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ORIGINAL ARTICLE

Emergency Versus Delayed Cholecystectomy After Percutaneous Transhepatic Gallbladder Drainage in Grade II Acute Cholecystitis Patients

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Abstract
Introduction In grade II acute cholecystitis patients presenting more than 72 h after onset of symptoms, we prospectively compared treatment with emergency (ELC) to delayed laparoscopic cholecystectomy performed 6 weeks after percutaneous transhepatic gallbladder drainage (PTGBD).
Methods Four hundred ninety-five patients with acute cholecystitis were assessed for eligibility; 345 were excluded or declined to participate. One hundred fifty patients were treated after consent with either ELC or PTGBD.
Results Both PTGBD and ELC were able to resolve quickly cholecystitis sepsis. ELC patients had a significantly higher conversion rate (24 vs. 2.7 %, $P < 0.001$), longer mean operative time (87.8 ± 33.06 vs. 38.09 ± 8.23 min, $P < 0.001$), higher intraoperative blood loss (41.73 ± 51.09 vs. 26.33 ± 23.86, $P = 0.008$), and longer duration of postoperative hospital stay (51.71 ± 49.39 vs. 10.76 ± 5.75 h, $P < 0.001$) than those in the PTGBD group. Postoperative complications were significantly more frequent in the ELC group (26.7 vs. 2.7 %, $P < 0.001$) with a significant increase in incidence (10.7 %) of bile leak ($P = 0.006$) compared to those in the PTGBD group.
Conclusion(s) PTGBD and ELC are highly efficient in resolving cholecystitis sepsis. Delayed cholecystectomy after PTGBD produces better outcomes with a lower conversion rate, fewer procedure-related complications, and a shorter hospital stay than emergency cholecystectomy.

Keywords Grade II acute cholecystitis · Delayed cholecystectomy · Emergency cholecystectomy · Percutaneous transhepatic · Gallbladder drainage

Introduction

Laparoscopic cholecystectomy has been shifted from being considered a contraindication in the management of acute cholecystitis to being the most commonly performed procedure in acute cholecystitis patients in the last decade. This shift was driven by the increase in laparoscopic experience and the improvement in the laparoscopic devices and instruments, which has led to improved safety and reduced morbidities.[1,2] A high level of evidence coming from meta-analysis of ten prospective, randomized clinical trials stated that laparoscopic cholecystectomy performed within 72 h after the onset of symptoms of acute cholecystitis had no increased risk of complications with an added benefit of shorter hospital stay compared to open cholecystectomy.[3]

Patients with acute cholecystitis may present with a wide spectrum of disease severity ranging from a mild, self-limited illness to a fulminant and potentially life-threatening disease with an overall mortality rate of approximately 0.6 %.[4,5] The severity assessment criteria for acute cholecystitis were first presented throughout the world in Tokyo guidelines in 2007.[6] It was graded according to severity as mild (grade I), moderate (grade II), or severe (grade III), with different

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recommendations of surgical treatment options. Severe (grade III) acute cholecystitis was defined as acute cholecystitis associated with organ dysfunction whereas mild (grade I) acute cholecystitis was defined as occurring in a patient who has no findings of organ dysfunction and mild disease in the gallbladder, enabling cholecystectomy as a safe and low-risk procedure.[6,7] Moderate (grade II) acute cholecystitis was defined as acute cholecystitis in which the degree of acute inflammation is likely to be associated with increased operative difficulty in performing cholecystectomy.[8–13] They fulfill any one of the following criteria: elevated white blood cell count (>18,000/mm^3), palpable tender mass in the right upper abdominal quadrant, duration of complaints >72 h, or marked local inflammation (pericholecystic abscess, gangrenous cholecystitis, hepatic abscess, biliary peritonitis, emphysematous cholecystitis). Those patients according to Tokyo guidelines may be treated with emergency cholecystectomy or urgent gallbladder drainage, medical treatment, and delayed cholecystectomy.[7,14]

