

EARLY VERSUS DELAYED LAPAROSCOPIC CHOLECYSTECTOMY IN PATIENTS WITH MILD ACUTE BILIARY PANCREATITIS

By

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ABSTRACT

Background: Acute biliary pancreatitis and timing of cholecystectomy has always been a challenge for surgeons dealing with biliary pathology. Both the diagnosis and treatment have evolved over the last years with the introduction, and universal application of advanced imaging modalities, as well as endoscopic and laparoscopic procedures.

Objective: To compare between index and interval laparoscopic cholecystectomy in the management of acute mild biliary pancreatitis.

Patients and methods: This study was carried out on 50 patients with mild acute biliary pancreatitis, period from April 2020 to December 2020. The study had been carried out at Al-Hussein Hospital, Al-Azhar University, and Damanhour National Medical Institute. They were divided into two equal groups: Group A underwent early cholecystectomy within a week of admission, and group B underwent delayed (interval) cholecystectomy 4-6 weeks after discharge.

Results: Early group included 3 males (12%) and 22 females (88%), while interval group included 5 males (20%) and 20 females. (80%) ,Regarding age ($p=0.209$) , mean age \pm SD for the index group was 39.40 ± 10.46 years, and range 23 – 59 years , while in the interval group mean age \pm SD was 43.40 ± 11.69 years ,and range 22 – 59 years. All cases were subjected to through history taking and complete clinical examination. Abdominal pain was the presenting symptom in all patients (100%), jaundice was present in 10cases (40%) in group A and in 8 cases (32%) in group B. Laparoscopic cholecystectomy (LC) was completed to all patients in group A and group B without conversion to open cholecystectomy. Peristalsis was audible and patients started oral fluid intake in the same day of surgery in all cases. No intraoperative complications took place, and no postoperative complications were recorded. Patients were followed for 3 months post-operatively, no mortality, and no complications were recorded.

Conclusion: Laparoscopic cholecystectomy in mild acute biliary pancreatitis was safe and feasible during index admission with no added risks. Postponing cholecystectomy did not alter intra-operative complications.

Keywords: Laparoscopic Cholecystectomy, Mild Acute Biliary Pancreatitis.

INTRODUCTION

Defined acute pancreatitis (AP) as an inflammatory disease of the pancreas that is associated with little or no fibrosis of the gland, and which may be followed by

clinical and biological restitution, if the primary cause is eliminated. Clinically, the severity of acute pancreatitis varies significantly. Most patients experience a mild form of the disease, which is self-limiting; while others suffer a more severe

and sometimes a fatal attack (*Chatila et al., 2019*).

Acute gallstone pancreatitis is a common condition throughout the world, marked by pancreatic inflammation. Acute pancreatitis is thought to be triggered by the passage of gallstone down the common bile duct (CBD). Patients who have small gall stones and a wide cystic duct may be at a higher risk of passing stone. Gall stone migration with obstruction of the CBD and pancreatic duct triggers acute biliary pancreatitis (*Kirkegård et al., 2018*).

According to *Van Geenen et al., (2010)* the mechanism by which the passage of gallstones induces pancreatitis is unknown. Two factors have been suggested as the possible initiating event in gallstone pancreatitis: reflux of bile into the pancreatic duct due to transient obstruction of the ampulla during passage of gallstones; or obstruction at the ampulla secondary to stone(s) or edema resulting from the passage of a stone.

Acute pancreatitis constitutes about 80% of cases with mortality around 1%, while severe attack occurs in rest 20% of cases which is associated with mortality ranging from 20% to 50%. One major cause of acute pancreatitis is biliary calculi, which accounts for about 50-70% of cases presenting with this disease (*Banks et al., 2012*).

Laparoscopic Cholecystectomy is the treatment of choice to prevent further attacks. Controversy regarding the timing of cholecystectomy in the patients with Acute Biliary Pancreatitis still exists (*Vege et al., 2018*).

Patients with severe AP with associated dysfunction of multiple organs are, unequivocally logical choice for the initial conservative approach with Delayed Laparoscopic Cholecystectomy (DLC), 4-6 weeks after the subsidence of acute phase. But, the optimal timing of surgery in mild pancreatitis (Ranson score ≤ 3) remains unclear (*Tan et al., 2019*).

The aim of this study was to evaluate the optimal timing of laparoscopic cholecystectomy (LC) in patients with mild gallstone pancreatitis.

