

The Outcome of Laparoscopic Cholecystectomy within the First 72 Hours of Acute Cholecystitis versus Laparoscopic Cholecystectomy Performed after 72 Hours Till the End of the First Week

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Abstract

Background: Cholecystectomy for acute calcular cholecystitis is the most frequent surgical procedure performed by general surgeons comprising approximately 500000 operations annually in USA. Laparoscopic cholecystectomy became the gold standard treatment for acute non-complicated calcular cholecystitis but the appropriate time remains controversial.

Aim of Study: The aim of this study was to compare between laparoscopic cholecystectomy within the first 72 hours of clinical presentation (Group A) and laparoscopic cholecystectomy after 72 hours till the end of the first week (Group B) in acute calcular cholecystitis regarding operative and postoperative outcome.

Patients and Methods: This study was a prospective comparative study including 30 patients who had been diagnosed with acute calcular cholecystitis in the period between November 2020 and November 2021. The cases were collected from emergency room and outpatient clinics in Ain Shams University hospitals and policehospitals in Egypt.

Results: Of the 30 patients, 16 were operated upon within 72 hours of presentation while 14 were operated beyond 72 hours till the end of the first week. The mean operative time in the early group was significantly higher than delayed the group (116.13 versus 86.67min, $p=0.003$). There was no significant difference regarding the intraoperative complications or conversion rate to open cholecystectomy in both groups. Regarding the postoperative data there was no significant difference according to the length of postoperative hospital stay and postoperative complications.

Conclusion: Early laparoscopic cholecystectomy for acute non-complicated cholecystitis within 72 hours from onset of symptoms (although longer operative time) is a safe procedure with similar hospital stay and comparable morbidity with late laparoscopic cholecystectomy after 72 hours.

Key Words: Acute calcular cholecystitis – Laparoscopic cholecystectomy.

Introduction

GALL stones are frequent and usually a Symptomatic disease, symptomatic gall stones and acute calcular cholecystitis are commonly facing general surgeons [1,2]. The reported prevalence of gallstones is up to 10% in adult eastern populations and up to 15% in adult western populations. It is estimated that 20-40% of individuals with gallstones will develop associated symptoms, and 12% will develop acute cholecystitis, acute cholecystitis due to gall stones in up to 90% of patients [1].

Gall stones are classified based on composition and location. More than 90% of gall stones are composed mainly of cholesterol (cholesterol gall stones) the other stone types (10%) are represented by black and brown pigment stones. Stones in the gallbladder (cholecystolithiasis) are the main entity and consist of cholesterol and black pigment gallstones (composed of polymerized calcium bilirubinate). By contrast, brown pigment stones, containing bilirubin and calcium fatty acid soaps, form in infected bile ducts [3].

Epidemiological studies have indicated a large number of risk factors for cholesterol stones. The formation of cholesterol stones is profoundly influenced by metabolic abnormalities. Obesity predisposes to gallstone formation symptomatic gallstones and cholecystectomy. Hyperinsulinemia is associated with increased hepatic cholesterol uptake biliary secretion and hyposecretion of biliary bile acids. In addition insulin resistance and type 2 diabetes mellitus act as independent factors that is associated with cholesterol gallstones and gallstone disease. Physical inactivity and over nutrition are known risk factors for obesity and metabolic syn-

drome also increase the synthesis of hepatic cholesterol and, therefore, increase the risk of developing cholesterol gall stones [4].

Patients with gallbladder stones can present with characteristic symptoms called biliarycolic, which is defined as episodic attacks of severe pain in the right upper abdominal quadrant or epigastrium for at least 20-30 minutes with radiation of the pain to the right back or shoulder, which improves with administration of analgesics. In addition, gallbladder stones can also cause nonspecific abdominal symptoms, such as epigastric pain and intolerance to fried or fatty foods (characterized by nausea, bloating and flatulence). However, only 60% of patients report the absence of abdominal pain after surgery, indicating that symptoms are neither characteristic nor predictive [5].

Acute cholecystitis (sudden inflammation of the gallbladder) should be suspected in a patient with fever, severe pain located in the right upper abdominal quadrant that lasts for several hours and/or Murphy's sign (that is, tenderness in the right upper quadrant below the costal margin on deep inspiration [6].