Percutaneous transhepatic gallbladder drainage (PTGBD) is reported as a treatment option for patients with acute cholecystitis.[15] Under ultrasound or CT guidance, this minimally invasive procedure is an alternative treatment to emergency cholecystectomy for critically ill patients with acute or complicated cholecystitis, who require urgent treatment.[16] PTGBD could help those high-risk patients to recover from the acute attack before delayed elective laparoscopic cholecystectomy is performed. However, its place in the management of low-risk patients with grade II acute cholecystitis is yet to be defined. In patients with acute cholecystitis, laparoscopic cholecystectomy is safe and feasible within 72 to 96 h after the onset of symptoms[17–21] before the development of fibrosis, where the anatomy is less obscure and the edema facilitates dissection.[22, 23] Most patients with grade II acute cholecystitis present more than 72 h after the onset of symptoms; treatment is controversial and results are unclear. They may have severe inflammation and dense adhesions that increase the risk of complications of laparoscopic cholecystectomy and conversion to open surgery.[24–26]

The aim of the present study is to compare the outcome of emergency laparoscopic cholecystectomy (ELC) to delayed laparoscopic cholecystectomy performed 6 weeks after percutaneous transhepatic gallbladder drainage (PTGBD) in management of patients with grade II acute cholecystitis presenting >72 h after the onset of symptoms.

Patients and Methods

The study was conducted at Alexandria Main University Hospital, Alexandria, Egypt. This is a 1000-bed teaching hospital owned by the Faculty of Medicine of the University of Alexandria. The ethics committee and review board at our institute approved the study and treatment protocol. An informed consent was obtained from all patients who agreed to participate in this study.

From December 2014 to May 2016, all patients presenting with acute calcular cholecystitis to our emergency department were assessed for eligibility on presentation.

Inclusion criteria:

1. Age ≥18 years
2. Written informed consent
3. Diagnosis and grading criteria: defined according to the Tokyo guidelines[7]

   (a) The diagnosis acute calculous cholecystitis:

   A. Local signs of inflammation: (1) Murphy's sign, (2) right upper quadrant mass/pain/ tenderness
   B. Systemic signs of inflammation: (1) fever, (2) elevated CRP, (3) elevated WBC count
   C. Imaging findings: imaging findings characteristic of acute cholecystitis

   Suspected diagnosis: one item in A + one item in B
   Definite diagnosis:

(1) One item in A and one item in B are positive.
(2) C confirms the diagnosis when acute cholecystitis is suspected clinically.

   (b) The grade: grade II (moderate) acute cholecystitis with duration of complaints >72 h: fulfilling any one of the following criteria:

   1. Elevated white blood cell count (>18,000/mm^3)
   2. Palpable tender mass in the right upper abdominal quadrant

Exclusion criteria:

1. Onset of symptoms <72 h or >7 days before first presentation
2. Marked local inflammation (pericholecystic abscess, gangrenous cholecystitis, hepatic abscess, biliary peritonitis, emphysematous cholecystitis)
3. Already admitted to ICU on presentation
4. Pregnancy
5. Acalculous cholecystitis
6. Decompensated liver cirrhosis, massive ascites
7. Mental illness prohibiting informed consent
8. Severe (grade III) acute cholecystitis
9. Mild (grade I) acute cholecystitis
10. Chose open cholecystectomy, a history of previous upper abdominal surgery, complication with

choledocholithiasis or intrahepatic bile duct stones requiring choledocholithotomy

A total of 495 patients were admitted because of a clinical diagnosis of acute calculous cholecystitis. All patients underwent the standard laboratory work-up with abdominal ultrasound performed to establish the diagnosis. A contrast-enhanced abdominal CT scan was performed if the findings on ultrasound examination were inconclusive. All patients with acute cholecystitis were diagnosed and graded according to the Tokyo guidelines.[6] Two hundred seventy-eight patients were excluded, as they did not meet our inclusion criteria or had an exclusion criterion whereas an additional 67 patients declined to participate in the study. The remaining 150 patients met our selection criteria. The patients were assigned after consent to the emergency laparoscopic cholecystectomy (ELC) group or PTGBD group (percutaneous transhepatic gallbladder drainage) using a closed sealed envelopes that were opened in order when assignments were made. An independent observer managed patients' allocation in either group. The allocated treatment was performed within 24 h.

