

## Complicated Acute Cholecystitis; Protocol of Management

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### ABSTRACT

**Objectives:** To evaluate the outcome of management plan for acute cholecystitis (AC) patients according to patients' general condition and disease severity. **Patients & Methods:** advanced cases of acute cholecystitis (grades II-III) were evaluated for fitness for general anesthesia (GA) according to criteria of American Society of Anesthesiologists and fit patients underwent laparoscopic cholecystectomy (LC), while unfit patients underwent percutaneous cholecystostomy (PC). **Results:** Eighteen fit patients underwent LC; two patients (11.1%) required open conversion. 13 patients developed PO morbidities, but only two complications were surgery-related. Only one patient died secondary to surgery-related cause (MR of 5.6%). Eight patients underwent PC; 6 patients developed PO morbidities and one patient died during hospital stay due to surgery related cause (MR of 12.5%). Patients had PC or LC showed non-significant difference as regards time till 1<sup>st</sup> ambulation or oral intake and for ICU stay, but PC patients required significantly longer hospital stay (12.6 vs. 14.6 days). **Conclusion:** LC is effective definitive therapy if patient was fit for GA. For patients who are unfit for GA, PC is a feasible, safe and effective option with acceptable outcomes.

**Keywords:** Acute cholecystitis, Laparoscopic cholecystectomy, percutaneous cholecystostomy, Mortality rate

### INTRODUCTION

Acute cholecystitis (AC) is an acute inflammation of the gallbladder wall. It may be calculous if the underlying etiology is the obstruction of the cystic duct or the neck of the gallbladder due to an impacted stone or acalculous cholecystitis which develop without associated cholelithiasis <sup>(1)</sup>.

Forty percent of AC patients develop complications <sup>(2)</sup> that mostly occur secondary to gallstone impaction especially in men and diabetic patients <sup>(1)</sup>. Regarding the relatively high complication rates of AC, the decision whether or not to perform surgery should be well considered <sup>(3)</sup>.

In medical practice, the tendency to remove an inflamed gallbladder is deeply rooted <sup>(4)</sup>. However, antibiotics and a variety of minimally invasive non-surgical interventions, although not definitive, play an adjunctive role in management of AC <sup>(5)</sup>.

Cholecystectomy remains the only definitive therapy for AC, but current guidelines recommend treatment on the basis of disease severity at presentation <sup>(5)</sup>. Urgent laparoscopic cholecystectomy has been established as the best

treatment for AC <sup>(6)</sup>. For some patients, the surgical risk-benefit profile may favor conservative treatment <sup>(4)</sup>. However, failure of conservative treatment can result in high-risk operations with relatively high rates of operative morbidity <sup>(6)</sup>.

According to Tokyo Guidelines; acute cholecystitis can be classified into 3 grades. Grade I (mild) shows limited pathology within the gall bladder without systemic organ dysfunction. Grade II (moderate) shows extensive local pathology but still without systemic organ dysfunction. While grade III (severe) shows systemic organ dysfunction <sup>(7)</sup>.

In high-risk patients with AC, percutaneous cholecystostomy (PC) can serve as a bridging option to cholecystectomy. The current study was designed to evaluate the outcome of our protocol in management of patients with acute cholecystitis according to their general condition and disease severity.

### PATIENTS & METHODS

The current prospective study was conducted at General Surgery Departments at Al-jedaani Hospital (KSA), Al-Zafer Hospital (KSA) and

Benha University Hospital after obtaining approval from local ethical committee and after fully informed written consent signed by patient. This study was carried out since March 2012 till June 2016 including a 30-day follow-up duration. Patients presented with grade II & III acute cholecystitis were recruited for this study.

#### **Preoperative evaluation**

Collected data included demographic data including age, gender and body mass index, duration of symptoms prior to hospital attendance, and associated co-morbidities. All patients underwent clinical assessment, laboratory investigations and imaging by abdominal ultrasound (US) and CT scan. US signs including gallbladder diameter, wall thickness, stones, pericholecystic fluid collection, intra-peritoneal free fluid, periportal tracking, inflammatory fat changes, common bile duct dilatation, intraluminal or intramural air, extra-luminal gallstones and mean number of sonographic findings.