Cholecystectomy for acute calculous cholecystitis is the most frequent surgical procedure performed by general surgeons comprising approximately 500000 operations annually in USA [7]. Laparoscopic cholecystectomy became the gold standard treatment for acute calculous cholecystitis but the appropriate time is remains controversial [3]. Two timing for intervention are available for the treatment of acute calculous cholecystitis. The first is early (within 72 hour of onset of symptoms) laparoscopic cholecystectomy (LC) as definitive treatment after establishing diagnosis and surgical fitness of the patient in the same hospital admission [8]. The second is conservative treatment which is successful in about 90% of the cases and then delayed cholecystectomy is performed in the second hospital admission after an interval of 6-12 weeks

Early diagnosis of patients with acute calculous cholecystitis requires specific diagnostic criteria of clinical data and imaging (abdominal ultrasound) [10]. The typical ultrasound image of acute calculous cholecystitis demonstrates gallbladder swelling, wall thickening with sonolucent layers, and the stone impaction in the cystic duct [11]. Surgeons began to recognize that early laparoscopic cholecystectomy is the preferred strategy for managing the acutely inflamed calculous gallbladder but still the other prefer delayed approach [12]. The aim of this study was to compare between laparoscopic

cholecystectomy in early (less than 72 hours of clinical presentation) and laparoscopic cholecystectomy after 72 hours till the end of the first week in acute calculous cholecystitis as regard operative and postoperative outcome.

Patients and Methods

This study was a prospective comparative study at Ain Shams University Hospitals and police hospitals in Egypt. It included 30 patients who had been diagnosed with acute calculous cholecystitis in the period between November 2020 and November 2021. The cases were collected from emergency room and outpatient clinics in Ain Shams University hospitals and police hospitals in Egypt. An ethical approval was obtained from general surgery department ethical committee and a written consent was taken from each patient after informing them the objectives of the study, the risks and benefits, with confidential handling of personal information. All participants had the right for the voluntary nature of participation and the rights to withdraw from the study.

Inclusion criteria:

We included adult patients between ages 18-60 years, both males and females with acute calculous cholecystitis based on presence of the following signs of acute cholecystitis; abdominal tenderness, rebound tenderness, rigidity in the right hypochondrium, fever, leukocytosis $>11 \times 10^9/L$ and sonographic signs of acute cholecystitis; edema and thickening of the gall bladder wall, pericholecystic collections, gall bladder distention (mucocele or pyocele) or impacted stone at Hartmann pouch.

Exclusion criteria:

We excluded patient with obstructive jaundice, pancreatitis, perforation or pericholecystic abscess, patient with cholangitis, diabetic patients and patient unfit for surgery for any medical reason as end-stage liver disease and significant cardiac disease.

Then the cases were subdivided into 2 groups according to the time of presentation to us; group A (16 cases) included the cases who presented within first 72 hours and group B (14 cases) included who presented after 72 hours till the end of the first week. Laparoscopic cholecystectomy was done for each case at the time of presentation by the same surgical team contributing in this study.

Preoperative workup:

Regarding the preoperative assessment, all patients had a complete history taking [medical-

history, surgical history, previous attacks, jaundice (change color of urine and stool)], general examination (pulse, temperature, blood pressure and jaundice), and local examination (tenderness, rebound tenderness, guarding, rigidity and murphy's sign).

The radiological workup was abdominal ultrasound, electrocardiogram (ECG), chest X-ray, and echocardiogram (ECHO) if needed. While the laboratory one was complete blood count, liver-function tests, kidney function tests, total and direct bilirubin, alkaline phosphatase, PT, PTT, INR, lipase and amylase.

Operative technique:

We used the standard four-port technique for laparoscopic cholecystectomy, with general anesthesia. Patients were on supine position with reverse Trendelenburg position. Surgeon made small incisions in the abdomen, and 10mm camera port was inserted supraumbilical at the midline, another 10mm trocar was used in the epigastrium which was the main right working port for the surgeon, one 5mm trocar in the right midclavicular line as the left working port for the surgeon, another 5mm trocar was inserted at the right ant-axillary line for gall bladder fundus traction.



Fig. (1): Severe adhesions were found between the liver and omentum and anterior abdominal wall.

The abdomen was inflated with carbon dioxide with verress needle at palmer's point at left sub-costal region. Identification of calot's triangle and critical view of safety then clipping of cystic duct and cystic artery (Figs. 1-4). The gall bladder was dissected from GB bed then good haemostasis was done (Fig. 5). Gall bladder was removed from the right 10mm epigastric working port, with a drain inserted in Marison's pouch, and port wounds were closed with sutures.

