

Exploring the Outcomes of Gallbladder Perforation: A Retrospective Observational Study

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ABSTRACT

Introduction: Gallbladder Perforation (GBP) is one of the most dangerous consequences of acute cholecystitis. It presents in a variety of ways, leading to diagnostic dilemmas and posing management challenges. There is high morbidity and mortality associated with this condition and management is not always straightforward in most cases.

Aim: To compare clinical presentation, associated co-morbidities and outcomes in ultrasound-guided open/percutaneous drainage followed by delayed cholecystectomy (DC-PCO group) and early laparoscopic/conversion to open cholecystectomy (EC group) for GBP.

Materials and Methods: The present study was a retrospective observational study in which case records of 2,366 patients over the last four years (from January 2019 to January 2023) with symptomatic cholecystitis were analysed at a tertiary care centre. A total of 44 adult patients aged over 14 years who had symptomatic cholecystitis on presentation and underwent cholecystectomy due to preoperative diagnosis of GBP were included. Patients with intraoperative findings of GBP, GBP secondary to abdominal trauma and perforation due to gallbladder malignancy were excluded. These 44 patients were classified into two groups. The first group included 24 patients who underwent ultrasound-guided open/percutaneous drainage followed by delayed cholecystectomy, termed the DC-PCO group. The second group included 20 patients who underwent early laparoscopic/conversion to open cholecystectomy, termed

the early cholecystectomy group (EC). Demographic profile, morbidities and postoperative outcomes were studied in both groups and the significance of differences was analysed using the Mann-Whitney U test and the Chi-square test.

Result: The median age was 49 (25-75) years, with a significantly higher proportion of females compared to males. An 86.4% of patients presented with abdominal pain as the most common complaint (38/44). According to Niemeier's classification, 13 patients had Type I, 27 patients had Type II and four patients had Type III perforation. The median duration of hospital stay was longer for the EC group compared to the DC-PCO group (p -value=0.028). Additionally, 75% of patients in the EC group had a proximal site of GBP (70% body and 5% neck), while 62.5% of patients in the DC-PCO group had fundus perforation (distal location). This suggests that the more proximal the site of perforation, the denser the adhesions, leading to more difficult dissection and increased perioperative complications (such as CBD injury).

Conclusion: The GBP is a serious complication of acute cholecystitis. Management in cases of GBP depends on the clinical condition of the patient, associated co-morbidities, type of GBP and imaging findings. The management revolves around the key decision of initial image-guided drainage versus early exploration. Early cholecystectomy is warranted for frank peritonitis, with the open procedure performed when dense adhesions complicate dissection and the risk of CBD injury is high.

Keywords: Acute cholecystitis, Laparoscopy, Niemeier classification

INTRODUCTION

The GBP is a critical complication of symptomatic cholecystitis due to various aetiologies [1]. In 1934, Niemeier classified this complication into three types: Type I—Acute perforation with generalised biliary peritonitis; Type II—Subacute perforation with localised abscess formation; and Type III—Chronic perforation with the possibility of fistula formation [2]. Risk factors for GBP include acute calculous cholecystitis, obesity, older age, malignancy, immunosuppressive status, trauma, ischaemia and vascular or systemic illness [3-7].

One of the most crucial considerations in the decision to perform initial image-guided management versus emergency surgery is based on clinical and imaging findings. Although ultrasound is readily available and does not involve radiation, its findings exhibit high interobserver variability. In contrast, abdominal Computed Tomography (CT) is highly sensitive and specific in detecting gallstones, air in the gallbladder wall and the pericholecystic fluid surrounding it; thus, it is the imaging modality of choice in GBP [8]. Most patients with localised GBP can initially be managed with ultrasound-guided interventions, including percutaneous and open drainage. However, cases requiring emergency

surgical intervention can be addressed with early laparoscopic cholecystectomy or conversion to open cholecystectomy in cases of difficult dissection or frozen Calot's triangle [9-11].

Currently, no standard protocol is established for managing such cases, which complicates the task of the on-floor emergency surgical team. An attempt was made to retrospectively study these cases and to identify the merits and demerits in the decision-making process, enabling us to objectively determine the management approach for similar scenarios in the future. Thus, present study aimed to compare clinical presentation, associated co-morbidities and outcomes in ultrasound-guided percutaneous cholecystostomy (PCO) drainage followed by delayed cholecystectomy (DC-PCO group) and early laparoscopic/conversion to open cholecystectomy (EC group) for GBP.