#### **Protocol of management:**

1. All patients diagnosed as acute cholecystitis were classified into 3 grades according to Tokyo guidelines <sup>(7)</sup>. Grade I patients were excluded from the study
2. Grade II and III patients were assessed by an anesthetist for evaluation for fitness for general anesthesia according to criteria of American Society of Anesthesiologists (ASA).
3. Patients with grade III cholecystitis and/or who were unfit for general anesthesia (ASA 3, 4) underwent percutaneous cholecystostomy (PC) under local infiltration anesthesia with sedation. PC indicates draining of the gallbladder content through placement of a drain or a tube under image guidance via ultrasound or computed tomography. Those patients were scheduled for elective latent cholecystectomy after 6-12 weeks.
4. Patients who were fit for general anesthesia underwent laparoscopic cholecystectomy (LC).

#### **Study outcomes:**

- The primary outcomes will include the in-hospital and 30-day mortality rates (MR), and the rate of PO complications.
- Secondary outcomes will include the frequency of conversion to open cholecystectomy (OC), the need for re-intervention, length of ICU stay and total length of hospital stay, and the frequency of re-admission for biliary complaints.

#### **Statistical analysis**

Obtained data were presented as mean±SD, ranges, numbers and ratios. Results were analyzed using One-way ANOVA with post-hoc Tukey HSD Test and Chi-square test ( $\chi^2$  test). Statistical analysis was conducted using the SPSS (Version 15, 2006) for Windows statistical package. P value <0.05 was considered statistically significant.

## **RESULTS**

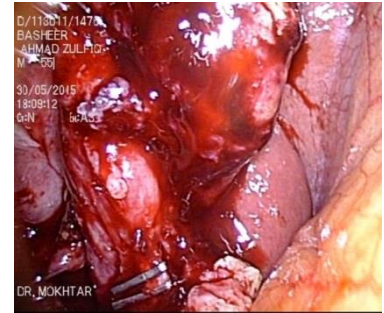
During the study period, 94 patients presented with acute abdomen secondary to acute cholecystitis. Sixty-eight patients presented with grade I (mild) acute cholecystitis and they were excluded from the study. 26 patients presented with either grade II (21 patients) or grade III (5 patients). All of them were assigned to emergency intervention. Clinical evaluation defined 8 patients who were unfit for general anesthesia; three patients had uncompensated cardiac lesion, three patients were still showing manifestations of severe sepsis, one patient had chronic obstructive pulmonary disease and the 8<sup>th</sup> developed severe sepsis-related acute kidney injury. These eight patients were assigned for PC (PC group). On the other side, clinical evaluation showed that 18 patients were fit for general anesthesia and underwent LC (LC group) as shown in figure 1 and 2. Patients underwent PC were significantly older and had significantly higher serum CRP levels. On US imaging, patients of PC group showed significantly wider gall bladder diameter with significantly higher wall thickness and significantly higher number of US findings. Details of patients' data are shown in table 1.



**Fig. (1a):** Insertion of the trochar under vision



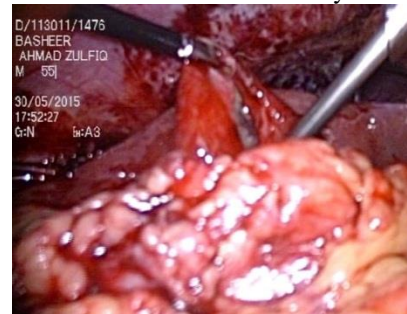
**Fig. (1b):** Adhesiolysis of the abdominal wall



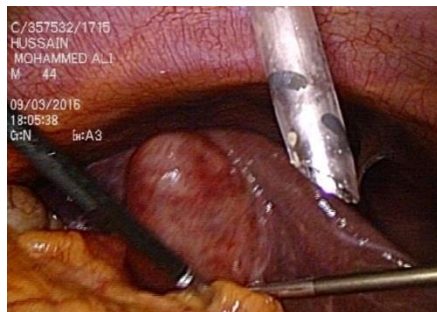
**Fig. (1e):** Clipping of the cystic artery



