The Outcome of Early Laparoscopic Cholecystectomy after Acute Biliary Pancreatitis ''on Same Admission''

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ABSTRACT

Background: An acute pancreatic inflammatory process that may or may not include nearby tissues or distant organ systems is known as acute pancreatitis.

Objectives: This study aimed to evaluate the possibility of early laparoscopic cholecystectomy at the same time of admission in patients with non-necrotizing biliary acute pancreatitis.

Patients and methods: This study was carried out on twenty patients to detect the outcome of early laparoscopic cholecystectomy in acute biliary pancreatitis on same admission, which will be performed in General Surgery Department of Faculty of Medicine Menoufia University and General Surgery Department of Damanhur Medical National Institute.

Results: MRCP was done in 4 cases only (20%), and revealed multiple small gallstones in these 4 cases, only minimal intra-hepatic biliary dilatation (IHBRD) in 2 cases (10%). IOC was done for the four cases revealed that two cases (10%) had no common bile duct (CBD) stones, the other two cases (10%) had a small stone in CBD, so CBD stone extraction was done through transcystic CBD exploration with IOC, the CBD diameter was within normal in these 4 cases, ranged from 7-9.5 mm, mean diameter was 8.25 ± 1.44 mm. The early laparoscopic cholecystectomy group experienced a considerably shorter overall hospital stay than the delayed laparoscopic cholecystectomy group.

Conclusion: In moderate acute biliary pancreatitis, laparoscopic cholecystectomy is safe and doable during index hospitalisation without any further risks.

Keywords: Acute biliary pancreatitis, Cholecystectomy, Laparoscopic.

INTRODUCTION

Acute pancreatitis (AP) is described as a sudden onset of pancreatic inflammation with varied involvement of nearby tissues or distant organ systems ^[1]. It is one of the most prevalent gastrointestinal disorders, which typically has a mild and self-limiting course. However, 10% to 20% of patients experience a rapidly progressing inflammatory response that is linked to a lengthy hospital stay as well as significant morbidity and mortality. Less than 1% of patients with mild pancreatitis die, whereas between 10% and 30% of patients with severe pancreatitis do. Resulting in a financial, physical, and emotional strain on people^[2]. It can range from a minor, self-limiting pancreatic inflammation to a serious condition with infected pancreatic necrosis, multiple organ failure, and a significant mortality risk. Even in the lack of particular therapies that target the pathophysiology that determines clinical result, the clinical outcome has improved in recent decades. This is likely due to a more uniform approach to diagnosis, monitoring, and care ^[3].

Small gallstones and sludge are the most frequent causes of acute pancreatitis. These obstructions temporarily block the same channel that empties both the biliary and pancreatic ducts, which causes inflammation of the pancreas ^[4]. In some older research, surgeons favoured delaying the procedure until all clinical indications and test results had disappeared. Patients may experience recurrent biliary events such as biliary pancreatitis, acute cholecystitis, cholangitis, or biliary colic following an episode of biliary pancreatitis. Following an incident of acute biliary pancreatitis, cholecystectomy is advised by worldwide standards to avoid these. A patient may be at risk for a deadly episode of acute pancreatitis if decisive therapy is not given ^[5, 6]. The aim of this study was to evaluate the possibility of early laparoscopic cholecystectomy at the same time of admission in patients with non-necrotizing acute biliary pancreatitis.

PATIENTS AND METHODS

This study was carried out on twenty patients to detect the outcome of early laparoscopic cholecystectomy in acute biliary pancreatitis on same admission to be performed in General Surgery Department, Faculty of Medicine, Menoufia University and General Surgery Department of Damanhur Medical National Institute.

Inclusion criteria: All patients of gall bladder stones as primary cause of acute pancreatitis with clinical and radiological evidence (Elevated serum levels of amylase and lipase associated with pancreatitis in ultrasonography and /or CT scan).

Exclusion criteria: Patients with severe pancreatitis with organ failure (severe pancreatitis is defined as the presence of more than three Ranson criteria at the time of admission). Patients unwillingness to cooperate, high suspicion of retained CBD stone (Elevated Bilirubin Level with Ultrasound demonstration of CBD stone), severe medical conditions that preclude cholecystectomy (such as uncontrolled diabetes or cardiac patients), pregnancy, prior to a gastric bypass, complications (such as pancreatic pseudo cyst, pancreatic abscess, and pancreatic fistula) and a history of prior upper abdominal surgery that should rule out laparoscopy.