PATIENTS AND METHODS

This study was carried out on 50 patients with mild acute biliary pancreatitis, during the period from April 2020 to December 2020. The study had been carried out at Al-Hussein Hospital, Al-Azhar University and Damanhour National Medical Institute.

Inclusion criteria:

- All adults between the age of 20 and 60 with mild gallstone pancreatitis were included.
- Diagnosis of:
 - a. **Acute pancreatitis (at least two of the three following features present):** 1. Upper abdominal pain. 2. Serum lipase or amylase levels above three times the upper level of normal 3. Characteristic findings of acute pancreatitis on cross-sectional abdominal imaging.
 - b. **Mild pancreatitis:** No pancreatic necrosis, No persistent organ failure > 48 hours.
 - c. **Biliary pancreatitis:** Any of the following: 1-Gallstones and/or

sludge diagnosed on imaging. 2-Alanine aminotransferase level >2 times higher than normal values, with serum alanine aminotransferase levels >aspartate aminotransferase level).

Exclusion criteria:

- Extreme of age under 20 and above 60 years.
- Severe pancreatitis (as defined by the presence of more than 3 Ranson criteria on admission).
- Suspected concomitant acute cholangitis.
- Patient refusal to participate.
- Severe preexisting medical comorbidities contraindicating cholecystectomy (as determined by the primary physicians).
- Patients with:
 1. Necrotizing pancreatitis.
 2. Pancreatic infected collection.
 3. Pancreatic fistula.
 4. American Society of Anesthesiologists (ASA) III patients.

Patients were randomly assigned to either one of two groups using a computerized random-number generator by simple odd even number randomization technique. All patients got a serial number starting from 1. First case was allocated into group A, and then all odd serial numbers were included in group A and even serial number in group B.

- Twenty five of the patients included in the study (Group A) underwent early

(index) laparoscopic cholecystectomy (within 7 days of the randomization).

- The other 25 patient (Group B) underwent delayed laparoscopic cholecystectomy (4-6 weeks after randomization).

A written informed consent from each patient was obtained before study participation and after full explanation of the technique and its possible complications. The study was approved by our faculty ethical committee.

All patients were informed about their bilio-pancreatic pathology and the suggested treatment according to their diagnosis, Also the possibility of conversion to open surgery was explained to each patient.

Pre-operative evaluation of the chest radiographs and electrocardiogram studies were performed. Patients' ASA scores were recorded.

All patients with characteristic abdominal pain of pancreatitis were subjected to:

1. Thorough history taking and physical examination.
2. Laboratory investigations.
3. Imaging: Abdomen ultrasonography, CT scan of the abdomen and magnetic resonance cholangiopancreatography (MRCP) (when indicated).
4. ERCP in patients with persistent calculi CBD obstruction.

Operative technique:

- Laparoscope: Karl Storz Endoscope set, telecam DX II, Hopkins II optics, code number 26003 BA.

- The protocol of general anesthesia was uniform in all patients; isoflurane 1-2% for maintenance.
- Prophylactic antibiotics were given at the time of induction of anesthesia, third generation cephalosporins.
- Position of the patient: supine.
- Laparoscopic instruments were placed on a separate stand located on the patient's left. This arrangement allowed efficient surgeon access to the instruments with ease.
- Insertion of a suitable size nasogastric tube to deflate the stomach.
- Laparoscopic ports were placed in the standard approach used in laparoscopic cholecystectomy. A four ports technique as described by Reddick was employed with a zero degree laparoscopic lens used. A 12 mm supraumbilical port was inserted. Another 12 mm epigastric and two 5

mm right subcostal ports were inserted under direct vision.

Statistical analysis:

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for the Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Wilk test. Qualitative data were represented as frequencies and relative percentages. Chi square test (χ^2) was used to calculate difference between two or more groups of qualitative variables. Quantitative data were expressed as mean \pm SD (Standard deviation). Mann Whitney test was used for the abnormally distributed quantitative variables. Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data). P value $<$ 0.05 was considered significant.

RESULTS

There was no significant difference between the two studied groups as regard demographic data. There was significant

difference between the two studied groups as regard ALT at admission time (**Table 1**).