In our hospital, being a tertiary referral center, serving a community of nine million people, almost all of our patients presenting more than 72 h after onset of symptoms of acute cholecystitis were already on antibiotic treatment prescribed to them at their local clinics and hospitals. They were referred to us after failed conservative treatment. They all represent failed medical treatment for over 24 h.

The primary endpoint was a conversion rate to open cholecystectomy while the secondary endpoints included the following:

- Postoperative duration of hospital stay after ELC versus postoperative duration of hospital stay after delayed LC in second admission in the PTGBD group
- In-hospital mortality, 30-day mortality
- All major morbidity: only procedure-related complications were analyzed since medical complications were not always procedure related. Major morbidity mainly including bleeding, biliary injury including all patterns of injuries of the intra- and extrahepatic biliary ducts including leakage of the biliary tree, bowel injury, intra-abdominal abscess (as defined by fever and/or elevated CRP/WBC and intra-abdominal fluid collection on CT imaging or ultrasound)
- Reintervention: any form of surgical, endoscopic, or radiologic intervention
- Readmission or emergency room visits for biliary complaints or related medical problems

All patients in the PTGBD group received at first empirical intravenous antibiotics (second-generation cephalosporins). This was changed to more appropriate agents according to identified causative microorganisms and their susceptibility testing results (antibiogram) with a duration of treatment from 5 to 7 days of oral antibiotics. In the ELC group also, all patients received empirical intravenous antibiotics (second-generation cephalosporins), which was continued postoperatively unless results of bile culture identified a causative microorganism requiring a change to a more appropriate agent according to its susceptibility testing results (antibiogram) with a duration of treatment from 5 to 7 days of oral antibiotics.

Sample Size Estimation Sample size was calculated using Epi-save software to conduct a clinical study to compare emergency laparoscopic cholecystectomy versus percutaneous transhepatic gallbladder drainage followed by delayed laparoscopic cholecystectomy in management of patients with low-risk grade II acute cholecystitis presenting >72 h after the onset of symptoms. Sample size was estimated to be 75 patients in each group with a total of 150 patients included in the study to detect reduction of the conversion rate to open surgery from 40 % among patients subjected to emergency laparoscopic cholecystectomy[27] to 19 % among patients subjected to percutaneous transhepatic gallbladder drainage followed by delayed laparoscopic cholecystectomy,[27] thus detecting a reduction in conversion rate by 21 %. The estimated sample size is made at assumption of 95 % confidence level and 80 % power of study.

In the ELC Group LC was performed by a qualified surgeon trained and experienced in laparoscopic surgery defined as >100 laparoscopic procedures on a yearly basis using a four-port technique. Patients received prophylactic antibiotics according to the local hospital protocol. Antibiotic therapy was routinely continued postoperatively for 5 days unless the performing surgeon has strong indications to continue further according to the clinical scenario (such as imminent sepsis or hemodynamic instability). Operative details were recorded with special attention to operative time, intraoperative difficulties, complications, and conversion to open surgery. The decision to convert to open cholecystectomy was made according to the operative situation including the difficulty of dissection, poor control of intraoperative hemorrhage, and adhesions of Calot's triangle or the liver bed. A drain was routinely inserted in all patients. Follow-up visits in the outpatient surgery clinic were scheduled 1 week after the patient's discharge.

In the PTGBD Group The PTGBD procedure was performed under local anesthesia (5 ml of 5 % lidocaine) using ultrasound-guided drainage by an experienced interventional radiologist. A puncture needle was advanced transhepatically into the gallbladder at its upper third. The aspirated material was sent for anaerobic and aerobic culture. Fluoroscopy

followed to confirm the guide wire placement in the gallbladder. After placing a guide wire and dilating the track, an 8–10-French pigtail catheter was inserted into the gallbladder to form a loop in the gallbladder, which was connected to an external drainage bag. The bag was sutured and fixed to the skin providing continuous external drainage. The drain was flushed daily with a saline solution.

