute gallstone pancreatitis (GSP). *Surg Endosc.* 2008;22(8):1832-7.
14. van Baal MC, Besselink MG, Bakker OJ. Timing of cholecystectomy after mild biliary pancreatitis: a systematic review. *Ann Surg.* 2012;255(5):860-6.
15. Ito K, Ito H, Whang EE. Timing of cholecystectomy for biliary pancreatitis: do the data support current guidelines? *J Gastrointest Surg.* 2008;12(12):2164-70
16. Mador BD, Panton ON, Hameed SM. Early versus delayed cholecystectomy following endoscopic sphincterotomy for mild biliary pancreatitis. *Surg Endosc.* 2014;28(12):3337-42.
17. Judkins SE, Moore EE, Witt JE, Barnett CC, Biffl WL, Burlew CC, et al. Surgeons provide definitive care to patients with gallstone pancreatitis. *Am J Surg.* 2011;202(6):673-8.
18. Osborne DH, Imrie CW, Carter DC. Biliary surgery in the same admission for gallstone associated acute pancreatitis. *Br J Surg.* 1981;68:758-61.
19. Waldemar U, Andrew W, Clement I, Claudio B, Colin J. Mackey, et al. IAP guidelines for the surgical management of acute pancreatitis. *Pancreatology.* 2002;2:565-73.
20. Schacter P, Peleg T, Cohen O. Interval laproscopic cholecystectomy in the management of acute biliary pancreatitis. *HPB Surg.* 2000;11(5):319-23.
21. Nealon WH, Bawduniak J, 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;23:741-51.
22. Rosing DK, de Virgilio C, Yaghoubian A, Putnam BA, El Masry M, Kaji A, et al. Early cholecystectomy for mild to moderate gallstone pancreatitis shortens hospital stay. *J Am Coll Surg.* 2007;205(6):762-6.

Cite this article as: Khan KH, Khan WY, Khan Z, Shahzad M, Khan S, Imran R. Cholecystectomy in mild to moderate acute biliary pancreatitis when to intervene: early versus delayed. *Int Surg J* 2020;7:2480-4.