Table (1): Comparison between the two studied groups according to demographic data and laboratory data at admission time

Parameters	Group I (n = 25)		Group II (n = 25)		p
	No.	%	No.	%	
Demographic data:					
Sex					
Male	3	12.0	5	20.0	>0.05
Female	22	88.0	20	80.0	
Age (years)					
Min. – Max.	23.0 – 59.0		22.0 – 59.0		>0.05
Mean ± SD.	39.40 ± 10.46		43.40 ± 11.69		
Presentation					
Pain	25	100.0	25	100.0	–
Jaundice	10	40.0	8	32.0	>0.05
Associated co morbidities					
Hypertension	5	20.0	5	20.0	>0.05
Diabetes	5	20.0	3	12.0	>0.05
Cesarian section	9	36.0	9	36.0	>0.05
Appendectomy	2	8.0	5	20.0	>0.05
Laboratory data at time of admission					
Amylase					
Min. – Max.	382.0 – 2300.0		395.0 – 2070.0		>0.05
Mean ± SD.	1003.0 ± 508.84		829.92 ± 434.46		
Lipase					
Min. – Max.	213.0 – 1950.0		234.0 – 1720.0		>0.05
Mean ± SD.	796.04 ± 365.69		648.56 ± 328.87		
AST					
Min. – Max.	29.0 – 180.0		22.0 – 140.0		>0.05
Mean ± SD.	73.28 ± 38.57		53.52 ± 27.55		
ALT					
Min. – Max.	28.0 – 182.0		21.0 – 112.0		0.018
Mean ± SD.	74.64 ± 44.84		47.40 ± 22.06		
Calcium ++					
Min. – Max.	8.70 – 10.30		8.89 – 10.20		>0.05
Mean ± SD.	9.38 ± 0.55		9.44 ± 0.31		
ALK Phosph					
Min. – Max.	40.0 – 312.0		39.0 – 390.0		>0.05
Mean ± SD.	131.56 ± 73.86		172.20 ± 109.34		
Bilirubin					
Min. – Max.	0.33 – 2.40		0.33 – 2.10		>0.05
Mean ± SD.	1.14 ± 0.68		1.01 ± 0.56		
CRP					
Min. – Max.	12.0 – 78.0		6.0 – 70.0		>0.05
Mean ± SD.	40.12 ± 24.12		29.96 ± 19.18		

There was no statistical difference between two groups according to ultrasound data collected. There was no

statistical difference between two groups according to CT results (**Figure 1**).

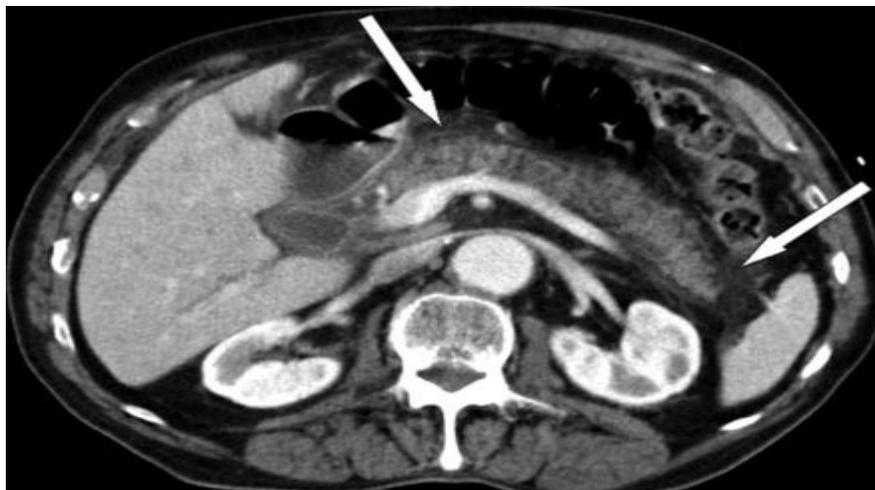


Figure (1): CT showing interstitial inflammation of the pancreas

There was no significant difference between the two studied groups as regard radiological data (**Table 2**).

Table (2): Comparison between the two studied groups according to radiological data

Radiological data	Group I (n = 25)		Group II (n = 25)		p
	No.	%	No.	%	
GB stones number					
Single	5	20.0	2	8.0	>0.05
Multiple	20	80.0	23	92.0	
Cystic dilation					
No	25	100.0	25	100.0	>0.05
Yes	0	0.0	0	0.0	
IHBRD					
No	20	80.0	22	88.0	>0.05
Minimal	5	20.0	3	12.0	
CBD diameter					
Normal	20	80.0	22	88.0	>0.05
Abnormal (Dilated)	5	20.0	3	12.0	
MRCP					
No	20	80.0	22	88.0	>0.05
Free	5	20.0	3	12.0	
Biltazar score					
A	0	0.0	3	12.0	>0.05
B	10	40.0	15	60.0	
C	10	40.0	5	20.0	
D	5	20.0	2	8.0	
E	0	0.0	0	0.0	

Surgical management: Laparoscopic cholecystectomy was performed early during the index hospitalization for 25 cases with mild biliary pancreatitis, while

25 other cases were discharged were re-admitted for delayed laparoscopic cholecystectomy at the appointed time.