The following criteria were used to define the success of PTGBD:

a. Improvement of the patient's clinical status including resolution of pain or tenderness at the right upper quadrant
b. Body temperature not exceeding 37.5 °C
c. Improvement of the patient's laboratory data with declining leukocytosis and C-reactive protein
d. Lack of complications related to the drain

After meeting the above-mentioned criteria, the patient was discharged from the hospital with the drain in place and scheduled for a weekly visit at the outpatient surgery clinic. Contrast imaging of the drain was performed 2 weeks after drain insertion to check cystic duct patency. The drain was closed but well kept in place under a sterile dressing in patients showing a patent cystic duct while in patients showing persistent obstruction of the cystic duct, the drain was left open till time of delayed cholecystectomy.

Data Collection and Follow-up Patients' data were recorded at time of admission including age, gender, associated comorbidities, BMI, history of previous abdominal surgeries, clinical findings including time of symptom onset, and vital signs in the emergency room and during admission. During admission, the patient's clinical, laboratory, and radiological data were recorded daily before and after the allocated intervention. The data regarding the allocated intervention including difficulty, duration, and complications was recorded immediately after the procedure by the performing surgeon or radiologist. Follow-up visits in the outpatient surgery clinic were scheduled 1 week after the patient's discharge.

Statistical Analysis of the Data

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. Comparisons between groups for categorical variables were assessed using the chi-square test and Fisher's exact or Monte Carlo correction. The Student *t* test was used to compare two groups for normally distributed quantitative variables. The Mann-Whitney test was used to compare two groups for abnormally distributed quantitative variables. Significance of the obtained results was judged at the 5 % level.

Results

Patients in the ELC and PTGBD groups had similar demographic, clinical, preoperative laboratory, and radiological characteristics as shown in Table 1. There was no significant difference between the two groups as regards to age, gender, BMI, associated comorbidities, ASA class, previous abdominal surgery, mean duration of symptoms before admission (time from onset of symptoms to admission), and the presence of high temperature on admission (mean body temperature). Preintervention laboratory findings including mean WBC counts, CRP, total bilirubin level, and liver function tests were similar in the two groups with all patients in both groups having a clinically palpable gallbladder mass with a positive ultrasound Murphy's sign (Table 2).

In the PTGBD group, percutaneous transhepatic gallbladder drainage was performed successfully in all 75 patients. All patients reported immediate relief of right upper abdominal quadrant pain following drainage with achievement of clinical improvement after a mean duration of 17.69 ± 3.06 h (range 14–25 h). There was no need for further aspiration or insertion of additional drains for pericholecystic fluid collections due to the clinical improvement of those cases. All PTGBD group patients were discharged after complete resolution of symptoms, with a mean time from percutaneous transhepatic gallbladder drainage to discharge of 27.69 ± 9.87 h (range 21–66 h). No patient developed recurrent biliary symptoms with all

Table 1 Comparison between the two studied groups according to demographic data

	ELC ($n = 75$)	PTGBD ($n = 75$)	*P*
Age (years)	50.19 ± 12.01	49.65 ± 11.63	0.783
Sex			
Male	27 (36.0 %)	30 (40.0 %)	0.614
Female	48 (64.0 %)	45 (60.0 %)	
BMI	34.43 ± 4.13	34.32 ± 4.34	0.878
Associated comorbidity			
No	57 (76.0 %)	55 (73.3 %)	0.988
DM	9 (12.0 %)	9 (12.0 %)	
Hypertension	6 (8.0 %)	7 (9.3 %)	
Cardiac	2 (2.7 %)	2 (2.7 %)	
Asthma	1 (1.3 %)	2 (2.7 %)	
ASA			
I	57 (76.0 %)	55 (73.3 %)	0.707
II	18 (24.0 %)	20 (26.7 %)	0.707

Qualitative data was expressed using number and percent and was compared using the chi-square test or Fisher test. Normally quantitative data was expressed in mean ± SD and was compared using the Student *t* test while abnormally quantitative data was expressed in median (min–max) and was compared using the Mann-Whitney test