Diagnosis: Once a working diagnosis of acute pancreatitis is established, laboratory tests such as the following are conducted to corroborate the clinical impression: Blood urea nitrogen (BUN), creatinine and electrolytes, blood glucose, serum amylase and lipase, liver-associated enzymes (alkaline phosphate, total and direct bilirubin, AST, ALT), serum cholesterol and triglyceride levels, complete blood count (CBC) (high WBCs), hematocrit, C-reactive protein (CRP), and arterial blood gas levels are all measured.

Diagnostic imaging: Abdominal imaging is helpful to confirm the diagnosis and complications of acute pancreatitis. This includes abdominal radiography, abdominal ultrasonography (the most effective initial test for determining the aetiology and the technique of choice for detecting gallstones), and abdominal computed tomography (CT) scanning.

Abdominal imaging: Mild acute pancreatitis: Organ failure and regional consequences are not present. **Moderately severe acute pancreatitis:** Local issues and/or temporary organ failure (less than 48 hours). **Severe acute pancreatitis:** Persistent organ failure lasting more than 48 hours.

Preoperative assessment: Analgesics and appropriate fluid resuscitation were administered to the patients. They had regular laboratory tests and abdominal ultrasonography during the first three days of hospitalisation, as well as any further tests that might be required. CT is used. Patients proved with biliary mild attacks of AP admitted doing laparoscopic cholecystectomy, if retained CBD stone should have extracted by ERCP first, patients with severe attacks were referred to ICU.

Work up: Once acute pancreatitis has been successfully diagnosed. To corroborate the clinical impression, laboratory tests were obtained. Clinical signs, blood tests, and contrast-enhanced computed tomography (CT) scans are often used to diagnose AP. Immediately after presentation, the patient's hemodynamic state should be evaluated, resuscitative treatments should be taken as needed, and the Ranson scoring system should be used to categorise patients into groups before beginning a therapy plan. Because severity is the major factor in management. Mild acute pancreatitis may be treated conservatively with little difficulty (less than 3 points on the Ranson scale), while severe acute pancreatitis, which is excluded, requires intensive care (greater than 3 points on the scoring system). Within 48 hours of admission, patients with mild cases of acute pancreatitis were determined by these criteria: Improvement of clinical, hemodynamic status, abdomen imaging and laboratory results as well as patients who were recommended to undergo laparoscopic cholecystectomy following an episode of acute biliary pancreatitis in order to avoid further attacks.

Operative technique: by laparoscopic

cholecystectomy in almost all cases and only additional intraoperative cholangiogram (I.O.C) for the two cases with CBD stone.

Postoperative management: Postoperative analgesia with ketolac ampules during the first 24 hours postoperatively and later at the request of the patient, start with warm oral liquids the evening after the operation.

Follow up of the cases: Patients were monitored for one month in the outpatient clinic by liver function tests and ultrasonography of the abdomen were done to exclude missing stones or other long-term complications.

Complications: Postoperative (30 days after the operation) event that changed the clinical course such as bleeding, only one case complicated post-operatively with bleeding, which was estimated as 400 ml. in tubal drain. Bleeding decreased gradually after receiving one blood unit andbleeding stopped within the third day, drain removed and patient discharged. Bile duct injury or stricture, we faced one case with suspecting CBD injury, so converted to open method.

Ethical approval: Menoufia Medical Ethics Committee of Menoufia Faculty of Medicine gave its approval to this study. All participants gave written consents after receiving all information. The Helsinki Declaration was followed throughout the study's conduct.

Statistical Analysis

SPSS version 23 for Windows® was used to collect, code, analyse, and analyse the data. To evaluate if the data had a normal distribution, the Shapiro Walk test was used. Frequencies and relative percentages were used to depict qualitative data. The Chi square test (χ^2) was used to compare the differences between two or more sets of qualitative variables. The mean \pm SD of quantitative data was used. To compare two independent groups of regularly distributed variables (parametric data), the independent samples t-test was utilised. P \leq 0.05 was considered significant.