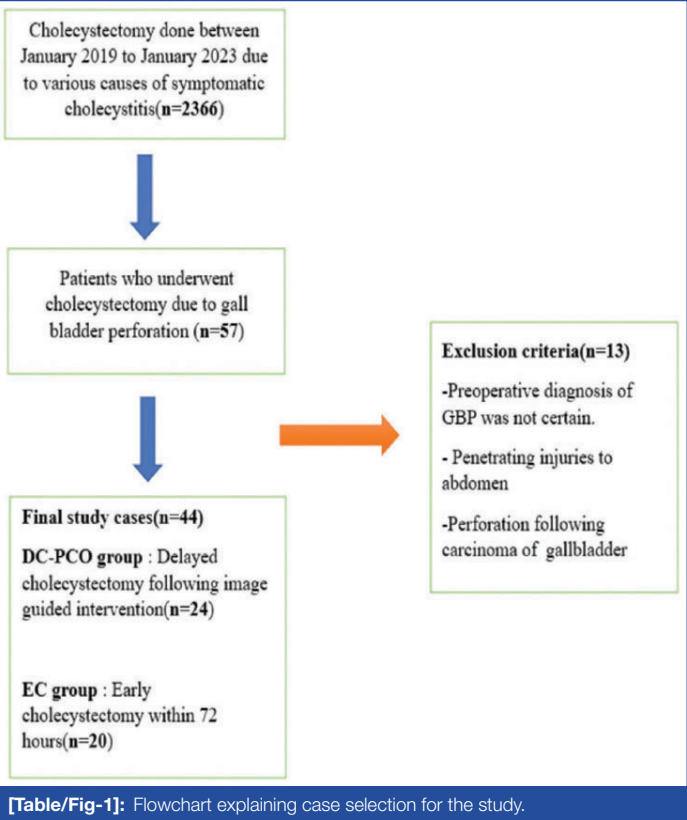
MATERIALS AND METHODS

A retrospective observational study was carried out in the Department of Surgery, Jawaharlal Nehru Medical College and Hospital, Aligarh Muslim University, Aligarh, Uttar Pradesh, India, from January 2019 to January 2023. The study protocol was approved by the Institutional Ethics Committee (IEC) (D. No. 355/IEC) and all patients

were masked during the analysis of clinical data. Subsequently, 57 patients who were managed for GBP were evaluated.

Inclusion criteria: Adult patients aged over 14 years who presented with symptomatic cholecystitis and underwent cholecystectomy due to a preoperative diagnosis of GBP were included in the study.

Exclusion criteria: Patients with intraoperative findings of GBP, GBP due to abdominal trauma and perforation due to gallbladder malignancy were excluded. [Table/Fig-1] demonstrates a flowchart for case selection.



Study Procedure

A routine blood profile, including preoperative total leukocyte counts, random blood sugar and liver function tests, was performed for all patients. Direct abdominal X-ray series, high-resolution ultrasound of the abdomen, abdominal Contrast-Enhanced Computed Tomography (CECT) and Magnetic Resonance Imaging (MRI) of the abdomen were conducted where necessary. Cases were divided into two groups based on the initial management approach: patients who underwent the ultrasound-guided approach, including percutaneous/ open drainage, were termed the DC-PCO group (n=24), while patients managed through emergency laparoscopic cholecystectomy and conversion to open cholecystectomy were referred to as the EC group (n=20). Demographic profiles, clinical features, morbidities, complications and culture reports were studied in the both groups. The gallbladder specimens were sent for histopathological examination after definitive management and the intraperitoneal collections were sent for pus culture and sensitivity testing for all patients.

Management approach: In the image-guided approach, a USG-guided percutaneous 16-F pigtail catheter was inserted under local anaesthesia using serial dilators, or an open drainage with a 20-F tube was conducted after opening the peritoneum under sedation. In the surgical approach, standard (4-port) laparoscopic cholecystectomy was initiated under general anaesthesia. Conversion to open cholecystectomy was performed in cases with dense adhesions and difficulty in achieving the critical view of safety via an open subcostal incision.

