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

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KEYWORDS
biliary pancreatitis;
cholecystectomy;
recurrent biliary events;
ERCP

Abstract *Background:* In patients with acute biliary pancreatitis (ABP), cholecystectomy is mandatory to prevent further biliary events, but the precise timing of cholecystectomy for mild to moderate disease remain a subject of ongoing debate. The aim of this study is to assess the outcomes of early versus delayed cholecystectomy. We hypothesize that early cholecystectomy as compared to delayed cholecystectomy reduces recurrent biliary events without a higher peri-operative complication rate.
Methods: Patients with mild to moderate ABP were prospectively randomized to either an early cholecystectomy versus a delayed cholecystectomy group. Recurrent biliary events, peri-operative complications, conversion rate, length of surgery and total hospital length of stay between the two groups were evaluated.
Results: A total of 72 patients were enrolled at a single public hospital. Of them, 38 were randomized to the early group and 34 patients to the delayed group. There were no differences regarding peri-operative complications (7.78% vs 11.76%; $p = 0.700$), conversion rate to open surgery (10.53% vs 11.76%; $p = 1.000$) and duration of surgery performed (80 vs 85 minutes, $p = 0.752$). Nevertheless, a greater rate of recurrent biliary events was found in the delayed group (44.12% vs 0%; $p \leq 0.0001$) and the hospital length of stay was longer in the delayed group (9 vs 8 days, $p = 0.002$).

Conclusion: In mild to moderate ABP, early laparoscopic cholecystectomy reduces the risk of recurrent biliary events without an increase in operative difficulty or perioperative morbidity.

1. Introduction

Gallstone disease is the leading cause of acute pancreatitis in developed nations, accounting for up to 75% of cases.[1] In Malaysia, a retrospective study done over a period of 7 years showed that in nearly one-half of the patients (45.1%) admitted for acute pancreatitis, the etiology was biliary calculi, followed by alcohol intake (19.7%).[2]

After biliary pancreatitis, patients may experience a recurrent episode of biliary pancreatitis, common bile duct (CBD) obstruction, cholangitis, or biliary colics.[3,4] Cholecystectomy and clearance of stones from the biliary tree remain the mainstay of treatment to prevent recurrent biliary events.[1,5]

Most cases of acute biliary pancreatitis (ABP) are mild and self limiting; however, 10—20% of patients develop severe pancreatitis, which is associated with high morbidity and mortality.[5] 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.[6] For mild to moderate ABP, international guidelines recommend early cholecystectomy.[1,3—5,7,8] 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 attacks,[1] whereas the British Society of Gastroenterology recommend cholecystectomy within the same hospital admission or up to 2 weeks after discharge.[4] The American Gastroenterological Association guidelines suggest that cholecystectomy should be performed as soon as possible and in no case beyond 2—4 weeks after discharge,[3] whereas the American College of Gastroenterology recommend cholecystectomy within index admission.[8] 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.

Several nonrandomized studies published recently favor cholecystectomy during the same index admission for ABP.[9—13] 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 al[14] 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.[14] This finding is crucial as recurrent attacks of biliary pancreatitis can be severe and life threatening.

Despite these guidelines and literatures, cholecystectomy during the same admission is not commonly practiced. A recent study of over 25,000 patients acutely admitted to hospitals in England with gallstone-related disease showed that only 14.7% underwent cholecystectomy during the same admission.[15] Another study in the US showed that only half of the patients admitted for ABP had cholecystectomy done during the same admission. Patients admitted to hospitals with smaller annual volumes of cholecystectomy or higher annual volumes of acute pancreatitis admissions were less likely to undergo cholecystectomy during the initial hospitalization for ABP.[16] A nationwide study in the Netherlands demonstrated that three-quarters of the patients admitted with mild biliary pancreatitis underwent cholecystectomy a median of 6 weeks after discharge.[13] The majority of specialists perform an interval cholecystectomy due to uncertainty regarding the efficacy and safety of an early cholecystectomy. The lack of evidence from prospective randomized controlled trials may contribute to that. Limitations to hospital resources, such as access to surgeons, operating room time, and postoperative intensive unit beds, may also contribute to noncompliance to recommendations for early cholecystectomy.

