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Original Research Article

Timing of cholecystectomy in mild gallstone pancreatitis: a single centre study over 10-year period

Yegi S. Kim[1]*, Maria K. Vanguardia[1], Charles Pilgrim[1], Rachel Giblin[2], Priyadarshini Selvaraj[2], Nuhansi Wijesinghe[2]

[1]Department of Surgery, Peninsula Health, Frankston, Victoria, Australia
[2]Faculty of Medicine, Monash University, Nursing and Health Sciences, Clayton, Victoria, Australia

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***Correspondence:**
Dr. Yegi S. Kim,
E-mail: sandy.kim.au@gmail.com

ABSTRACT

Background: The recommended management of mild gallstone pancreatitis (GSP) is to perform index admission cholecystectomy. This study is to assess the timing of cholecystectomy in patients presented with mild GSP in a single centre, over 10-year period, and assess the rates of complications in different timings of the surgery.
Methods: Patients diagnosed with gallstone pancreatitis between 2009 and 2022 in Peninsula Health were identified using a diagnosis coding system.
Results: A total of 198 patients were diagnosed with mild GSP between 2009 and 2022. 24 (12%) patients underwent early cholecystectomy (within 48 hours of admission), 106 (54%) underwent delayed cholecystectomy (over 48 hours) and 68 (34%) underwent interval cholecystectomy. The average length of hospital stay (LOS) was lower in patients who had early cholecystectomy (3 days) than patients who had delayed (6 days) or interval cholecystectomy (8 days). The complication rates were higher in patients who were in delayed cholecystectomy group (14%) or in interval cholecystectomy group (26.5%) than patients who underwent early cholecystectomy (4%) which was statistically significant (p=0.024).
Conclusions: The gold standard management of mild GSP is to perform cholecystectomy at index admission. This study showed that the patients who underwent cholecystectomy within 48 hours of admission had no increased rate of perioperative complication and significantly reduced LOS.

Keywords: Mild gallstone pancreatitis, Timing of cholecystectomy, Complications, LOS

INTRODUCTION

Gallstones are one of the most common causes of acute pancreatitis in Australia and in most cases the gallstone pancreatitis is classified as 'mild'. The definitive management of gallstone pancreatitis is cholecystectomy to prevent its recurrence.[1,2]

In the past, it was recommended to perform laparoscopic cholecystectomy in a delayed fashion to manage biliary acute pancreatitis which was not considering different severity of the disease.[3] More recent studies have demonstrated that performing cholecystectomy during the same admission have shown great benefits for patients by reducing gallstone-related complications, readmission rates and length of hospital stay (LOS).[4,5]

Furthermore, performing cholecystectomy early, that is within 48 hours of admission have shown to be safe and cost effective.[6-9] This study aims to show the comparisons of index in early and delayed versus interval cholecystectomy in mild gallstone pancreatitis (MGP) in a single institution in Australia and its trend in the practice.

METHODS

Patient selection

Retrospective data was collected using a diagnosis code as gallstone pancreatitis (GSP) between May 2009 and December 2022. Patients treated at Peninsula health, Melbourne, Australia with mild gallstone pancreatitis and underwent cholecystectomy during that period were included in this study. The patient data was accessed through the online medical records. This study was approved by the Peninsula Health Ethics Committee.

Inclusion criteria

The diagnosis of acute pancreatitis was confirmed by meeting two of three criteria: (i) epigastric pain consistent with pancreatitis, (ii) elevated serums lipase more than three times the upper normal limit and (iii) radiological evidence of acute pancreatitis.[10] The severity of pancreatitis was defined by the Atlanta Classification of acute pancreatitis and the use of C-reactive protein (CRP) levels taken within 24-48 hours of the admissions.[11,12]

Exclusion criteria

Those with end-organ dysfunction either transient (<48 hours), persistent (>48 hrs) or the presence of local complications were considered moderate to severe pancreatitis hence excluded from the study. Organ dysfunction and failure was classified by the Marshall scoring system.[10] Additionally, those with CRP levels above 150 mg/dl were considered to have moderate to severe GSP hence were excluded from the study.