Table 2 Comparison between the two studied groups according to preoperative clinical and laboratory characteristics

	ELC ($n = 75$)	PTGBD ($n = 75$)	P
Duration of symptoms (h)	92.75 ± 11.52	93.2 ± 12.27	0.816
Previous abdominal surgery			
No	71 (94.7 %)	70 (93.3 %)	0.620
Appendectomy	1 (1.3 %)	3 (4.0 %)	
Hysterectomy, BSO	1 (1.3 %)	0 (0.0 %)	
Lap tube adhesiolysis	1 (1.3 %)	0 (0.0 %)	
Lap right cyst removal	1 (1.3 %)	0 (0.0 %)	
Oophorectomy	0 (0.0 %)	1 (1.3 %)	
Stone bladder	0 (0.0 %)	1 (1.3 %)	
Temperature (°C)	38.4 (37.8–39.1)	38.3 (37.7–39.4)	0.848
WBCs ($10^3/mm^3$)	19.7 (18.2–24.0)	19.6 (18.2–23.8)	0.551
CRP (mg/dl)	96.0 (56.0–151.0)	99.0 (78.0–155.0)	0.281

Qualitative data was expressed using number and percent and was compared using the chi-square test or Fisher test. Normally quantitative data was expressed in mean ± SD and was compared using the Student t test while abnormally quantitative data was expressed in median (min–max) and was compared using the Mann-Whitney test

patients entered into remission till time of delayed cholecystectomy. There were no major complications related to PTGBD. Seven patients (9.3 %) experienced a PTGBD-related minor complication, two cases of catheter dislodgement requiring further reposition and fixation, three cases of small subhepatic hematoma treated conservatively, and two cases of minor bile leak around the catheter resolved spontaneously with no need for repeat catheterization with a larger catheter. Those seven patients required more outpatient clinic visits to monitor their minor complications, but no readmission was needed. Two weeks after the placement of the PTGBD catheter, cholangiography was performed; in 60 patients (80 %), the cystic duct was patent and the catheter was closed but well kept in place under a sterile dressing till delayed cholecystectomy; in 11 patients (14.6 %), the cystic duct was still obstructed, and the catheter was left for open drainage until surgery. In the remaining four patients (5.4 %), cholangiography revealed common bile duct stones in the absence of clinical symptoms or jaundice. Endoscopic sphincterotomy with stone extraction was achieved successfully through endoscopic retrograde cholangiopancreatography before delayed cholecystectomy. In all patients, laparoscopic cholecystectomy was performed 6 weeks after PTGBD.

Comparing emergency and delayed laparoscopic cholecystectomy in the two groups revealed a significantly longer mean operative time in the ELC group than in the PTGBD group (87.8 ± 33.06 vs. 38.09 ± 8.23 min, $P < 0.001$) with a significant increase in intraoperative blood loss ($P = 0.008$). The conversion rate from laparoscopic to open cholecystectomy was significantly more frequent in the ELC (18 patients) than the PTGBD group (2 patients) (24 vs. 2.7 %, $P < 0.001$). In the ELC group, the decision to convert to open surgery was taken in 14/18 patients because of the difficulty with dissection at Calot's triangle with adhesions, tissue friability, or unclear anatomy, making Calot's triangle dissection unsafe, whereas 4/18 patients were converted due to uncontrolled bleeding (Table 3). Conversion due to bleeding was more frequent in ELC group patients than in PTGBD group patients but with no significant difference (5.3 vs. 1.3 %, $P = 0.367$). Intraoperative cholangiography was required in all 14 patients converted in the ELC group due to difficult dissection and unclear anatomy at Calot's triangle. In spite of a higher conversion rate and increased use of intraoperative cholangiogram, there was a significant increase ($P < 0.001$) in the number of subtotal cholecystectomies performed in ELC (13 patients) compared to successful complete cholecystectomy in all cases of the PTGBD group. Abdominal drains were used in all patients in both groups.