RESULTS

A flow chart of the study population is presented in figure (1). Of the 29 patients who attended to the General Surgery Department, Faculty of Medicine Menoufia University and General Surgery Department of Damanhur Medical National Institute. 9 patients were excluded from the study (3 patients declined consent and 6 patients did not meet the inclusion criteria) and 20 patients agreed to participate in the study 14 women (70%) and 6 men (30%), mean age was 42 ± 16.26 years and median age was 39 years, ranged from 22 to 60 years. Regarding history, two cases (10%) had past medical history of hypertension, all the other cases 18 cases (90%) were medically free. All our patients were ASA (American Society of Anesthesiology) grade I or II, we excluded patients with ASA grade III and IV from our study due to unfitness for laparoscopic surgery (Table 1).

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Figure (1): Flowchart of the studied patients.

Table	(1)	Distribustion	of the	at a dia d		a a a a a dia a da	dama a anamin'a	and aliminal data
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	No.	%	
Gender			
Male	6	30.0	
Female	14	70.0	
Age/year			
Min. – Max.	22.0-60.0		
Mean ± SD	42.0 ± 16.26		
Median	39.0		
Clinical presentation			
Pain	20	100.0	
Jaundice	12	60.0	
History of jaundice	0	0.0	
Cholangitis	2	10.0	
No jaundice	8	40.0	
History of pancreatitis	2	10.0	
Duration (days)			
Min. – Max.	2.0 -6.0		
Mean ± SD	4.50 ± 2.08		
Median	4.00		

Concerning laboratory investigations, the most important eight laboratory investigations that were observed in our patients were: ALT (Alanine Aminotransferase), AST (Aspartate Aminotransferase), ALP (Alkaline Phosphatase), total bilirubin, direct bilirubin, white blood cell count, serum amylase and lipase. The mean value for ALP was (ranged from 79-445 U/L), the mean value for total bilirubin was (ranged from 0.6-6.3 mg/dl), the mean value for direct bilirubin was (ranged from 0.1-5.9 mg/dl), the mean value for AST was (ranged from 27-914 U/L), the mean value for ALT was (ranged from 17-580 U/L), the mean value of WBC count was (ranged from 4.1-18.9 c/cm³), the mean value of serum amylase was (ranged from 47 -2933 U/L), and the mean value of serum lipase was (ranged from 52 - 5182 U/L). Alkaline phosphatase was elevated in14 cases (70%). Total bilirubin was elevated in 12 cases (60%), levels higher than 4 mg were found in 8 cases (40%). Direct bilirubin was elevated in 10 cases (50%). AST was elevated in 14 cases (70%), ALT was elevated in 8 cases (40%), and WBC count was elevated in 14 cases (70%). Serum amylase was elevated in 18 cases (90%), while serum lipase was elevated in 16 cases (80%) (Table 2).

Table (2): Descriptive of the studied cases according to preoperative laboratory investigations

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	Range	Median
ALT (SGOT) (U/L)	17.0 - 580.0	29.0
AST (SGPT) (U/L)	27.0 - 914.0	156.50
Total bilirubin (mg/dl)	0.60 - 6.30	1.50
Direct bilirubin	0.10 - 5.90	0.70
(mg/dl)		
ALP (U/L)	79.0 - 445.0	148.0
WBC (c/cm ³)	4.10 - 18.90	11.95
PA (%)	80.0 - 99.0	91.50
Amylase (U/L)	47.0 - 2933.0	478.0
Lipase (U/L)	52.0 - 5182.0	724.50

Median and Range: nonparametric test. SD; standard deviation, AST; Aspartate Aminotransferase, ALT; Alanine Aminotransferase, ALP;Alkaline Phosphatase, WBC; White Blood Cell count, PA; Prothrombin Activity.