Other definitive biliary interventions such as endoscopic retrograde cholangiopancreatography (ERCP) with endoscopic sphincterotomy (ES) can also independently reduce rates of recurrence of ABP but may result in higher rates of biliary complications when compared with cholecystectomy.[17] ERCP and ES alone without cholecystectomy as definitive therapy for ABP still remain controversial. ERCP with its higher incidence of postprocedure pancreatitis resulted in longer hospital length of stay when compared with laparoscopic cholecystectomy and intraoperative cholangiogram (IOC) even when common bile duct exploration was performed.[18] Nevertheless, ES can be used as an accepted definitive treatment in elderly patients who have multiple comorbid conditions and are not fit for surgery to prevent recurrence of pancreatitis.

To date, there is only one published prospective randomized controlled trial in the US looking into the timing of cholecystectomy after ABP in 50 patients.[19] In this study, there was no comparison group randomized to undergo cholecystectomy electively after discharge.

Moreover, this trial did not assess the efficacy of early cholecystectomy on long term outcomes such as recurrent biliary events. In this study, we performed a comparative study of the outcomes of patients with early (cholecystectomy done within index admission) versus delayed cholecystectomy (cholecystectomy done on an elective basis after discharge, at ~ 6 weeks), concentrating only on patients with mild to moderate acute biliary pancreatitis. We hypothesize that early cholecystectomy compared with delayed cholecystectomy in patients with mild to moderate ABP reduces recurrent biliary events without a higher perioperative complication rate.

2. Research setting and methodology

2.1. Study setting

This study was carried out in Selayang Hospital, a public hospital in the state of Selangor, Malaysia, over a period of 1 year (November 2013 to November 2014).

2.2. Study design and randomization

This is an open-label, prospective randomized controlled study. Patients diagnosed to have mild to moderate ABP who meet the inclusion criteria and gave informed consent to participate in the study were prospectively randomized to either an early or delayed cholecystectomy group. Concealing the allocation for investigators or study participants is unfeasible due to the nature of this study, because study participants need to be scheduled for an early or delayed cholecystectomy. Random assignment was performed by drawing a sealed, unlabeled, unordered envelope from a container by an independent party immediately after informed consent was obtained. In patients randomized to the early group, cholecystectomy with IOC was performed within the index admission when patients no longer required opioid analgesics, could tolerate a normal oral diet and had serum C-reactive protein concentration $<$ 100 mg/L. In the delayed group, interval cholecystectomy with IOC was performed on an elective basis after hospital discharge from the index admission, at approximately 6 weeks after the pancreatitis episode. Cholecystectomy was performed as a laparoscopic procedure unless contraindicated, in which case, open cholecystectomy would be performed. All the operations were performed by a single consultant hepatobiliary surgeon. All patients received appropriate perioperative antibiotic prophylaxis.

2.3. Sample size calculation

To demonstrate a reduction of recurrent biliary events with power of 80% and two sided test of 5%, 55 patients will have to be included in each group (PS Calculations, version 2.1.3; Vanderbilt University, Nashville, TN, USA). With an estimated a drop-out rate of 10%, a sample size of 60 in each group is needed.

2.4. Inclusion criteria

All patients aged 18 years and older who were admitted to Selayang Hospital with mild to moderate ABP and consented to participate in this study were included.

A participant was diagnosed as having acute pancreatitis if they had at least two of the three following features[20]: (1) clinical signs of pancreatitis, e.g., upper abdominal pain, nausea, vomiting, and epigastric tenderness; (2) an 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 defined by the presence of the following: (1) confirmatory diagnosis of gallstones and/or sludge on radiological imaging; and (2) absence of ethanol abuse (males $>$ 3 units/d, female $>$ 2 units/d). The classification of mild to moderate pancreatitis was defined by the presence of the following[20]: (1) no pancreatic necrosis and/or peripancreatic 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.

2.5. Exclusion criteria

Patients were excluded if they had any of the following: (1) severe pancreatitis (as defined by the presence of 3 or more of Ranson's or Imrie criteria on admission); (2) admission to ICU or HDU; (3) suspected concomitant acute cholangitis; (4) severe preexisting medical comorbidity contraindicating cholecystectomy (as determined by the primary physician); (5) pregnancy; and (6) prior gastric bypass surgery (rendering ERCP difficult).

2.6. Ethical consideration

Approval was obtained from the National University of Malaysia Medical Centre Clinical Research Ethics Committee and Medical Research Ethics Committee, Ministry of Health prior to initiating this study. Permission for data collection and analysis was obtained from the relevant authorities in Selayang Hospital with regards to the reviewing of patients' medical records and reports. All patient information sheets were kept privy throughout the study.