No 30-day mortality occurred in either group. Postoperative complications were significantly more frequent in the ELC group (20 patients) compared to two patients in the PTGBD group (26.7 vs. 2.7 %, $P < 0.001$). There was a significant increase in incidence of bile leak in the ELC group (10.7 %) compared to no case in the PTGBD group ($P = 0.006$). The diagnosis of the bile leak was made through the drainage results from the drain placed at surgery. 5/13 subtotal cholecystectomies in ELC developed postoperative bile leak. 5/8 bile leaks in ELC required endoscopic retrograde cholangiopancreatography, sphincterotomy, and stenting. Subhepatic collection (biloma) occurred in five patients in the ELC group and required additional percutaneous ultrasound-guided drainage in three patients. There was also a significant increase in mean intraoperative blood loss in the ELC group compared to the PTGBD group (41.73 ± 51.09 vs. 26.33 ± 23.86, $P = 0.008$). The two groups showed similar incidence of wound, port site infection, and bowel injury rate. Bowel injury during dissection of dense adhesions of the gallbladder occurred in two patients in the ELC group (duodenal serosal injury); one of them required direct seromuscular suture. Patients in the ELC group had a significantly longer mean postoperative hospital stay than those in the PTGBD group (51.71 ± 49.39 vs. 10.76 ± 5.75 h, $P < 0.001$). On the long-term follow-up, obstructive jaundice due to choledocholithiasis was diagnosed with magnetic resonance cholangiopancreatography in one patient at 4 months in the ELC group. The stone was successfully extracted through ERCP and sphincterotomy. Total duration of hospital stay in the PTGBD group (sum of the two admissions, first admission for PTGBD and second admission for delayed LC) was 39.45 ± 10.71 h compared to 58.41 ± 38.42 h in ELC (single admission) with no statistically significant difference ($P = 0.058$).

Table 3 Comparison between the two studied groups according to operative and postoperative data

	ELC ($n = 75$)	PTGBD[a] ($n = 75$)	P
Conversion	18 (24.0 %)	2 (2.7 %)	<0.001*
Conversion due to difficult dissection	14 (18.7 %)	1 (1.3 %)	<0.001*
Conversion due to bleeding	4 (5.3 %)	1 (1.3 %)	0.367
Intraoperative bleeding (ml)	41.73 ± 51.09	26.33 ± 23.86	0.008*
Operative time (min)	87.8 ± 33.06	38.09 ± 8.23	<0.001*
Subtotal cholecystectomy	13 (17.3 %)	0 (0.0 %)	<0.001*
Postoperative hospital stay (h)	51.71 ± 49.39	10.76 ± 5.75	<0.001*
Combined PTGBD and postoperative complications	20 (26.7 %)	9 (12.0 %)	0.023*
Postoperative complications	20 (26.7 %)	2 (2.7 %)	<0.001*
Bleeding	0 (0 %)	0 (0 %)	–
Bile duct injury (leak)	8 (10.7 %)	0 (0.0 %)	0.006*
Subhepatic collection	5 (6.7 %)	0 (0.0 %)	0.058
Wound infection	7 (9.3 %)	2 (2.7 %)	0.166
Bowel injury	2 (2.7 %)	0 (0.0 %)	0.497
Ileus	3 (4.0 %)	0 (0.0 %)	0.245
Choledocholithiasis	1 (1.3 %)	0 (0.0 %)	1.000
PTGD complications	–	7 (9.3 %)	–
Catheter dislodgement	–	2 (2.7 %)	–
Subhepatic hematoma	–	3 (4.0 %)	–
Bile leak	–	2 (2.7 %)	–
Clavien-Dindo classification			
Nonsevere (grades I and II)	17 (22.7 %)	2 (2.7 %)	<0.001*
Severe (grade III)	9 (12.0 %)	0 (0.0 %)	0.004*
Clinical improvement after PTGBD (h)	–	17.89 ± 3.06	–
WBC after insertion	–	11.1 ± 1.25	–

Qualitative data was expressed using number and percent and was compared using the chi-square test or Fisher test. Normally quantitative data was expressed in mean ± SD and was compared using the Student t test while abnormally quantitative data was expressed in median (min–max) and was compared using the Mann-Whitney test

*Statistically significant at $P \leq 0.05$

[a] Postoperative data under the PTGBD group in this table represent the data of their second admission of delayed cholecystectomy

Discussion

The optimal treatment of patients with grade II acute cholecystitis admitted to the hospital over 72 h after the onset of symptoms has not yet been well defined. There is only limited evidence in the literature about whether PTGBD first or immediate cholecystectomy (laparoscopic or open) gives a better outcome. Both approaches are currently used, and specific indications on which approach to be used are mostly dependent on local experience and personal preferences.