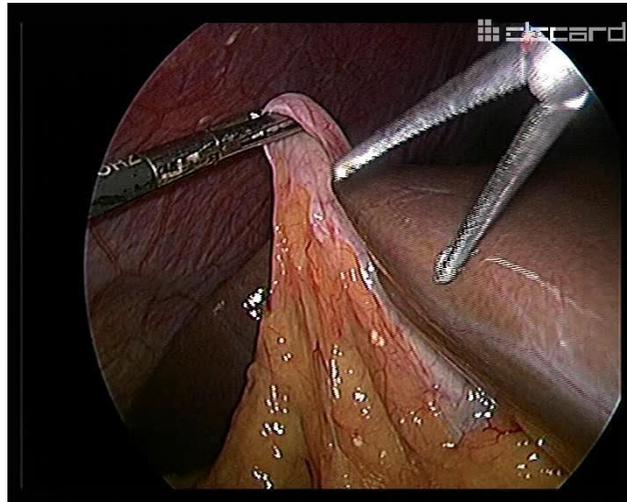


Figure (2): Adhesions with omentum

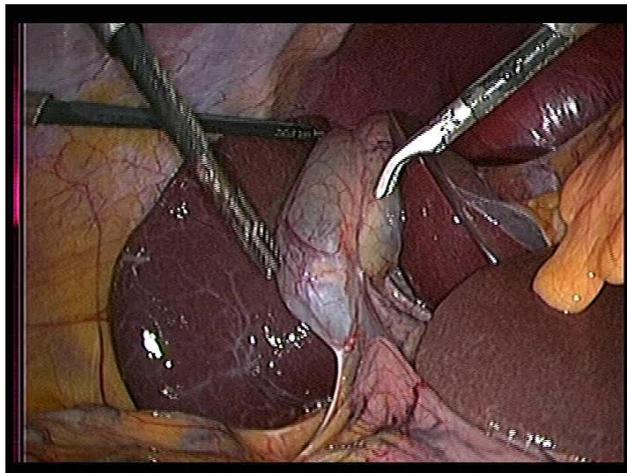


Figure (3): Adhesions between gallbladder and duodenum

There was no significant difference between the two studied groups as regard surgical data (Table 3).

Table (3): Comparison between the two studied groups according to recorded surgical data

Recorded surgical data	Group I (n = 25)		Group II (n = 25)		p
	No.	%	No.	%	
Adhesions					
Absent	10	40.0	13	52.0	>0.05
Present	15	60.0	12	48.0	
Callots dissection					
Easy	15	60.0	17	68.0	>0.05
Difficult	10	40.0	8	32.0	
Operative time (minutes)					
Min. – Max.	20.0 – 95.0		25.0 – 100.0		>0.05
Mean ± SD.	47.08 ± 23.02		49.0 ± 23.07		
Conversion to open cholecystectomy					
No	25	100.0	25	100.0	>0.05
Yes	0	0.0	0	0.0	
Postoperative hospital stay (days)					
Min. – Max.	1.0 – 3.0		1.0 – 3.0		>0.05
Mean ± SD.	1.24 ± 0.52		1.24 ± 0.52		
Morbidity					
No	25	100.0	25	100.0	–
Yes	0	0.0	0	0.0	
Bleeding					
Min. – Max.	20.0 – 160.0		20.0 – 160.0		>0.05
Mean ± SD.	51.80 ± 40.90		47.64 ± 35.32		

There was no significant difference between the two studied groups as regard 1st week follow (Table 4).