2.7. Data collection

Data collection was commenced in Selayang Hospital after the study was approved. Preoperative, operative, and postoperative data were prospectively collected for each patient participating in the study.

2.8. Data analysis

Data entry utilizing codes were performed using the SPSS software version 16.0 (Chicago, IL, United States of America) licensed to National University of Malaysia. Computer assisted analysis was carried out at the end of the study. Results were expressed as means with 95%

confidence intervals (CI) or medians with interquartile ranges (IQRs) for continuous variables and Mann–Whitney *U* tests were performed to assess for significant differences between two groups. Frequencies were presented for categorical variables and Fischer's exact test or chi-square tests were used as appropriate.

2.9. Termination of study

An interim analysis was performed midway through the study which revealed a significant difference in the rate of recurrent biliary events and that which required hospital readmissions in the delayed cholecystectomy group compared with the early cholecystectomy group. After discussion with the supervising and ethics committee, a decision was made to terminate the study. At the time of termination, a total of 72 patients had completed participation in the study.

3. Results

3.1. Demographic pattern of patients

A total of 82 patients who were diagnosed with a primary episode of mild to moderate ABP and had fulfilled the criteria of the study were recruited. The patients were randomized into two groups as mentioned in the methodology above. Ten patients subsequently withdrew from the study due to reasons which included opting for alternative medicine therapy, change of mind on undergoing surgery, and deciding to undergo surgery in another institution. A total of 72 patients were enrolled in the final analysis of this study.

There were 31 male (43.06%) and 41 female (56.94%) patients in this study. The age range was from 18 to 75 to with a mean of 41.93 years. In the study population, the majority of patients were Malays (55.56%), followed by foreigners (19.44%), Chinese (18.06%), and Indians (6.94%). This ethnic distribution reflected the ethnic composition of the general Malaysian population of patients seeking treatment in the public health system.

Thirty eight patients were randomized into the early group and 34 patients into the delayed group. There is no significant difference between the two groups in age, gender, and ethnic demographics (Table 1).

The median time interval from diagnosis of ABP to cholecystectomy in the early group was 6 days whereas the median time in the delayed group was 44 days (Table 1).

Nineteen patients (50%) in the early group and 15 patients (44.12%) in the delayed group underwent an ERCP prior to cholecystectomy due to a strong suspicion of CBD stones, based on laboratory biochemical parameters and imaging findings. Of these 34 patients, 33 patients underwent ES and stone extraction. The remaining patient did not have evidence of CBD stone on ERCP. There is no significant difference between the two groups in reference to the patients undergoing precholecystectomy ERCP (Table 1).

Two patients in the delayed group underwent ERCP postcholecystectomy for removal of a small CBD stone which was incidentally found on IOC during cholecystectomy (Table 1).

3.2. Perioperative outcomes

Perioperative outcomes are shown in Table 2. All 72 patients underwent laparoscopic cholecystectomy. In 64 patients (89.47% in the early group and 88.24% in the delayed group), laparoscopic cholecystectomy was completed successfully. Conversion to open surgery was necessary in eight patients (4 in the early group and 4 in the delayed group; $p = 0.99$). These included five patients who were found to have severe inflammatory adhesions that precluded safe dissection of the Calot's triangle, and three patients who had impacted CBD stones discovered on the IOC and required open surgical exploration. Among the latter three patients, two had undergone precholecystectomy ERCP during which stones were removed and an occlusion cholangiogram had shown complete clearance. The remaining one patient was not suspected preoperatively to have CBD stones and did not undergo preoperative ERCP.

There is no difference between the two groups in the duration of surgery (median of 80 minutes in the early group and 85 minutes in the delayed group, $p = 0.752$).

There is also no statistically significant difference in the complication rates between the two groups. There was one intraoperative complication which occurred in the delayed group; this was an injury to duodenal serosa during mobilization which was recognized and repaired immediately during surgery. This case was among the five patients who required

Table 1 Patient demographics in relation to timing of cholecystectomy.