In this study, we assessed the role and outcomes of emergency compared to delayed LC after percutaneous transhepatic gallbladder drainage in the treatment of 150 patients with grade II acute cholecystitis admitted to hospital over 72 h after the onset of symptoms. Both PTGBD and ELC were able to resolve quickly cholecystitis sepsis in 100 % of the patients, and the mortality rates did not show any difference. The rate of conversion to open surgery was significantly higher in ELC with a significant increase in duration of postoperative hospital stay. Mean blood loss and postoperative complications were also significantly higher among patients who underwent emergency laparoscopic cholecystectomy compared to those who had delayed laparoscopic cholecystectomy 6 weeks after percutaneous transhepatic gallbladder drainage.

Published literature yielded controversial data in studies comparing emergency versus delayed laparoscopic cholecystectomy after PTGBD. The conversion rate to open surgery was reported to be higher among patients undergoing emergency LC in one retrospective study[25], in contrast to others reporting the higher frequency of conversion associated with the delayed cholecystectomy after PTGBD.[28, 29] The operative time was consistently reported to be shorter among patients undergoing delayed laparoscopic cholecystectomy after

PTGBD.[25, 28, 30] Other studies including the study of Tsumura et al.[31] showed no significant difference in surgery results with or without PTGBD treatment. A report from one study group[29] showed that PTGBD not only did not shorten the operation time for the delayed LC group or the postoperative hospitalization time. These differences in results yielded may be due to the fact that the timing for delayed LC after PTGBD was different, with the grade and severity of acute cholecystitis not strictly defined among the studied population.

There is a significantly higher open conversion rate during laparoscopic cholecystectomy in acute cholecystitis (11–28 %) than the less than 5 % rate reported for chronic cholecystitis.[32–36] Conversions mean that the costs and risks of complications are increased.[33, 35] Although the present study was conducted at a tertiary care university hospital with all laparoscopic procedures in both groups performed by the same two qualified and experienced laparoscopic hepatobiliary surgeons, the conversion rate after emergency laparoscopic cholecystectomy was high (24 %). However, this high conversion is comparable to those high rates previously reported in other studies reaching 40 % in emergency settings.[24, 37, 38] In the ELC group, the first surgeon converted 8/18 LC, whereas the second surgeon converted 10/18 LC. They each converted one case in the PTGBD group. There was no difference in the conversion rate between the two surgeons who performed the procedures.

In the setting of acute cholecystitis, laparoscopic cholecystectomy is still considered a challenging procedure due to anticipated anatomical difficulties with reported higher incidences of common bile duct injuries.[34, 39] In severe cholecystitis, the reported complication rates lie between 0 and 40 %.[12, 40, 41] The overall frequency of complications was significantly higher in patients undergoing emergency laparoscopic cholecystectomy. We had a significantly higher rate (10.7 %) of postoperative bile leak in ELC versus 0 % in the PTGBD group ($P = 0006$). We had no case of bile duct transection or ligation, but bile leaks were encountered. Bile leaks occurred more in patients who had subtotal cholecystectomy (5/8 bile leak patients). In two cases, bile leak was from the cystic duct stump, caused by slipped surgical clips which was likely due to resolution of inflammation in a thickened inflamed cystic duct, and one patient was leaking from the accessory bile duct at the gallbladder bed which was not identified intraoperatively among the surgical inflamed field. More than half of bile leak patients (5/8 patients) required intervention in the form of ERCP and stenting, which led to an increase in their duration of hospital stay. Also, those patients had a higher incidence of bilomas that required further ultrasound-guided drainage. Subtotal cholecystectomy was performed in patients where there was failure of anatomical identification of the critical view of safety with unclear anatomy even after intraoperative cholangiogram with dense adhesions at Calot's triangle making further dissection unsafe.