In Ultra sonographic findings, preoperative ultrasound studies were available for all patients and were interpreted, by the radiologist, as suggestive of acute pancreatitis by the presence of bulky pancreas in 14 cases (70%). Gallstones were present in all patients (20 patients). Intra-hepatic biliary dilatation (IHBD) was detected in 4 patients (20%), always minimal degree. In 16 cases (80%), no IHBD was found, the number of gallstones were single in 4 cases (20%), and multiple stones were detected in 16 cases (80%). The size of gallstones was small (less than 5 mm) in 14 cases (70%), and large stones in 6 cases (30%). The CBD was described as dilated (more than 6 mm) in 4 cases (20%), the mean CBD diameter of the dilated cases was 12 \pm 3.9 mm (ranged from 9-17 mm). No CBD stones were detected in ultrasonography. In the four cases where CBD were dilated, further imaging (MRCP) was performed to verify the cause of CBD dilatation or trans-cystic intraoperative cholangiography was used to verify the cause of CBD dilatation and exclude the presence of CBD stones. Peri-pancreatic fluid collection was detected by ultrasonography in 14 cases (70%), in 12 cases (60%) this collection was minimal in amount, and in 2 cases (10%) this collection was mild in amount. No peripancreatic fluid collection was detected in 6 cases (30%). Concerning computed tomography (CT) findings, gallstones were present in 14cases (70%), the CBD was normal in 16 cases (80%), and dilated in 4 cases (20%). In the dilated cases, it was ranging from 9-17 mm and mean value was 12 ± 3.9 mm and IHBRD was present only in 2 cases (10%). Two scoring systems were included based on CT findings: The first was Bilthazar score, grade A where normal CT findings (not present in any cases), grade B where focal or diffuse enlargement of the pancreas was present in 4 cases (20%), grade C with peri-pancreatic inflammation was present in 11 cases (55%), grade D with fluid collection in a single location was present in4 cases (20%), grade E with two or more fluid collections were found adjacent to the pancreas and present in one cases (5%) (Table 3).

Table (3): Distribution of the studied cases according to ultrasound and CT

U/S	No.	%		
GB stones number				
Single	4	20.0		
Multiple	16	80.0		
Size of gallbladder	stones			
Small	14	70.0		
Large	6	30.0		
IHBRD				
No	16	80.0		
Minimal	4	20.0		
CBD diameter				
Normal	16	80.0		
Dilated	4	20.0		
Peri-pancreatic collection				
No	6	30.0		
Minimal	12	60.0		
Mild	2	10.0		
Bulky pancreas	14	70.0		
СТ	No.	%		
Gall stones	14	70.0		
CBD diameter				
Normal	16	80.0		
CBD dilated	4	20.0		
Min. – Max.	9.0 - 17.0			
Mean \pm SD	12.0 ± 3.90			
IHBRD	2	10.0		
Biltazar score				
А	0	0.0		
В	4	20.0		
С	11	55.0		
D	4	20.0		
E	1	5.0		

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In the current study, magnetic resonancecholangiopancreatography (MRCP) was done in 4 cases only (20%), and revealed multiple small gallstones in these 4 cases, only minimal IHBRD in 2 cases (10%). IOCwas done for the four cases revealed that two cases (10%) CBD was already free and the other two cases (10%) showed small stones found, so CBD stone extraction needed through transcystic CBD exploration with IOC. The CBD diameter was with in normal in these 4 cases, ranged from 7-9.5 mm with mean diameter 8.25 ± 1.44 mm. Regarding operative time, the mean duration of laparoscopic cholecystectomy was 53 ± 12.61 . From insertion of versus needle till the end of the operation, median 52.5 minutes, range 30 to 75 minutes. In the present study, the mean postoperative hospital stay was 1.8 ± 1.2 days (range from one to 4 days). As for postoperative pain, 18 patients (90%) experienced mild pain that relieved completely with the intake of two intravenous injections of NSAID followed by oral intake of NSAIDs, as if laparoscopic cholecystectomy for chronic calacular cholecystitis was done. In 2 cases (10%), the pain was moderate, only partially improving with NSAIDs (Table 4).

Table (4): Distribution of the studied cases according to MRCF	CP, and postoperativedata
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	No.	%		
GB stone				
Single	0	0.0		
Multiple	4	20.0		
Size				
Large	0	0.0		
Small	4	20.0		
IHBRD				
No dilatation	2	10.0		
Minimal	2	10.0		
CBD Diameter				
Min. – Max.	7.0-9.50	7.0-9.50		
Mean ± SD	8.25 ± 1.44	4		
CBD stones	2	20.0		
Other	0	0.0		
Postoperative hospital stays/days				
0	0	0.0		
1	12	60.0		
2	4	20.0		
3	0	0.0		
4	4	20.0		
Min. – Max.	1.0 - 4.0			
Mean \pm SD	1.80 ± 1.20	1.80 ± 1.20		
Postoperative pain				
Mild	18	90.0		
Moderate	2	10.0		
Severe	0	0.0		
Peristalsis audible and oral intake				
Day1	2	10.0		
Same day	18	90.0		
Drain removal/days				
1	12	60.0		
2	4	20.0		
3	4	20.0		
Min. – Max.	1.0 - 3.0			
Mean \pm SD	1.60 ± 0.82	2		