	Early group ($n = 38$)	Delayed group ($n = 34$)	p*
Patients			
Age (y), median and IQR	42.5 (29.75–52)	42.5 (30.75–54.25)	0.977
Sex			0.435
Male	18 (47.37%)	13 (38.24%)	
Female	20 (52.63%)	21 (61.76%)	
Race			0.353
Malay	24 (63.16%)	16 (47.06%)	
Chinese	6 (15.79%)	7 (20.59%)	
Indian	1 (2.63%)	4 (11.76%)	
Foreigner	7 (18.42%)	7 (20.59%)	
Procedures			
ERCP	19 (50%)	17 (50%)	> 0.99
Preop	19	15	0.644
Postop	0	2	0.220
Time to cholecystectomy (d), median, and IQR	6 (5–9)	44 (36–56)	[a]

* p value < 0.05 was classed as significant.
ERCP = endoscopic retrograde cholangiopancreatography; IQR = interquartile range.
[a] Not performed.

Table 2 Perioperative outcomes in relation to timing of cholecystectomy.

	Early group ($n = 38$)	Delayed group ($n = 34$)	p*
Conversion to open	4 (10.53%)	4 (11.76%)	> 0.99
Duration of surgery (min), median, IQR	80 (60—95)	85 (60—120)	0.752
Overall complications	3 (7.89%)	4 (11.76%)	0.700
Perioperative complication	0	1 (2.94%)	0.472
Postoperative complication	3 (7.89%)	3 (8.82%)	> 0.99
Mortality	0	0	[a]
Total LOS (d), median, IQR	8 (6—10)	9 (8—11)	**0.002**

* p values < 0.05 were classed as significant and are highlighted in bold.
IQR = interquartile range; LOS = length of stay.
[a] Not performed.

conversion to open surgery due to dense adhesions and difficult mobilization. The overall operative mortality was 0%.

Postoperative complications occurred in six out of 72 patients (3 in the early group and 3 in the delayed group). Five out of six patients had surgical site infections which were treated with daily outpatient dressing. One patient in the delayed group had an episode of pancreatitis post operatively. The patient was readmitted 2 days after discharge with mild pancreatitis and was treated conservatively and warded for 3 days.

The total length of stay (LOS) (which includes the index admission plus admission for precholecystectomy recurrences plus admission for cholecystectomy) is longer in the delayed group compared with the early group. In the delayed group, median total LOS is 9 days (interquartile range [IQR] = 8—11) whereas it is 8 days (IQR = 6—10) in the early group ($p = 0.001$).

3.3. Recurrent biliary events

In the 38 patients who underwent cholecystectomy during the index admission, there was no recurrent biliary event in the short interval between recovery from pancreatitis and cholecystectomy. Fifteen patients (44.12%) in the delayed group had gallstone-related symptoms prior to cholecystectomy. The difference between the two groups is significant (0% vs. 44.12%, $p < 0.0001$). Eight of the 15 patients (53.33%) required hospital readmission due to severity of the biliary events. Ten patients (29.41%) had biliary colic, three patients (8.82%) developed acute cholecystitis, and two patients (5.88%) had recurrent biliary pancreatitis. No incidence of cholangitis occurred in this study. The median time between discharge and readmission is 20 (12—29) days. Eleven admissions (73.33%) occurred within 4 weeks after discharge. Biliary events requiring readmission before cholecystectomy are summarized in Table 3.

Table 3 Recurrent biliary events in 34 candidates for delayed cholecystectomy.

	No. of patients	No. of readmissions
No. of recurrent biliary events	15 (44.12%)	8 (53.33%)
Biliary colic	10 (29.41%)	3 (20.00%)
Acute cholecystitis	3 (8.82%)	3 (20.00%)
Recurrent biliary pancreatitis	2 (5.88%)	2 (13.33%)
Time of onset of recurrent biliary events after discharge		
Within 2 weeks	4 (26.67%)	
Within 4 weeks	11 (73.33%)	
After 4 weeks	4 (26.67%)	
Time after discharge (d), median, IQR	20 (12—29)	

IQR = interquartile range.

3.4. Role of ES

ES was performed in 33 (45.83%) of 72 patients. Stones or sludge were found in the CBD during ERCP in all 33 patients. All stones and sludge were cleared before cholecystectomy. There is no statistically significant difference in recurrent biliary events in patients who had ES performed compared with patients who did not have ES performed (8 vs. 7; $p = 0.569$). The rates of recurrent biliary events in patients who did or did not undergo ES before cholecystectomy are shown in Table 4.