STATISTICAL ANALYSIS

The Statistical Package for the Social Sciences software (version 24.0; SPSS Inc., Chicago, IL, USA) was used to conduct statistical

analyses. Categorical variables were expressed as frequency and percentage, while descriptive statistics were used to present numerical values in the form of median (min-max). Continuous variables were compared between groups using the Mann-Whitney U test. Pearson's Chi-square test was employed to compare categorical variables between groups. A p-value <0.05 was considered statistically significant.

RESULTS

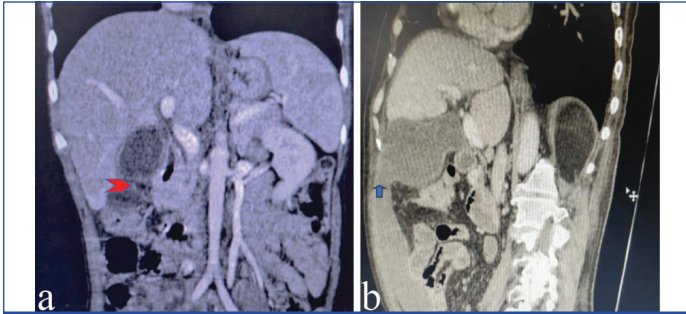
The age distribution differs significantly between the DC-PCO group (median 51.50 years) and the EC group (median 55 years). The median duration of stay was 8.6 days in the DC-PCO group and 9.8 days in the EC group, with a significant statistical difference indicating a longer stay for the EC group [Table/Fig-2].

Parameters	Total, n (%)	DC-PCO group (n=24), n (%)	EC group (n=20), n (%)	p-value
Age (years) median (range)	49 (25-75)	51.5 (25-75)	55 (30-85)	0.024*
Sex (F:M)	28:16	17:7	11:9	0.013*
History of calculus	35 (79%)	21 (87.5)	14 (70)	0.075*
Chief symptoms				
Abdominal pain	38 (86.4)	23 (95.8)	15 (75)	0.238**
Fever	11 (25)	6 (25)	5 (25)	0.50**
Jaundice	15 (34.1)	5 (20.8)	10 (50)	0.021**
Preoperative TLC (/cu.mm), median(range)	12300 (8500-26800)	10500 (9400-22100)	12100 (8400-22900)	0.264*
Random blood sugar (mg/dL)	154	152	146	0.769*
Modes of diagnosis				
Ultrasound (HR)	15 (34.1)	10 (41.6)	5 (25)	0.30**
CECT	26 (59.1)	12 (50)	14 (70)	0.13**
MRI	3 (6.8)	2 (8.3)	1 (5)	0.331**
GB wall thickness (mm)	7 (3-13)	9 (8-15)	8 (4-11)	0.682*
Co-morbidities				
Hypertension	27 (61.4)	14 (58.3)	13 (65)	0.214**
DM	19 (43.2)	7 (29.1)	12 (60)	0.011**
COPD	4 (9.1)	3 (12.5)	1 (5)	0.34**
Pregnancy	2 (4.5)	1 (4)	1 (5)	0.44**
Niemeier classification				
Type-I	13 (29.5)	5 (20.8)	8 (40)	0.082**
Type-II	27 (61.4)	16 (66.7)	11 (55)	0.015**
Type-III	4 (9.1)	3 (12.5)	1 (5)	0.194**
Hospital stay median number of days(range)	6.5 (3-18)	8.6 (5-15)	9.8 (7-18)	0.028*

[Table/Fig-2]: Table showing preoperative clinical characteristics of patients, various ways of management in DC-PCO group and EC group. *Mann Whitney U test; **Chi-square test; Bold values indicate statistically significant p-values (p<0.05)

Abdominal X-rays were performed on all the patients and a whole-abdomen CECT scan was conducted in 26 patients. Two patients with Type I GBP had air-fluid levels on direct abdominal radiographs. Abdominal ultrasonography showed gallstones in 35 patients, with defects or discontinuities in the gallbladder wall identified in 15 patients on high-resolution ultrasound. High-resolution ultrasonography of the abdomen can reveal a focal abnormal bulge in the gallbladder wall, underlying loss of continuity in the mucosal lining and echogenic omentum adhered to the gallbladder, which may suggest contained GBP. Contrast-enhanced abdominal CT revealed gallbladder wall thickening in all the patients, gallstones in 22 patients, extensive intraperitoneal free fluid in 13 patients and mild to moderate amounts of pericholecystic free fluid in 20 patients, as well as gallbladder perforation

sites in 18 patients. Abdominal CT and ultrasonography detected liver abscesses in six patients and dilated extra- and intrahepatic bile ducts in four patients. In [Table/Fig-3a,b], CECT of the abdomen shows coronal and oblique sagittal sections, revealing loss of continuity in the enhancing mucosal lining at the fundal region of the gallbladder with a loculated hypodense collection formed in the subhepatic region in 3a, suggestive of contained intraperitoneal ruptured gallbladder (Niemeier Type II) and a hypodense lenticular collection tracking along the right paracolic gutter in 3b (Niemeier Type I).