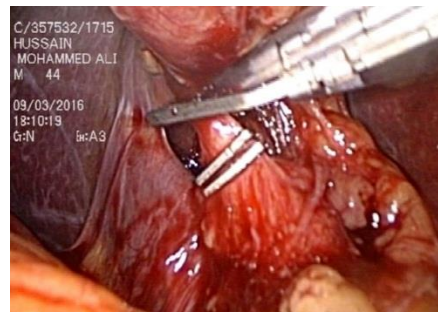
**Fig. (1c):** Fundus of the gall bladder was gangrenous and perforated (arrowed)



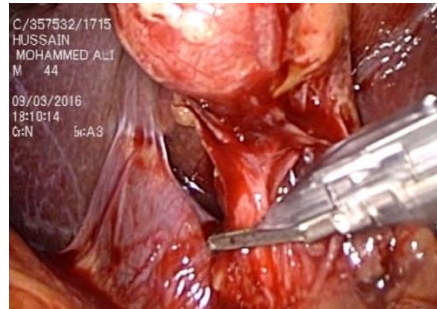
**Fig. (1d):** Dissection of gall bladder



**Fig. (2a):** Dissection of the gall bladder



**Fig. (2b):** Clipping of the cystic duct



**Fig. (2c):** Dissection of the cystic duct



**Fig. (2d):** Clipping of the cystic artery

**Table (1): Data of enrolled patients categorized according to operative procedure**

Data		LC (n=18)	PC (n=8)	P value	
Age (years)		60.9±5.9	66.4±7.1	0.049	
Gender	Males	14 (77.8%)	5 (62.5%)	NS	
	Females	4 (22.2%)	3 (37.5%)		
BMI data	Weight (kg)	92.5±8.5	94.5±10.1	NS	
	Height (cm)	166.2±3.2	167.5±4.2	NS	
	BMI (kg/m <sup>2</sup> )	33.4±2.4	33.6±3.2	NS	
Associated co-morbidities	No		7 (38.9%)	2 (25%)	NS
	Yes		11 (38.9%)	6 (75%)	
	Type	Diabetes mellitus	5 (27.8%)	3 (37.5%)	NS
		Coronary artery disease	3 (16.7%)	4 (50%)	
		COPD	2 (11.1%)	1 (12.5%)	
Chronic kidney disease		1 (5.6%)	1 (12.5%)		
Clinical manifestations	Duration of symptoms (days)		5.3±1.2	5.6±1.5	NS
	Temperature (°C)		38.5±0.5	38.8±0.4	NS
	RUQ pain & tenderness		17 (94.4%)	7 (87.5%)	NS
	Epigastric pain & tenderness		12 (66.7%)	5 (62.5%)	NS
	Murphy's sign		10 (55.6%)	6 (75%)	NS
	Nausea &/or vomiting		11 (61.1%)	6 (75%)	NS
Cholecystitis grade	Grade II		18(100%)	3(37,5%)	NS
	Grade III		0	5(62.5%)	NS
ASA grade	Grade I		8 (44.4%)	0	NS
	Grade II		6 (33.3%)	0	
	Grade III		3 (16.7%)	4 (50%)	
	Grade IV		1 (5.6%)	4(50%)	
Laboratory findings	Total leucocytic count (10 <sup>3</sup> /ml)		15.3±0.77	17±1.2	NS
	Total bilirubin (mg/ml)		1.31±0.17	1.36±0.22	NS
	ALT (mg/ml)		125.2±44.5	147.9±56.2	NS
	AST (mg/ml)		73.3±27.5	87.8±22.2	NS
	Creatinine (mg/ml)		1.41±0.37	1.73±0.54	NS
	CRP (mg/ml)		124.9±22.8	148.3±19.2	0.019
US findings	Presence of stone	Calculous	8 (44.4%)	3 (37.5%)	NS
		Acalculous	10 (55.6%)	5 (62.5%)	
	Gall bladder diameter (cm)		4.1±0.8	5.1±0.7	=0.005
	Gall bladder wall thickness (mm)		4.2±1	5.35±1.3	=0.024
	Number of US findings		3.8±0.7	4.5±0.8	=0.04