Post-operative follow-up:

Regarding post-operative follow-up, the care in ward was done including; starting intravenous fluids, antibiotics, analgesics, and proton pump inhibitor (PPI), starting oral fluids once patient become open bowel, drain was removed if the total amount was less than 50ml serosanguinous in 24hrs. Wound dressing and follow-up in outpatient clinic were done for all patients.

The operated patients fulfilling inclusion and exclusion criteria were divided into two groups according to time of presentation and we compared between two groups regarding: Rate of conversion to open surgery, operative complication: Bleeding, bile duct injury and subtotal cholecystectomy, operative time and post-operative hospital stay.



Fig. (2): Critical view of safety.



Fig. (3): Dissection of cystic artery.



Fig. (4): Clipping of cystic duct.

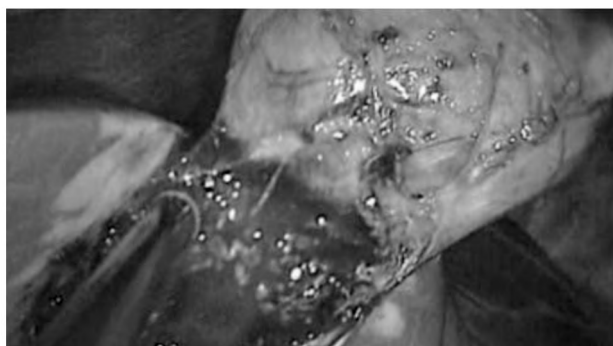


Fig. (5): Dissecting of the gallbladder from its bed.

Statistical analysis:

All data was recorded, tabulated, analyzed and statistically compared between both groups to identify any significant differences between them. The collected data was revised, coded, tabulated and introduced to a PC using statistical package

for social sciences (IBM SPSS 20 for windows). Data was presented and suitable analysis was done according to the type of data obtained for each parameter. The comparison between two groups with qualitative data were done by using Chi-square test. The comparison between two independent groups with quantitative data and parametric distribution was done by using Independent *t*-test.

Results

Of the included 30 patients the male percentage was 26.7% with mean age 44.9 ± 3.68 . With 7 patients had different previous abdominal surgeries. The detailed demographic and clinical data is illustrated in Table (1).

There was no significant difference between both groups regarding the preoperative demographic and clinical data (p -value > 0.05).

Table (1): Comparison between study groups regarding the preoperative demographic and clinical data.

	Groups		<i>p</i> -value	Significant
	Group A (within 72 hours) N=16	Group B (more than 72 hours) N=14		
Age (years) (mean \pm SD)	45 \pm 3.98	44.8 \pm 3.49	0.89**	NS
<i>Gender (No. %):</i>				
Male	5 (31.25%)	4 (28.57%)	0.66*	NS
Female	11 (68.75%)	10 (71.43%)		
BMI (kg/m ²) (mean \pm SD)	30.93 \pm 4.28	30.87 \pm 4.26	0.96**	NS
Mean duration of symptoms (days) (mean \pm SD)	1.9 \pm 0.54	1.9 \pm 0.47	1**	NS
<i>Previous abdominal surgery (No. %):</i>				
Yes	3	4	0.5*	NS
No	13	10		
Fever (No.%)	2 (12.5%)	1 (7.14%)	0.14*	NS
Previous acute attack (No.%)	9 (56.25%)	8 (57.14%)	0.69*	NS
Palpable GB (No.%)	2 (12.5%)	1 (7.14%)	0.43*	NS
<i>WBCs (No.%) (4000-11000/cm³):</i>				
Normal	12 (75%)	12 (85.71%)	0.41*	NS
High	4 (25%)	2 (14.29%)		
<i>U/S Data:</i>				
Pericholecystic collection	0 (0%)	0 (0%)	1*	NS
Wall thickness:				
<4mm	7 (43.75%)	8 (57.14%)	0.34*	NS
>4mm	9 (56.25%)	6 (42.86%)		

BMI = Body mass index.

GB = Gallbladder.

U/S = Ultrasound.

NS = Non-significant.

WBCs = White blood cells.

SD = Standard deviation

* Chi-square test.

**Independent *t*-test.

Regarding the general intraoperative data there was no significant difference between both groups (p -value >0.05) except the operative time there was significant more operative time for group A (p -value <0.05) is illustrated in Table (2).

We had one case of bile duct injury in Group A with no cases in Group B. This case had minor lateral injury of common hepatic duct and underwent laparoscopic primary repair. Also we had two cases (one in each group) with injury to proper

hepatic artery and we converted them to open approach and did primary repair.