[Table/Fig-3]: Coronal and oblique sagittal images in cases of Type-II and Type-I GBP respectively with focal defect seen as non enhancing mucosal lining at GB fundus region with contained localised collection seen in subhepatic region in 3a (Red arrow) and free intraperitoneal fluid seen in right paracolic gutter in 3b (blue arrow).

All patients were treated with analgesics and antibiotics (third-generation cephalosporins) within the first 36 hours of admission and antibiotics were changed when necessary based on the culture and sensitivity of aspirated pericholecystic fluid. In the DC-PCO group (n=24), USG-guided pigtail/malecot catheter insertion was performed in 18 patients under local anaesthesia (Lox 2%), while the remaining six patients required USG-guided open drain placement under sedation (ketamine 1 mg/kg slow i.v.). About 66.7% of patients in the DC-PCO group were classified as Type II Niemeier GBP (16/24), highlighting the effectiveness of initial image-guided management in Type II GBP cases. All patients who underwent image-guided drainage subsequently received delayed laparoscopic cholecystectomy as a definitive treatment.

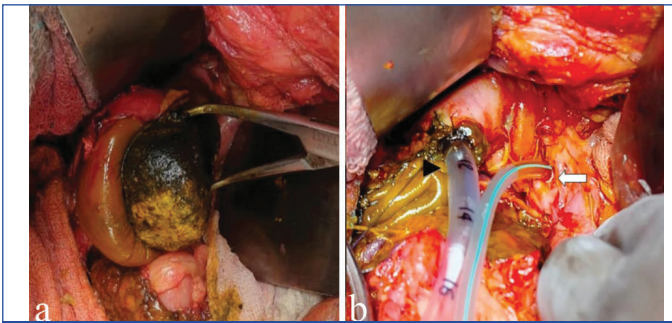
A comparative tabulation of initial management is demonstrated in [Table/Fig-4]. A total of five patients underwent open cholecystectomy due to frozen Calot's triangle and dense adhesions. One patient had a giant gallbladder calculus (approximately 6 cm) with Type III Mirizzi syndrome, for which open tube cholecystostomy (black arrowhead) was performed with T-tube placement (white arrowhead) in the proximal CBD following injury [Table/Fig-5a,b]. One patient underwent open partial cholecystectomy due to frozen Calot's triangle [Table/Fig-6a-c]. In the EC group, 15 cases were successfully managed by early laparoscopic cholecystectomy, with only five cases undergoing open/conversion to open cholecystectomy [Table/Fig-7].

In the DC-PCO group, the fundus was the most common site of perforation, whereas in the EC group, the gallbladder body was the most common site. This highlights the importance of the site of perforation in the management of GBP; since the more proximal the site of perforation, the denser the adhesions expected at Calot's