Table (4): Comparison between the two studied groups according to laboratory data one week post-operative

Groups	Group I (n = 25)	Group II (n = 25)	P
Laboratory data one week postoperative			
Amylase			
Min. – Max.	24.0 – 54.0	28.0 – 50.0	>0.05
Mean ± SD.	36.2± 8.46	35.68 ± 5.65	
Lipase			
Min. – Max.	15.0 – 35.0	12.0 – 36.0	>0.05
Mean ± SD.	22.96 ± 5.96	21.64 ± 7.11	
AST			
Min. – Max.	8.0 – 37.0	9.0 – 31.0	>0.05
Mean ± SD.	18.12 ± 7.28	15.28 ± 5.66	
ALT			
Min. – Max.	10.0 – 34.0	12.0 – 40.0	>0.05
Mean ± SD.	20.76 ± 6.70	23.8 ± 7.12	
ALK Phosph			
Min. – Max.	35.0 – 84.0	38.0 – 92.0	>0.05
Mean ± SD.	51.76± 13.07	52.48± 13.85	
Bilirubin			
Min. – Max.	0.39 – 1.1	0.38 – 0.90	>0.05
Mean ± SD.	0.73± 0.26	0.59 ± 0.18	

DISCUSSION

There is no universally accepted definition of 'early' laparoscopic cholecystectomy.

In our study early laparoscopic cholecystectomy within one week of the randomization, and delayed laparoscopic cholecystectomy 4 -6 weeks after randomization.

Yuan et al. (2020) suggested early laparoscopic cholecystectomy within 72 h after index admission, regardless of whether the abdominal symptoms were relieved or the laboratory test results backed to normal.

Delayed laparoscopic cholecystectomy (DLC), which was performed after

alleviation of abdominal symptoms and normalization of laboratory test results and usually beyond 72 h after index admission.

In *Aboulian et al. (2010)* and *Falor et al. (2012)* studies, patients were divided into 2 groups according to the timing of the LC. Patients who underwent an early LC (performed within 48 hours of admission) were compared with patients who underwent a delayed LC (after 48 hours).

In *Nebiker et al. (2011)* study, early cholecystectomy was defined as cholecystectomy within 14 days after onset of symptoms (group A). Delayed cholecystectomy was defined as initial conservative treatment followed by

cholecystectomy >14 days after first admission (group B). The majority of patients in group A were operated during the same hospitalization (only 8 patients left hospital before the operation), whereas those in group B normally left hospital after the first attack and were readmitted later for cholecystectomy.

Gurusamy et al. (2013) considered any laparoscopic cholecystectomy performed within three days after onset of pancreatitis as early laparoscopic cholecystectomy while considered laparoscopic cholecystectomy performed after three days as 'delayed' laparoscopic cholecystectomy.

In our study all patients in the early and delayed group reached the end point and have done laparoscopic cholecystectomy with no second attack of mild biliary pancreatitis.

Van Geenen et al. (2010) concluded that interval cholecystectomy carries a substantial risk of recurrent bilio-pancreatic events after discharge and before IC after mild gallstone pancreatitis. This risk is high even when the IC takes place within 2 weeks after discharge from the acute pancreatitis. Early cholecystectomy may be indicated to prevent such biliary events, which are associated with patient discomfort, hospital admission and additional costs.

In our study, no statistical difference between two groups as regard intra-operative measured parameters no difference in between two groups as regard intra operative complications which is consistent with other studies.

In our study, and in *Aboulian et al. (2010)*, no intraoperative complications in both groups.

In *Yuan et al. (2020)* study, the peri-operative and post-operative complications such as bleeding, bile leak, bile duct injuries, intra-abdominal abscess, and fever and port site infection were comparable in both groups and there was no significant difference between two groups.

In *Falor et al. (2012)* study, no statistical difference between two groups. Complications in the early LC group included urinary tract infection, CBD leak, recurrent pancreatitis, choledocholithiasis, and postoperative pain. In the delayed LC group, complications included intraoperative hypotension, cystic duct leak, presence of pancreatic pseudo cyst, CBD leak, wound infection, and recurrent pancreatitis. there was no statistical difference in complication rates 4.2% in early LC group vs 4.8% in delayed LC group.

In our study, all operated cases in the early and delayed group were completed laparoscopically with no conversion to open surgery.

In *Yuan et al. (2020)* study, 3 patients converted to open cholecystectomy in early group and 2 patients in delayed group. The difference was statistically insignificant.

In *Nebiker et al. (2011)* study, conversion to open surgery was necessary in 6% in group A and 3% in group B

In *Falor et al. (2012)* study, conversion from LC to open cholecystectomy 2.5% in early LC group vs 7.5% in delayed LC group.

Delayed cholecystectomy was associated with recurrent biliary attacks in 25-61%, and delaying cholecystectomy has no advantage regarding intraoperative complications.

This emphasized the safety and feasibility of early cholecystectomy in patients with mild biliary pancreatitis.

In our study ultrasonography was the first radiological investigation. *Nebiker et al. (2011)* based on ultrasonography for detection of gallstones, and confirmation of the biliary etiology as the cause of pancreatitis, and if CBD stones were suspected further radiological investigations were required.