Data are presented as numbers & mean±SD; percentages are in parenthesis; LC: Laparoscopic cholecystectomy; PC: Percutaneous cholecystostomy; BMI: Body mass index; RUQ: Right upper quadrant; ASA: American Society of Anesthesiology; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; CRP: C-reactive protein; US: Ultrasonography; NS: indicates non-significant inter-group difference; p<0.05 indicates significant inter-group difference

Laparoscopic exploration detected dense adhesions between gall bladder and transverse colon in one patient that was converted to open approach. In another patient laparoscopic exploration detected gangrenous gall bladder with very friable wall that showed difficult manipulations, so converted to open cholecystectomy (Fig. 3).



**Fig. (3a):** A case of gangrenous cholecystitis during laparoscopy, gall bladder wall was friable and it was converted to open cholecystectomy



**Fig. (3b):** Gangrenous gall bladder completely dissected and removed without perforation

**Table (2): Operative data of patients categorized according to operative procedure**

Data	LC (n=18)	PC (n=8)	P value
Open conversion	2 (11.2%)	0	NS
Operative time (min)	75.8±12	49.8±12.2	=0.014
Operative blood loss (ml)	361±148.2	226.6±127.1	=0.047

Data are presented as numbers & mean±SD; percentages are in parenthesis; LC: Laparoscopic cholecystectomy; PC: Percutaneous cholecystostomy; NS: indicates non-significant inter-group difference; p<0.05 indicates significant inter-group difference

All patients could ambulate within 33.5±7.3 hrs and received their 1<sup>st</sup> oral intake within 45.5±10.9 hrs with non-significant (p>0.05) difference between both groups. Nineteen patients developed PO morbidities with non-significant (p>0.05) difference between both groups as regards frequency and types of PO morbidities. Mean duration of ICU stay was non-significantly longer, while total duration of hospital stay was significantly (p=0.048) longer in patients of PC group (Fig. 5).

**Table (3): Postoperative data of patients categorized according to operative procedure**

Data		LC (n=18)	PC (n=8)	P value
Time till 1 <sup>st</sup> ambulation (hr)		34±7.7	32.5±6.7	NS
Time till 1 <sup>st</sup> oral intake (hr)		48±10.8	40±9.7	NS
Frequency of PO morbidities	Yes	13 (72.2%)	6 (75%)	NS
	No	5 (27.8%)	2 (25%)	
Type of PO morbidities	PO bleeding	0	1 (12.5%)	NS
	Biliary leakage	1 (5.6%)	2 (25%)	
	Subhepatic abscess	1 (12.5%)	1 (12.5%)	
	Cardiac attack	1 (5.6%)	1 (12.5%)	
	Pneumonia	2 (11.1%)	1 (12.5%)	
	Pulmonary embolism	1 (5.6%)	0	
	General edema	3 (16.7%)	1 (12.5%)	
	GIT troubles	7 (38.9%)	3 (37.5%)	
Frequency/patient		1.15	1.83	NS
Duration of hospital stay (days)		12.6±4.2	14.6±6	=0.048

Data are presented as numbers & mean±SD; percentages are in parenthesis; LC: Laparoscopic cholecystectomy; PC: Percutaneous cholecystostomy; NS: indicates non-significant inter-group difference; p<0.05 indicates significant inter-group difference



During PO hospital stay, one patient had PC developed biliary leakage; radiologic imaging detected the sub hepatic collection. Another tube drain was inserted by US guidance to drain this biliary leak. Patient was maintained at ICU but patient showed progressive deterioration and died on the 3<sup>rd</sup> PO day secondary to septicemia-related acute respiratory failure. Another patient in PC group was re-admitted to ICU for management of acute myocardial infarction, but died on the 2<sup>nd</sup> day of ICU re-admission; for a mortality rate (MR) of 25% after PC with a surgery-related MR of 12.5%. Concerning patients underwent LC, only one patient died during hospital stay for a MR of 5.6%. This patient developed biliary leakage leading to sub hepatic collection and abscess formation that resulted in reactionary empyema. This patient required CT-guided

abscess drainage, insertion of chest-drainage tube and re-admission to ICU, but died on the 6<sup>th</sup> PO day (Fig. 4).