Regarding postoperative follow up, one week post-operative clinical and laboratory follow up was done. WBC count, serum amylase and lipase levels were done, mean WBC count was 6.53 ± 1.94 (range 4-10.5), mean serum amylase was 86 ± 54.26 ranged from 25 to 170 U/L (the normal range 30-110 U/L,) mean serum lipasewas 106.6 ± 79.55 ranged from 31 to 185 U/L (the normal range 10-140 U/L) (Table 5).

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Table (5): Distribution of the studied cases according to Follow up

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	Mean ± SD
WBC	6.53 ± 1.94
Amylase	86.0 ± 5.26
Lipase	106.60 ± 9.55



Fig. (6): Extraction of the gallbladder from the epigastric port if retrieval bag is not available.

DISCUSSION

The mean age of patients in our study was 42 ± 16.26 years with median age of 39 years, ranged from 22 to 60 years. In the study of **Rosing** *et al.* ^[7] the mean age was close toour patients (40 years and ranged from 28 to 54 years), **Judkins** *et al.* ^[8] reported mean age of 38.2 ± 16.0 years (range 20–80 years), while **Nguyen** *et al.* ^[9] reported mean age of 59.6 ± 20.2 years. The reason that mean age in our study was younger than most similar studies that we selected these cases to be generally fit for anaesthesia and laparoscopy.

With regard to female to male ratio, among 20 cases 14 cases were females (70%), and 6 patients were males (30%), this was predictable because the incidence of gallstones and biliary pancreatitis is higher in females. This is in accordance with most similar studies; Nguven et al. ^[9] reported 63% females and 37% males, Ito et al. ^[10] also showed femalepredominance of 67% and males 33%. All patients presented with abdominal discomfort (100%), and jaundice was detected in 12 instances (60%), history of previous attackof pancreatitis in two patients (10%). Rosing et al. ^[7] defined gallstone pancreatitis by proper history and physical examination, (epigastric, right upper quadrant abdominalpain, nausea, vomiting), elevated serum levels of amylase, lipase or both, and sign of gallstones in either ultrasonography or CT scan, so all cases in their study were complaining of abdominal pain as main presenting symptom.

The mean duration of symptoms before admission was 4.50 ± 2.08 days, average(2-6 days) and median of 4 days. In the study of **Rosing** *et al.* ⁽⁷⁾, the duration of symptoms before diagnosis was short less than 48 hours, which mirrors that our patients were presented and sought medical advice late.

The most important laboratory investigations that were observed in our study were ALT, AST, ALP, total bilirubin, direct bilirubin, whiteblood cell count, serum amylase and lipase. The range of ALT in our study was 17-580U/L, the range of AST was 27-914 U/L, the range of ALP was 79-445 U/L, the range of total bilirubin was 0.6-6.3 mg/dl, the range of direct bilirubin was 0.1-5.9 mg/dl, therange of WBC count was 4100-18900 c/cm, the range of serum amylase was 47-2933 U/L, the range of serum lipase was 52-5182 U/L. Serum amylase level in study of Rosing et al. (7) ranged between 530 and 2092U/L, which was elevated in all cases of this study. Wilson and De Mova [11] depended on Ranson score below or equal to 3 to diagnose cases of mild biliary pancreatitis however in our study we mainly depended on improvement of clinical and hemodynamic status (no nausea and vomiting, oral feeding can be initiated), revision of laboratory data (improvement of serum amylase lipase and WBCs) and abdominal imaging (ultrasonography and CT).