Primary outcome

The primary outcome of interest was the complication rates. These included biliary pathology such as readmission with recurrent gallstone pancreatitis, biliary colic or cholecystitis, wound complication, perioperative complication both medical and surgical complications. The perioperative complications included acute myocardial infarction, deep vein thrombosis or pulmonary embolism. The surgical complications included return to theatre, bleeding or bile leak. We have compared the complication rates between early, delayed and interval groups.

Secondary outcomes

The secondary outcomes were hospital length of stay (LOS) and 30-day mortality. The total LOS for interval cholecystectomy group included the number of hospital-stay during the admission of mild gallstone pancreatitis plus time spent during the admission for the interval cholecystectomy. Additionally, we have identified different reasons for delaying or performing interval cholecystectomy by evaluating patients' medical records.

Statistical analysis

All the statistical analyses were performed using STATA version 16. The distribution of continuous data was checked using the Shapiro-Wilks test for normalcy. As all continuous variables failed this test, data has been described as median (Interquartile range (IQR)). Categorical data has been described as frequency (%) and compared using Fisher's exact test. The results with p values <0.05 were considered statistically significant.

RESULTS

A total of 332 patients were retrospectively identified and 198 patients of those were included in this study. 134 patients were excluded as they did not meet the criteria. Of note, 27 were excluded because the CRP level was >150, 44 patients were excluded as the CRP levels were not recorded and the rest were excluded as they were not gallstone pancreatitis or moderate to severe gallstone pancreatitis with local or systemic complications. As shown on Table 1 73 (37%) were male and 125 (63%) were female within the MGP group. The median age of patients with MGP was 52. The median age of Early group was 45, Delayed group, 53 and the Interval group, 57. The median ASA score of the study population was 2 (57%).

There were 24 (12%) patients who underwent cholecystectomy early (<48 hours of admission), 106 (54%) patients had delayed cholecystectomy (>48 hours of admission) and 68 (34%) patients underwent interval cholecystectomy (Table 2). 194 (98%) of patients had laparoscopic cholecystectomy, 1 (0.5%) patient had open cholecystectomy, and 3 (1.5%) patients had laparoscopic converted to open cholecystectomy. As shown in Table 2, five different reasons were identified for delaying or performing interval cholecystectomy. Overall, 48 (28%) patients were delayed or had interval cholecystectomy due to ongoing pain or abnormal biochemical markers. 21 (12%) patients were delayed due to no theatre access, 39 (22%) patients delayed because of either the surgeons' or patients' preferences or no reasons given. 66 (38%) patients were delayed as they were waiting for radiological work up including needing for further biliary imaging or medical work-up such as waiting for anaesthetic or medical review pre-operatively.

Complications

One (4%) developed complication in the early group, 15 (14%) patients in the delayed and 18 (26%) patients in the interval group (Table 3). The difference amongst three groups was statistically significant with the p-value of 0.024. As shown on Table 4, there was no significant difference in complication rates between the early and delayed groups (4% vs 14%, p=0.3), however, it was significantly different between the early and interval groups (Table 5) (4% vs 27%, p=0.02). The total median LOS, in all groups combined, was 6 days. The median

LOS for the early group was 3 days, 6 days for delayed and 6 days for interval group (Table 6) and this was significantly different between the groups (p<0.001). Furthermore, the median LOS between early and interval groups have shown significant difference (3 vs 6 days, p<0.001) (Table 7). All groups had zero 30-day mortality rate. Conversion to open cholecystectomy was seen in one patient in the delayed group and three patients in the interval group. One patient, due to the pre-existing large incisional hernia, underwent a planned open cholecystectomy with a concurrent incisional hernia repair.