Throughout 30-day PO follow-up, another two patients of the twenty three patients who were discharged alive died for a 30-day MR of 10%. Fortunately, both died secondary to causes unrelated to surgery. One patient had PC developed diabetic hyperosmolar hyperglycemic coma, admitted to ICU for intensive insulin therapy but could not respond to medical treatment and died on 2<sup>nd</sup> day of ICU admission. Another patient had LC had cerebral hemorrhage and died on admission to ICU. The mortality rate in PC group was 50%, one case was surgery related (12.5%) while other 3 cases (37.5%) was due to general conditions and other systems affection.

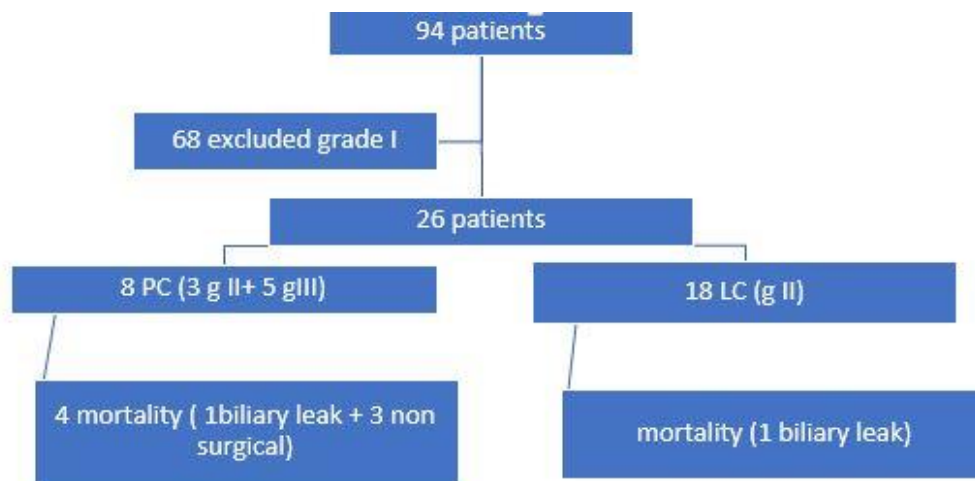


Fig 4: flow chart of studied patients

## DISCUSSION

In the current study, 94 patients presented with manifestations of acute abdomen secondary to acute cholecystitis (AC). Sixty eight patients presented with grade I cholecystitis and were excluded from the study. Other 26 patients presented with grade II and III cholecystitis.

Surgical decision for management of those patients was adjusted according to fitness for general anesthesia as judged by ASA grades and tolerability of abdominal insufflations during laparoscopic cholecystectomy (LC) not only on

severity of local disease. In support of this rationale for surgical-decision making, Liu et al.<sup>(8)</sup> found LC is a suitable procedure for treating selected patients with severe cardiovascular diseases (CVD) and gallbladder disease with operative morbidity and mortality rates compared to patients with gallbladder disease alone. Also, Ozkan et al.<sup>(9)</sup> documented that treatment choice in acute complicated cholecystitis in the elderly depends on the patient's general condition, severity of the disease, and ASA score.

Eighteen patients were fit for general anesthesia and underwent LC; two cases required

open conversion because of friability of gall bladder wall in one case and presence of dense adhesions to transverse colon in the other. The conversion rate was 11.1%. Similarly, McGillicuddy et al. <sup>(10)</sup> and Teckchandani et al. <sup>(11)</sup> reported an open conversion rate of 20.3% and 16% respectively. Moreover, Bouassida et al. <sup>(12)</sup> found the open conversion rate of LC in patients had gangrenous AC was higher than in non-gangrenous AC patients