4. Discussion

The timing of cholecystectomy in patients with ABP has been a contentious issue for a long time. It is an established practice that patients admitted for severe ABP have their cholecystectomy delayed until local complications have resolved, typically after some 6 weeks.[6] Sanjay et al[21] concluded that ES and interval cholecystectomy in severe ABP is associated with minimal morbidity and readmission rates. Several studies published are relevant to determining the optimal timing of cholecystectomy in patients with mild ABP but randomized prospective data are limited. As a result, available guidelines vary with respect to recommendations on the ideal timing of cholecystectomy.[1,3—5,7,8] Indeed, there is no consensus on whether or not patients

Table 4 Recurrent biliary events in patients who did or did not undergo ES before cholecystectomy.

	ES ($n = 33$)	No ES ($n = 39$)	p*
Biliary events	8 (24.24%)	7 (17.95%)	0.569
Recurrent pancreatitis	1 (3.03%)	1 (2.56%)	> 0.99
Cholecystitis	2 (6.06%)	1 (2.56%)	0.590
Biliary colic	5 (15.15%)	5 (12.82%)	> 0.99

* p values < 0.05 were classed as significant.
ES = endoscopic sphincterotomy.

who suffer an episode of ABP can be safely discharged prior to undergoing cholecystectomy.

For several decades surgeons have legitimated the choice for interval cholecystectomy on the belief that cholecystectomy during index admission would be associated with difficult dissection due to edema caused by pancreatitis, which could lead to more surgical complications and unnecessary conversion. However, recent studies including three meta analyses and one cohort study showed that delaying cholecystectomy has no advantage regarding intraoperative complications.[12,22–24] In this study, early cholecystectomy did not lead to an increase in overall complication rate, overall conversion rate, duration of surgery, and mortality rate. Below is a table comparing complication rates in our study to those in the literature (Table 5).

The rate of conversion to open surgery is notably higher in this study compared with those in other series. A possible reason may be that the patients with gallstone disease in Malaysia tend to have a higher incidence of chronic cholecystitis and impacted stones which lead to a higher frequency of adhesions and 'difficult gallbladder', and therefore, the higher rate of conversion.

Several, mostly retrospective, studies have suggested that there is a substantial risk of recurrent biliary events after discharge from hospital following an episode of ABP and before interval cholecystectomy. The reported incidence of recurrent biliary events in these literatures is between 9% and 60%.[11–14,22,25–28]

Our study demonstrated a significant difference in recurrent biliary events (44% vs. 0%) and this rate was comparable to that reported in the literatures. A total of 6% of patients in our study had relapse of mild ABP. One patient had recurrent CBD stone and the other patient probably had migration of biliary sludge. An incomplete or partially reoccluded sphincterotomy may also have a role in the recurrence of symptoms.

Recurrent biliary events in our study are also clinically significant in that $>$ 50% of patients with recurrent biliary events had symptoms severe enough to warrant admission to hospital. A recent investigation by Ito et al suggested that an interval of 2 weeks between discharge and cholecystectomy might be too long as 31% of recurrences occurred within 2 weeks after discharge.[14] In accordance with the literature, our study demonstrated a recurrence rate of 27% within 2 weeks after discharge.

In this study, patients who underwent delayed cholecystectomy had longer overall LOS than patients who underwent cholecystectomy during index admission because 24% of them required readmission for recurrent biliary events. These readmissions could have been prevented if cholecystectomy had been performed at index admission. In a randomized controlled trial, Aboulian et al[19] compared early laparoscopic cholecystectomy (within 48 hours of admission) with control laparoscopic cholecystectomy (performed after resolution of symptoms and normalizing trend of laboratory enzymes). There was no statistically significant difference in the need for conversion to open surgery or in perioperative complication rates between two groups. However, early cholecystectomy was associated with a significantly shorter length of hospital stay, 3 days compared with 4 days in the control group ($p = 0.0016$).[19] This approach was supported by Rosing et al[10] who instituted a practice of early cholecystectomy in a prospective study of 43 patients. The conclusions of these studies are consistent with the present study which reports early cholecystectomy results in a significantly reduced length of hospital stay with no increase in complications or mortality.