Regarding the general postoperative data there was no significant difference regarding the length of postoperative hospital stay is illustrated in Table (3).

There were no postoperative complications in form of postoperative hemorrhage, leakage, wound infection or postoperative ileus.

Table (2): Comparison between study groups regarding the intraoperative data.

	Groups		p -value	Significant
	Group A (within 72 hours) N=16	Group B (more than 72 hours) N=14		
Conversion to open (No.%)	1 (6.25%)	1 (7.14%)	1*	NS
Bile or stone spillage (No.%)	7 (43.75%)	5 (35.71%)	0.21 *	NS
Injury to bile duct (No.%)	1 (6.25%)	0 (0%)	0.43 *	NS
Injury to artery (proper Hepatic artery) (No.%)	1 (6.25%)	1 (7.14%)	1*	NS
Visceralinjury	0 (0%)	0 (0%)	1*	NS
<i>Blood loss (ml) (No.%):</i>				
<50	5 (31.25%)	2 (14.29%)	5*	NS
50-200	10 (62.5%)	8 (57.14%)	10*	NS
>50	1 (6.25%)	4 (28.57%)	1*	NS
Mean operation time (minutes) (mean \pm SD)	116.13 \pm 15.83	86.67 \pm 30.86	0.003 **	HS

NS= Non-significant. HS = Highly significant. SD = Standard deviation. *Chi-square test. **Independent t -test.

Table (3): Comparison between study groups regarding the post operative data.

	Group A (within 72 hours) N=16	Group B (more than 72 hours) N=14	p -value	Significant
Post-operative length of hospital stay (days) (mean \pm SD)	1.87 \pm 0.61	2.07 \pm 0.8	0.45**	NS

**Independent t -test. NS= Non-significant. SD = Standard deviation.

Discussion

The optimal timing of surgery for patients with AC has been a topic of controversy in the past. Initially, patients were managed conservatively with the aim of "cooling down" the inflammation, and then perform cholecystectomy weeks later.

The heterogeneity of patients suffering from AC and their medical co-morbidities make it difficult to standardize a proper treatment [13].

At the start of the laparoscopic era, acute cholecystitis was regarded a relative contraindication for LC, owing to high rates of complications and conversion. However, when laparoscopy became more advanced, this pattern shifted. Laparoscopic cholecystectomy is now considered the gold standard for the treatment of benign gall bladder diseases

and one of the most routinely performed surgical procedures [14]. According to the current evidence, early LC for acute cholecystitis is preferable than late or delayed LC in terms of treatment success and cost [15]. Otherwise, some surgeons prefer delayed LC in non-complicated AC due to less tissue edema and adhesions and so less incidence of injury theoretically [16].

Our study was a prospective comparative study on patients with non-complicated AC underwent LC. Sixteen patients with AC operated within 72 hours from presentation were compared to fourteen patients operated after 72 hours.

The preoperative demographics data was comparable between both groups. Regarding the intraoperative data, there was no significant difference between both groups except for the operative time

which was significantly longer in early cholecystectomy group. Also, regarding the postoperative data, there was no significant difference according to the length of postoperative hospital stay. There were no postoperative complications in form of postoperative hemorrhage, leakage, wound infection, or postoperative ileus in both groups.

In general, an early cholecystectomy is conducted within 72 hours, the so-called golden 72 hours with debate about the definition of the term "early". In some series, the term "early" refers to the onset of symptoms, where as in others, it refers to the period of admission. The term "early" was used in this study to refer to onset of symptoms [17].

Gutt et al., did a multi-center randomized trial to compare between early and delayed cholecystectomy. In their study, "early" referred to cases received immediate surgery within 24 hours of hospital admission and delayed referred to delay laparoscopic cholecystectomy at following 6-12 weeks of discharge as soon as acute attack subsided. The authors concluded that laparoscopic cholecystectomy done within 24 hours of admission was superior to delayed LC in terms of outcome besides, the total hospital stay in the delayed group was double that in the early group. So early laparoscopic cholecystectomy is more economic for operable patients with AC, urgent LC should be the therapy of choice [18].

A second retrospective analysis of 61 patients who were operated before and after the 72-hours revealed no significant difference between both times, indicating that the degree of inflammation was not always a time-dependent. This might explain why ELC was not linked to a higher conversion rate or bile duct damage even after 72 hours of symptoms [17]. According to the Cochrane study, gallstone-related morbidity occurred in 18.3% of patients during the waiting period comparable to the 29.5% described in this study. These patients subjected to such a non resolution of symptoms under initial conservative treatment or recurrence of symptoms during the waiting period requested an emergency LC with a high conversion rate of 45% [19].