In our study, magnetic resonance cholangiopancreatography (MRCP) was done in all cases that showed CBD dilation by ultrasound, in 20% cases in the index group and in 12% cases in the interval group.

Nebiker et al. (2011) performed MRCP in 31% of group A and 53% of group B because of increased serum bilirubin concentrations or clinical signs of cholestasis. 20% of group A and 31% of group B, CBD stones were detected on MRCP, and were extracted successfully after endoscopic sphincterotomy.

CONCLUSION

Laparoscopic cholecystectomy in mild acute biliary pancreatitis was safe and feasible during index admission with no added risks. Postponing cholecystectomy did not alter intra-operative complications.

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الإستئصال المبكر مقابل الاستئصال المتأخر للمرارة في المرضى الذين يعانون من التهاب البنكرياس الحاد الصفراوي الخفيف

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خلفية البحث: يعتبر الالتهاب الحاد للبنكرياس الناتج عن حصوات الحويصلة المرارية وتوقيت استئصال المرارة تحدياً دائماً للجراحين وقد تطورت طرق التشخيص و العلاج على مدى السنوات الماضية خاصة مع إدخال طرق التصوير المتقدمة والمناظير.

الهدف من البحث: المقارنة بين الاستئصال المبكر و المؤجل للمرارة بالمنظار في حالات التهاب البنكرياس المراري الحاد البسيط.

المرضى وطرق البحث: أجريت هذه الدراسة على 50 مريضاً يعانون من إتهاب حاد بسيط بالبنكرياس ناتج عن حصوات الحويصلة المرارية, و تم تقسيم المرضى إلى مجموعتين متساويتين، المجموعة الأولى تم إجراء إستئصال للمرارة بالمنظار للمرضى أثناء فترة الحجز الأولى خلال اسبوع و المجموعة الثانية أجريت لهم إستئصال للمرارة بالمنظار بعد 4-6 أسابيع من خروجهم من المستشفى بعد فترة الحجز الأولى. وعمل أشعة الرنين على القنوات المرارية في الحالات التي كانت تعاني من إتساع بالقناة المرارة أجريت في عشرة حالات في المجموعة الأولى و ثمانية حالات بالمجموعة الثانية. كل المرضى الذين شملتهم الدراسة كانوا يعانون من إتهاب خفيف بالبنكرياس ووجود حصوات بالقناة المرارية, بينما استبعد من الدراسة المرضى الذين يعانون من إتهاب شديد بالبنكرياس أو إتهاب مضاعف أو عدم اللياقة لإجراء منظار البطن الجراحي.

نتائج البحث: احتوت المجموعة الأولى على 3 ذكور (12%) و 22 انثى (88%) بينما احتوت المجموعة الثانية على خمسة ذكور (20%) و 20 انثى (80%) وكان متوسط العمر في المجموعة الأولى 39.40 ± 10.46 سنة, و تراوحت أعمارهم بين 23 الى 59 سنة, متوسط العمر في المجموعة الثانية كان $43.40 \pm$

11.69 سنة, و تراوحت أعمارهم بين 21 الى 59 سنة, و كانت آلام البطن هى العرض الأساسى فى كل الحالات, وكانت الصفراء موجودة فى أربعة مرضى من المجموعة الأولى و ثلاثة مرضى بالمجموعة الثانية. وقد أظهرت الموجات فوق الصوتية حصوات بالحويصلة المرارية فى كل الحالات, بينما استخدمت الأشعة المقطعية لتأكيد التشخيص وتحديد درجه الألتهاب, تم إجراء عملية استئصال الحويصلة المرارية بواسطة منظار البطن الجراحى لجميع الحالات بالمجموعة الاولى والثانية بدون تحويل أى حالات للفتح الجراحى. ولم تحدث مضاعفات أثناء العملية أو بعد العملية, وتم متابعة المرضى لثلاثة أشهر بعد العملية و لم تحدث مضاعفات أو وفاة أثناء هذه الفترة.

الاستنتاج: إستئصال المرارة بالمنظار فى إلتهاب البنكرياس الصفراوي الحاد الخفيف آمن وممكن أثناء إدخال المؤشر دون مخاطر إضافية. ولا يغير تأجيل استئصال المرارة من المضاعفات أثناء العملية.

الكلمات الدالة: إستئصال المرارة بالمنظار، إلتهاب البنكرياس الصفراوي الخفيف.