Three cases with LC had a smooth postoperative course. While thirteen LC patients developed 16 PO morbidities for a frequency of 1.15 complications / patient and only two complications were surgery-related. Regarding mortality, we had only one case died secondary to surgery-related complications. So, surgery-related MR was 5.6%. In line with these data, McGillicuddy et al. <sup>(10)</sup> detected a PO morbidity rate of 20% after LC for elderly patients had AC with a frequency of 1.66/ patient and mostly included acute respiratory failure, pneumonia, myocardial infarction and sepsis. Also, Bouassida et al. <sup>(12)</sup> found the number of complications of LC was comparable to open surgery in patients had either gangrenous or non-gangrenous AC. Moreover, Radunovic et al. <sup>(13)</sup>, in AC patients undergoing LC, reported an intraoperative complication rate of 13.1% and PO complications included bleeding from abdominal cavity (3.64%), biliary duct leaks (1.89%), and surgical wound infection (0.94%) with high incidence of complications in patients with elevated white blood cell count, US finding of gallbladder empyema and increased thickness of the gallbladder wall > 3 mm.

Eight patients (30.8%) on preoperative evaluation were unfit for general anesthesia; 3 had uncompensated cardiac lesion, 3 patients were still showing manifestations of severe sepsis, one patient had chronic obstructive pulmonary disease and the 8<sup>th</sup> developed severe sepsis-related acute kidney injury. These eight patients underwent biliary drainage using percutaneous cholecystostomy (PC) under US guidance. In line with that surgical decision, Bala et al. <sup>(14)</sup> documented that high operative risk due to older age and coronary artery disease preclude LC in more than one-third of AC patients, especially those presenting with sepsis and elevated alkaline phosphatase, but PC may be a safe treatment option in this group of high-risk patients. Also,

Bickel et al. <sup>(15)</sup> found PC decreases conversion rate of delayed LC, possibly by halting propagation of the inflammatory process and its consequences, so when decision regarding the necessity to perform drainage of the severely inflamed gallbladder is established, it is suggested to be done as soon as possible.

Six patients assigned to PC developed PO morbidities. Two patients died during the first admission; one secondary to surgery-related complication and the other was non-surgery related cause for a crude MR of 25% and surgery-related MR of 12.5%. Two more cases were died in the post-operative follow up period due to non-surgical causes. Yun et al. <sup>(16)</sup> reported a MR of 18.2% after PC, but these mortalities were unrelated to surgery.

Recently, in 2017, Dimou et al. <sup>(17)</sup> reported that the use of cholecystostomy tubes in patients with grade III cholecystitis has increased and was associated with lower rates of definitive treatment but with higher re-admission and mortality rates and Alvino et al. <sup>(18)</sup> reported 7% procedure-related complications rate after PC and concluded that PC is a highly successful treatment for AC and is associated with low complication rate. Also, Zarour et al. <sup>(19)</sup> documented that in AC, drainage by a PC catheter is a safe and effective procedure, so has to be used as a bridge to elective cholecystectomy.

Ansaloni et al. <sup>(20)</sup> documented that as soon as diagnosis is made and after the evaluation of choledocholithiasis risk, LC should be offered to all patients except those with high risk of morbidity or mortality and Wang et al. <sup>(21)</sup> documented that PC has been effectively used for the treatment of AC for patients unsuitable for early cholecystectomy.

The current study detected non-significant difference between patients had PC or LC as regards time till 1<sup>st</sup> ambulation or oral intake and for ICU stay. However, patients had significantly longer total hospital stay (12.6 vs. 14.6 days) and this could be attributed to the higher frequency of preoperative associated co-morbidities. Similarly, Yun et al. <sup>(16)</sup> found patients had PC resumed oral intake within 2.9 to 3.9 days and concluded that PC is an effective bridge procedure before cholecystectomy in patients with AC and ASA grade of  $\geq 3$ . In line with the obtained results, Bouassida et al. <sup>(12)</sup> found that LC significantly reduce total hospital stays and medical costs.

## CONCLUSION

Classification of AC patients according to its grade and also according to patient grade of ASA system was helpful in decision making. LC is effective definitive therapy if patient was fit for general anesthesia and could be conducted with minimal conversion rate, PO surgery-related morbidities and mortalities. For patients who are unfit for general anesthesia, PC is a feasible, safe and effective option with acceptable outcome despite of the long PO hospital stay.

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