However, this result can not be extended to all levels of patient care. Further more, for a variety of reasons, quick LC may not always be available, a number of individuals with AC may require specific consultations and correction of comorbidities and experienced laparoscopic surgeons may not be available within 24h [18]. In a tertiary

center like our center, this logistic problem to deal with these cases is not present.

Zafar et al., in a matched analysis of over 95 000 patients, they discovered that operations performed within the first 48 hours of presentation were associated with the lowest rates of complications, length of stay, mortality, and hospital cost, adding to the growing body of evidence supporting very early LC for acute cholecystitis. Surgery for acute cholecystitis should be done within two days after the onset of symptoms. Despite the fact that causative relationships could not be shown in this retrospective study, delays in surgery were found to be linked to increased morbidity, mortality, length of stay, and hospital expenses. The practice of uncertain postponing cholecystectomy for acute cholecystitis should be avoided [20].

Banz et al., published data on 4113 patients from the Swiss Association of Laparoscopic and Thoracoscopic Surgery, and Brooks et al., utilized data from 5268 patients in the National Surgical Quality Improvement Program database to conduct the only other big database analysis. Delaying LC for acute cholecystitis beyond 48 hours of presentation led with higher conversions to open surgery, more complications, and a longer postoperative hospital stay, according to Banz et al.

However, one significant critique of their research was that individuals who had surgery later may have been sicker from the start and hence had poorer results [21].

We have many limitations in our study including small sample size without randomization and we did not comment on the cost for each group.

Conclusion:

Early laparoscopic cholecystectomy for acute non-complicated cholecystitis within 72 hours from onset of symptoms (although longer operative time) is a safe procedure with similar hospital stay and comparable morbidity with late laparoscopic cholecystectomy after 72 hours.

Financial support and sponsorship: Nil.

Conflicts of interest:

There are no conflicts of interest.

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نتيجة استئصال المرارة بالمنظار خلال أول ٧٢ ساعة من التهاب المرارة الحاد مقابل استئصال المرارة بالمنظار بعد ٧٢ ساعة حتى نهاية الأسبوع الأول

يعتبر استئصال المرارة من أجل التهاب المرارة الحاد الإجراء الجراحي الأكثر شيوعاً الذي يقوم به الجراحون العاملون ويتكون من حوالي ٥٠٠٠٠٠ عملية جراحية سنوياً في الولايات المتحدة الأمريكية.

أصبح استئصال المرارة بالمنظار العلاج القياسي الذهبي للالتهاب المرارة الحصى الحاد ولكن الوقت المناسب لا يزال مثيراً للجدل يتوفر توقيتان للتدخل لعلاج التهاب المرارة الحصى الحاد. الأول هو استئصال المرارة بالمنظار مبكراً (خلال ٧٢ ساعة من ظهور الأعراض أو بعد ٧٢ ساعة بعد استخدام العلاج التحفظي) كعلاج نهائي بعد تحديد التشخيص واللياقة الجراحية للمريض في نفس المستشفى.

الهدف من هذه الدراسة هو مقارنة استئصال المرارة بالمنظار في وقت مبكر (أقل من ٧٢ ساعة من العرض السريري) مقابل استئصال المرارة بالمنظار بعد ٧٢ ساعة حتى نهاية الأسبوع الأول في نتسجة التهاب المرارة الحصى الحاد ونتائج ما بعد الجراحة.

من خلال دراسة مستقبلية مقارنة في مستشفيات جامعة عين شمس ومستشفيات الشرطة في مصر من نوفمبر ٢٠٢٠ إلى نوفمبر ٢٠٢١.

من بين ٣٠ مريضاً المشمولين كانت النسبة المئوية للذكور ٢٦.٧٪ بمتوسط عمر 44.9 ± 3.68 . حيث خضع ٧ مرضى لعمليات جراحية سابقة مختلفة في البطن فيما يتعلق بالبيانات العامة أثناء العملية لم يكن هناك فرق كبير بين المجموعتين. من خلال تحليل وقت العملية، كان هناك وقت جراحي كبير للمجموعة التي خضعت لاستئصال المرارة خلال ٧٢ ساعة، مع عدم وجود فرق كبير فيما يتعلق بطول الإقامة في المستشفى بعد الجراحة.