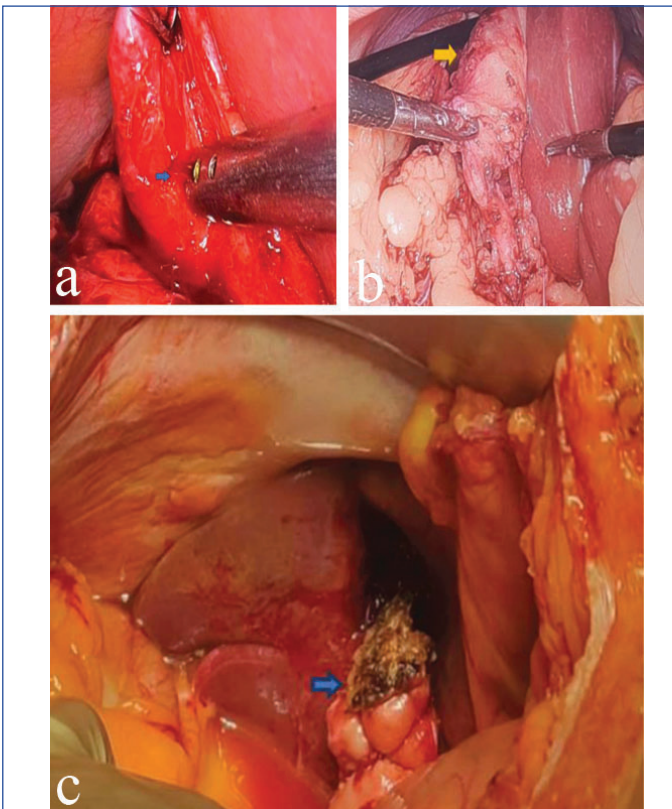
Surgical complications				
No complication	11 (25)	9 (37.5)	2 (10)	0.043**
Paralytic ileus	14 (31.8)	5 (20.8)	9 (45)	
Adhesion	10 (22.7)	7 (29.1)	3 (15)	
Biliary leakage	3 (6.8)	1 (4.2)	2 (10)	
SSI	6 (13.6)	2 (8.3)	4 (20)	
Number of patients needed post-operative ICU care	7 (15.9)	2 (8.3)	5 (25)	
Duration of surgery, median (range), minutes	110 (50-140)	90 (60-120)	118 (75-150)	0.325*
Bile culture				
Sterile	37 (84)	19 (79)	18 (90)	0.550**
Growth after 48 hour	7 (16)	5 [§] (20)	2* (10)	

[Table/Fig-4]: Tabulated comparison of operative complications, clinical characteristics of DC-PCO group and EC group.

*Mann-Whitney U test; **Chi-square test; Bold value indicates statistically significant p-value (p<0.05); [§]*P. aeruginosa* as growth; **E.coli* as growth



[Table/Fig-5]: a) Intraoperative picture of a large gallbladder calculus (approx. 6x6 cm) causing GB perforation; b) Intraoperative picture of open Tube cholecystostomy (black arrowhead) and T tube placement (white arrowhead) in proximal CBD following injury. (Images from left to right)



[Table/Fig-6]: Perop findings in three cases: a) Laparoscopic identification of site of GBP seen at the body region at site of bile leak being suctioned after dissecting the adherent omentum (blue arrow); b) Laparoscopic cholecystectomy showing site of perforation in contracted GB after dissection of adherent omentum (yellow arrow); c) Subtotal (conversion to open) cholecystectomy following frozen Calot's triangle found on laparoscopy (bold blue arrow).

	Total (n=44), n (%)	DC-PCO group (n=24), n (%)	EC group (n=20), n (%)	p-value
GB perforation site				
Fundus	20 (45.5)	15 (62.5)	5 (25)	<0.001**
Body	20 (45.5)	6 (25)	14 (70)	
Neck	4 (09)	3 (12.5)	1 (5)	
Definitive procedure				
Cholecystectomy	42 (95.5)	23 (95.8)	19 (95)	
Sub-total cholecystectomy	2 (4.5)	1 (4.2)	1 (5)	

Definite procedure	Emergency management (n=44)	Type-I	Type-II	Type-III
Delayed Cholecystectomy (DC-PCO group)	USG guided percutaneous drainage under local anaesthesia	03	12	3
	USG guided open drainage under sedation.	02	04	0
Early Cholecystectomy (EC group)	Early laparoscopic converted to open cholecystectomy/ early open cholecystectomy	03	02	0
	Early laparoscopic cholecystectomy	05	09	01

[Table/Fig-7]: Niemeier's classification of GBP and various procedures done in different types of GBP patients (Niemeier's classification).

triangle, making USG-guided procedures less feasible for initial management and laparoscopic dissection more challenging during definitive cholecystectomy, often necessitating conversion to open surgery.

There were two mortalities (4.5%), both of which occurred early during hospital stay. The first case involved a diabetic patient with uncontrolled blood sugar levels (455 mg/dL) and severe sepsis (28,000/cu mm) who underwent USG-guided drainage. The second case followed emergency open cholecystectomy in a seven-month antenatal patient with intrauterine foetal demise. Mortality did not differ significantly between the two groups. The mortalities were attributed to sepsis and multiple organ failure in the early post-intervention/postoperative period.