Trend towards index cholecystectomy

There were 60 cholecystectomies performed between 2012 and 2016. In this period, the number of index cholecystectomy was 27 (45%) and interval cholecystectomy 33 (55%), p value of 0.27. There were 138 cholecystectomies between 2017 and 2022. In this period, 103 (75%) patients underwent index cholecystectomy and 35 (25%) underwent interval cholecystectomy, p<0.001 (Table 8).

Table 1: Patient characteristics.

	Early cholecystectomy, <48 h	Delayed cholecystectomy (within same admission) >48 h	Interval cholecystectomy	P value
Age median	45	53	57	0.05
Male (%)	73/198 (37)			
Female (%)	125/198 (63)			
CRP median (IQR)	7.5 (7)	9 (18.5)	16 (36)	0.04
ASA (%)				
1	6/24 (25)	13/105 (12.3)	3/68 (4.4)	
2	15/24 (62.5)	63/105 (59.4)	33/68 (48.5)	0.008
3	3/24 (12.5)	29/105 (27.4)	30/68 (44.1)	
4	0/124 (0)	1/105 (0.9)	2/68 (2.9)	

Table 2: Cholecystectomy types, and reasons for delay.

	Early cholecystectomy, <48 h	Delayed holecystectomy within same admission) >48 h	Interval cholecystectomy	P value
Cholecystectomy type (%)	24/198 (12)	106/198 (54)	68/198 (34)	
Laparoscopy (%)	24 (100)	105 (99)	65 (96)	
Open (%)	0 (0)	0 (0)	1 (1)	0.21
Lap to open (%)	0 (0)	1 (1)	2 (3)	
Reasons for delay (%)	**Total (delayed and interval combined) N (%)**	**Delayed cholecystectomy**	**Interval cholecystectomy**	
1	33/174 (19)	20/106 (19)	13/68 (19)	
2	15/174 (9)	10/106 (9)	5/68 (7)	
3	21/174 (12)	14/106 (13)	7/68 (10)	
4	39/174 (22)	10/106 (9)	29/68 (43)	
5	66/174 (38)	52/106 (49)	14/68 (21)	

*Reasons for delay: 1=Waiting for resolution of pain, 2=Waiting for resolution of biochemical markers, 3= No theatre time, 4=Other: Consultant preference/Patient preference/No reason given, 5= Radiological or Medical Work-up required, i.e. anaesthetic review, or further radiological investigation required.

Table 3: Complications between all groups.

Cholecystectomy type	Early	Delayed	Interval	P value
Complications (%)				
No	23/24 (96)	91/106 (86)	50/68 (74)	
Yes	1/24 (4)	15/106 (14)	18/68 (26)	
Complication types (%)				
Biliary related readmissions	0 (0)	4/15 (27)	13/18 (72)	0.024
Wound complication	0 (0)	1/15 (6)	0 (0)	
Perioperative complication	0 (0)	3/15 (20)	0 (0)	
Surgical complication	0 (0)	3/15 (20)	3/18 (17)	
ERCP post op	1/24 (4)	4/15 (27)	2/18 (11)	

Table 4: Complication between early and delayed groups.

	Early	Delayed	P value
Complications (%)			
No	23/24 (96)	91/106 (86)	0.3
Yes	1/24 (4)	15/106 (14)	

Table 5: Complication between early and interval groups.

	Early	Interval	P value
Complications (%)			
No	23/24 (96)	50/68 (74)	0.02
Yes	1/24 (4)	18/68 (27)	

Table 6: Total length of hospital stays between all groups.

Cholecystectomy type	Early	Delayed	Interval	P value
Total LOS days median (IQR) N	3 (1) 24	6 (3) 106	6 (7) 68	<0.001

Table 7: Total length of hospital stays between early and interval groups.

Cholecystectomy type	Early	Interval	P value
Total LOS days median (IQR) N	3 (1) 24	6 (7) 68	<0.001

Table 8: Trend towards index cholecystectomy.