The role and timing of ERCP for ABP is also controversial and is another contributor to delaying cholecystectomy. In a meta-analysis of randomized controlled trials, Moretti et al[29] demonstrated that early ERCP reduces pancreatitis-related complication in patients with predicted severe pancreatitis but has no advantage in predicted mild pancreatitis compared with conservative management. In a prospective randomized study by Chang et al,[30] patients with mild to moderate gallstone pancreatitis without cholangitis were randomized to preoperative ERCP versus post operative ERCP if CBD stones were seen on IOC. There was no difference in complication rate, but length of stay and costs were significantly less in the postoperative ERCP group. According to the American Society for Gastrointestinal Endoscopy guidelines, there is no role for early ERCP in the evaluation and management of patients with mild acute pancreatitis in the absence of clear evidence of a retained stone.[3] In this current study, there is no difference in the use of ERCP between the early and delayed groups. In 38 patients who did not have preop ERCP done, only three patients demonstrated CBD stone on IOC. All three patients were treated successfully; one with intraoperative CBD exploration and another two patients with postoperative ERCP and stone extraction. Therefore our current approach for mild to moderate ABP is to limit preoperative ERCP to patients with cholangitis, a strong suspicion of CBD stones or apparent cholestasis, which would be done within same index admission.

ERCP and ES apgallstones pancreatitis, and this has increasingly been used in elderly and frail people.[17,27,31–33] Bignell et al[31] demonstrated that 94% of patient treated with ERCP and ES alone had no recurrence of pancreatitis in a large retrospective study with a long follow-up (up to 10 years). Although these studies showed that ES alone is effective in reducing recurrent pancreatitis, patient who undergo only ES are at further risk of complications related to the gallbladder. Due to the high risk of biliary

Table 5 Results of a review of complications in the literature.

Author and year	No. of patients	Complications (early)	Complications (delayed)	Conversion (early)	Conversion (delayed)
Van Baal et al, 2012 [12]	998	4%	6%	9%	6%
Randial Perez et al, 2014 [26]	636	4.83%	4.42%	—	—
Johnstone et al, 2014 [25]	523	13%	9%	2%	8%
Current study	72	7.89%	8.82%	10.53%	11.76%

complications (ranging from 10% to 23%),[27,31-33] it was suggested that ERCP and ES should be used as an alternative to cholecystectomy in treatment of ABP in high risk surgical patients and elderly. However, for patients who are deemed fit for surgery, current literatures recommend ES followed by cholecystectomy in the treatment of ABP.[33—35] In the current study, ES did not appear to have a protective role in recurrent ABP as well as other biliary complications before cholecystectomy, though this did not reach statistical significance (Table 4). It may perhaps be noted that the majority of recurrent biliary events in the study were nonpancreatitis conditions, namely biliary colic and cholecystitis, which are typically not reduced by ES.

Postcholecystectomy pancreatitis has been shown to occur and indeed, there have been reports of pancreatitis recurring after cholecystectomy. These may be due to retained CBD stones or sludge. In this study, there was a patient who had postcholecystectomy pancreatitis. Though the IOC did not show evidence of CBD stone, a possible explanation may be fine 'sandy' stones or sludge that may not have been picked up. Nevertheless, pancreatitis recurrence after cholecystectomy in ABP is very low, and cholecystectomy remains the best modality of treatment in preventing recurrent pancreatitis.

A larger sample size in this study would have been more ideal for the statistical significance. The surgical procedure performed in this study was undertaken by a hepatobiliary surgeon, and though the uniformity of having a single surgeon in all procedures reduces bias in operative data and results, the results may not reflect that of cholecystectomy procedures in daily practice which are usually performed mostly by general surgeons. However, this should not affect analysis as the aim of the study is to compare the results between the two groups.

In conclusion, the findings of this study of patients with mild to moderate ABP demonstrate that laparoscopic cholecystectomy with IOC performed within the same index admission reduces recurrent biliary events and decreases the total length of hospital stay compared with delayed laparoscopic cholecystectomy. In addition, there is no difference in the need for conversion to open surgery, duration of surgery, or complication rate between performing early or delayed cholecystectomy. Therefore, we recommend early laparoscopic cholecystectomy in patients with mild to moderate ABP and we hope that with more supporting data and studies, early laparoscopic cholecystectomy will become the standard of care in treating mild to moderate ABP in the near future.

Appendix A. Supplementary data

Supplementary data related to this article can be found online at http://dx.doi.org/10.1016/j.asjsur.2016.07.010.

References