DISCUSSION

The GBP accounts for 2-10% of all emergency gallbladder surgeries [12]. Almost always, patients with Type I GBP require immediate medical attention and surgical intervention [13,14]. Thirteen patients operated on for GBP had Niemeier Type I perforation (29.5%). Gupta V et al., reported an incidence of 8.6% for Type I GBPs [15], whereas Rajput D et al., indicated it to be 60% in their findings [16]. Variable rates have been documented in the literature, which may be attributed to the overall lower prevalence rates of GBPs or the wide variation in sample sizes across different studies.

At initial presentation, GBPs can manifest with nausea, vomiting and abdominal pain [17]. According to Krishnamurthy G et al., abdominal discomfort was the most common presenting symptom in 93.9% of patients. Present study aligned with this finding. They also observed that the highest associated co-morbidities included diabetes mellitus (80.0%), hypertension (60.0%) and ischaemic heart disease (33.3%) [11]. According to Stefanidis D et al., diabetes mellitus (25.0%) was second most prevalent, while heart conditions (50.0%) were the most common concomitant ailments in their study [18]. Upon analysing the co-morbid conditions of the patients in present study, most prevalent co-morbid conditions were hypertension (61.3%), Type 2 diabetes mellitus (43.2%) and COPD (9.1%). Two patients were antenatal upon presentation. Given the lower incidence of GBPs, the sample size in all these studies, including present study was small.

According to studies by Xiao Y et al., and Krishnamurthy G et al., the fundus was the most frequently perforated site in 60% of cases [8,11]. In present study, the fundus and body region of GB were the most frequently perforated regions (45.5% each) In the literature, this observation has been attributed to decreased blood flow to the fundal region due to its distal location and supply by the cystic artery. In terms of initial management decisions, the site of perforation identified on imaging can play a role in determining whether early cholecystectomy (EC) as initial management should be followed; the more proximal the site of perforation, the denser the adhesions expected at Calot's triangle, making early laparoscopic dissection difficult during cholecystectomy and often requiring conversion to open cholecystectomy. We adhered to the

Enhanced Recovery After Surgery (ERAS) protocol for every patient. Adhesions at Calot's triangle complicate safe surgery and this is the most frequent reason for conversion to open cholecystectomy. We anticipate that adhesions develop near Calot's triangle due to the inflammatory process associated with more proximal GBPs.

According to Sahbaz NA et al., the most prevalent complication across any category was wound infection (5.26%) [19]. In present study, paralytic ileus (31.8%) was the most frequent complication of GBPs. Rajput D et al., observed that patients with Type I GBPs had an average hospital stay of 12 days following open surgery, while those who underwent laparoscopic surgery had a shorter duration, which was consistent with present study findings [16]. The literature does not provide comparable information on culture and sensitivity data. The growth rate was significantly higher in a study assessing patients who had gallbladder surgery for acute cholecystitis [20]. The small sample size and the preoperative broad-spectrum empirical antibiotic coverage administered to patients may account for the sterile bile cultures observed in most patients in present study.

This study highlights the role of image-guided early interventions undertaken in cases of GBP, given their wider availability, acceptance and associated lower morbidities. While present study found no significant difference between the two management routes concerning mortality and long-term outcome data, the morbidity data, including the average duration of hospital stay, was lower for the DC-PCO group.

Limitation(s)

The retrospective design and small sample size are limitations of present study. Furthermore, this study only included patients who had a GBP identified by preoperative imaging and who underwent minimally invasive interventions in response to this diagnosis. The exclusion of patients who did not have a preoperative diagnosis of GBP and who underwent laparotomy due to other causes of acute abdomen, suspected perforation, peritonitis, or free gas in the abdomen, with intraoperative diagnosis of GBP, may have impacted the study's findings.

CONCLUSION(S)

Gallbladder perforation, unlike other hollow viscus perforations, is unique as it poses significant challenges in diagnosis and management. Both the DC-PCO and EC groups carry similar risks and outcomes, with no significant difference in mortality rates. Therefore, the decision to pursue emergency versus delayed cholecystectomy (DC) depends on the clinical condition, associated co-morbidities and imaging findings of the patient. In resource-limited settings, patients with unstable vital signs but without obvious clinical features of peritonitis can initially be managed with image-guided drainage. In cases of obvious peritonitis, early laparoscopic surgery or conversion to open cholecystectomy should be performed. In cases of chronic perforation or localised abscess formation, ultrasound-guided drainage may be utilised as initial management, as dense adhesions are expected in subacute to chronic cases.

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