In our study MRCP was done in 4 cases (20%), which revealed calcular gallbladderdisease, with minimal IHBRD in 2 cases (10%). Two cases (10%) CBD was already freeand the other two cases (10%) showed small stones, so CBD stone extraction needed through transcystic CBD exploration with IOC. When used to rule out CBD stones, MRCP is a secure and accurate imaging tool for common bile duct disease. According to Hallal et al. ^[12], MRCP is related with advantageous properties (such as high sensitivity and negative predictive value) in choledocholithiasis identification among patients with biliary pancreatitis. MRCP is a desirable alternative for those who have a minimal risk of developing choledocholithiasis since it is noninvasive. Laparoscopic cholecystectomy (without CBD exploration) was done in 18 cases (90%), no CBD dilatation was present (by US or CT) or dilated CBD but stones were excluded using MRCP. There were no intraoperative difficulties, Calot's triangle dissection was simple, only minor adhesions, cystic duct was dilated in most cases indicating its abilityto pass stones to the CBD and confirming the biliary etiology for pancreatitis, operativetime was close to that consumed in similar studies.

We employed the laparoscopic technique since it has become the accepted method for cholecystectomy, resulting in a shorter hospital stay and quicker return to regular activity. There is disagreement about the best time to do cholecystectomy for gallstone pancreatitis, but some experts believe it should be done right away to prevent recurring biliary problems. According to Rosing et al.^[7], patients with mild to severe gallstone pancreatitis can safely receive early laparoscopic cholecystectomy (LC) without holding off until laboratory results have returned to normal or their symptoms have subsided. Hospital stays decreased as a result of an early LC strategy. **Taylor and Wong**^[13] examined the methods used by two surgeons. Surgeon 1 delayed the surgery until the amylase level returned to normal and the abdominal soreness completely disappeared, while surgeon 2 started the laparoscopic procedure as soon as the amylase level was dropping and the stomach discomfort was getting better. For surgeons 1 and 2, the complications rate was 10% and 11%, respectively. Patients of surgeon 1 spent 4.7 days in the hospital, whereas patients of surgeon 2 spent 3.7 days there. Additionally, this study's problems rate and hospital stay were comparable to ours.

Ito *et al.* ^[10] accepted that in certain patients having cholecystectomy for acute biliary pancreatitis who are at low risk for choledocholithiasis, direct ductal assessment can be performed safely. Furthermore, IOC might not be required in patients having cholecystectomy after biliary pancreatitis attack if there are no abnormalities in liver function tests or bile duct dilatation seen on preoperative non-invasive imaging.

In our study the range of postoperative hospital stay was between 1-4 days, and this was one of the main advantages of early cholecystectomy to shorten the hospital stay and to prevent recurrent attacks of pancreatitis that require readmission. In the study of **Rosing** *et al.* ^[7], strategy of early cholecystectomy resulted in considerably shorter hospital stays for patients with mild to severe biliary pancreatitis, with no increase in complications or death. Retrospective research by Tang and Cuschieri ^[14] showed that early surgery was safe in cases with moderate gallstone pancreatitis, which resulted in 4.2-days decrease in the average duration of stay. Delaying cholecystectomy offers no advantage in terms of intraoperative problems and may significantly increase overall morbidity and length of hospital stay. Delayed cholecystectomy is related with recurrent biliary episodes in 25-61% of patients. Ammori et al. [15] found no indication that patients with biliary pancreatitis experienced intraoperative or postoperative problems more frequently than those having LC. This illustrates the necessity of the "same admission" cholecystectomy protocol for biliary pancreatitis patients.

Recurrent biliary pancreatitis may be severe and according to surgeons who advocate lethal. cholecystectomy on first admission. Despite this, an early cholecystectomy may potentially result in a simpler dissection than a later one. According to the research of Costi et al. ^[16], a single final intervention may be used in the future to address gallstone pancreatitis with choledocholithiasis. The concept of "laparoscopy first" combines cholecystectomy with laparoscopic exploration of the common bile duct in a single setting on first admission. Surprisingly several investigations revealed that only a small percentage of individuals had an early cholecystectomy, despite the UK guidelines for acute pancreatitis being published. Also surprisingly, only a small percentage of individuals had cholecystectomy procedures done too late in research from the USA and Australia.

CONCLUSIONS

Postponing cholecystectomy does not change intra-operative complications, laparoscopic cholecystectomy in mild acute biliary pancreatitis is safe and practical at index admission without additional risks, delayed cholecystectomy in case of mild biliary pancreatitis carries risk of recurrent biliary pancreatitis and other gallstones complications during interval period like acute cholecystitis and biliary colic and delayed cholecystectomy takes the risk of patient drop outs during interval period before cholecystectomy leaving those patient at persistent risk of recurrent biliary pancreatitis that maybe severe and fatal.

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