	Index (eSarly+delayed)	Interval	P value
2012-2016 (N, %)	27/60 (45)	33/60 (55)	0.27
2017-2022 (N, %)	103/138 (75)	35/138 (25)	<0.001
Comparison between 2012-2016 vs 2017-2022			<0.001

DISCUSSION

In the past, index cholecystectomy was thought to be associated with difficult operation and potentially increased risk of conversion to open due to oedema and adhesions from ongoing acute pancreatitis.[3,13,14] Hence, for the past few decades surgeons opted for interval cholecystectomy. However, recent literatures have demonstrated that the index cholecystectomy high success rate in mild GSP with no significant post operative complications when compared to interval cholecystectomy.[3,13]

Moreover, many studies are recommending early cholecystectomy as management of MGP. However, there has been a discrepancy between the recommendation and clinical practice in many institutions.[9,13,14] The timing of surgery has been delayed for patients for varies reasons including lack of ability to access to theatres, the notion that the clinicians should wait until the pancreatitis 'settles' with improving pain and biochemical markers, need for further investigations or workup.[13,14] Early cholecystectomy is associated with significant reduction in LOS, complication rates which include biliary related pathologies, need for endoscopic retrograde cholangiopancreatography (ERCP) and with no increased risk of conversion to open cholecystectomy.[9,14-17] The findings of our study were consistent with many literatures on this topic. The complication rate in the early cholecystectomy group was 4% which was significantly lower than the delayed (14%) or interval group (26%, p=0.024). There was one patient (4%) who required an ERCP in the early group. This complication rate was significantly lower than the delayed (27%) or the interval group (11%). Similar result was demonstrated in a meta-analysis study where early cholecystectomy group had significantly lower rate of ERCP usage than the delayed group.[13]

It is thought to increase the risk of ERCP usage in an untreated or delayed gallstone pancreatitis due to its pathophysiology of gallstone pancreatitis.[13] On the side note, Bignell et al, demonstrated that the use of ERCP and sphincterotomy was higher in elderly and frail patients with gallstone pancreatitis.[18] However, this may be an alternative treatment option over cholecystectomy in this patient population as ERCP alone can be effective in minimizing the risk of recurrent gallstone pancreatitis and cholecystectomy can be quite risky for this group of patients.[17,18] 72% of the complication in the Interval group was related to biliary pathologies including recurrent gallstone pancreatitis, biliary colic, cholecystitis or cholangitis. This was higher than previously quoted rates in several retrospective studies demonstrating rates

between 20-60%.[17,19] A few studies have shown that the incidence recurrent biliary events would increase up to 31% within 2 weeks of discharge from the hospital prior to interval cholecystectomy.[17,20]

Most of the cases in this study, the patients did not have early cholecystectomy as they were waiting for further medical or radiological work-up. Interestingly, our study showed only a small proportion of patients (12%) being delayed due to difficulty in accessing operating theatres. Most of the cases were delayed due to preferences of patients or surgeons. Also, our data showed that 19% of the patients were delayed or underwent interval cholecystectomy for unresolved pain which was historically a recommended practice in managing gallstone pancreatitis regardless of the severity.[21]

However, the trend has been towards index cholecystectomy over interval cholecystectomy in the last 5 years. This may be due to a shift of surgeon or patient preference rather than a logistical reason. This was a positive finding as the clinical practice is based on the evidence shown on many literatures that have demonstrated significant benefits for patients with MGP.

This study, however, has a few limitations. This was a retrospective study. We have used C-reactive protein as one of markers to indicate the severity of the disease. As a result, some patients were excluded when this information was missing despite meeting other criteria of mild gallstone pancreatitis. Lastly, the number of patients undergoing early cholecystectomy was small.

CONCLUSION

The index cholecystectomy is a gold standard in managing mild gallstone pancreatitis. And furthermore, early cholecystectomy in mild gallstone pancreatitis is safe and cost-effective. These results should be confirmed with larger patients, by obtaining data from multiple institutions.

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