Since it was first reported by Radder[42] in 1980 for the treatment of suppurative cholecystitis, the percutaneous transhepatic gallbladder drainage has gained wide acceptance in the management of acute cholecystitis and its treatment efficacy has been increasingly accepted by researchers. The aim and rationale of percutaneous transhepatic gallbladder drainage is to alleviate symptoms and relieve sepsis of acute cholecystitis in a less invasive method than emergency surgery. This is achieved by relieving the gallbladder tension through external drainage under local anesthesia in combination with antibiotic therapy.[22] This allows time to optimize and prepare critically ill patients with acute cholecystitis for elective surgery instead of undergoing emergency cholecystectomy. The indication for the use of PTGBD in the management of acute cholecystitis differs in various centers but commonly includes the high-surgical-risk patients having comorbid illness with severe (grade III) acute cholecystitis. The latest issued "Tokyo guideline" cites moderate (grade II) acute cholecystitis also as an indication[7, 14] due disease duration of more than 72 h, the latter of which is likely to be associated with severe inflammation and dense adhesions and, thus, higher risk of conversion and complications of cholecystectomy.[17, 43] We adopted those criteria but excluded cases with gangrenous cholecystitis, hepatic abscess, biliary peritonitis, and emphysematous cholecystitis.

Gallbladder drainage can be performed via two routes, the transperitoneal and transhepatic approach (PTGBD). The transhepatic approach through the bare area of the GB was the most commonly used in the majority of published series to prevent catheter dislodgement and bile leakage[30, 44], despite the potential risks of pneumothorax, intrahepatic bleeding, or hemobiliary fistula.[22] Due to the popularization of ultrasonography, PTGBD has become a standard interventional procedure[23]; thus, in the present study, we adopted this approach. In addition to minimizing the risk of intraperitoneal bile leakage, the transhepatic approach avoids inadvertent injury to the hepatic flexure of the colon.

The safety and efficacy of percutaneous transhepatic gallbladder drainage in the treatment of critically ill high-risk acute cholecystitis patients with the reduction in their mortality were illustrated in published literature.[45, 46] It is a rather uncomplicated procedure with a low complication rate that is reported to range from 3 to 13 % and the mortality was 0 to 11 %.[19, 47–55] The complication rate in this current series was 9.3 % with no major complication. Only two interventional radiologists with a vast experience in biliary intervention performed all the PTGBD procedures, which were reflected in our low complication rate. Relief of sepsis was achieved in 100 % of our patients, with no patients developing recurrent biliary symptoms during the long-term follow-up till reaching laparoscopic cholecystectomy time. This was in agreement with Melloul et al.[46] who, after reviewing 14 published studies on percutaneous gallbladder drainage between 1998 and

2010, found that the success rate of puncture was close to 100 % and alleviation of symptoms with patients entering into the remission rate reached 78 to 100 %.

The best time of delayed cholecystectomy after PTGBD is controversial and differs among various centers according to their policy and experience. We scheduled delayed laparoscopic cholecystectomy at 6 weeks (over 4 weeks) after PTGBD to avoid marked inflammation that is likely to be present before 4 weeks. Published data also concluded that patients treated with immediate laparoscopic cholecystectomy within 72 h after PTGBD may have a shorter mean hospital stay and lower hospital costs than those who underwent delayed laparoscopic cholecystectomy more than 72 h after PTGBD, but the latter subjects had lower frequency of complications and a shorter operative time.[29]

Another controversial issue is management of the PTGBD catheter till time of delayed cholecystectomy especially whether it should be removed during or before delayed cholecystectomy. In the present study, we did not remove the catheter until delayed laparoscopic cholecystectomy. We performed elective cholangiography for all patients after 2 weeks of PTGBD and adopted the policy of open drainage to all patients with cystic duct obstruction whereas, for those with a patent duct, the catheter was closed and left in place. The latter was done to decrease the risk of recurrent acute exacerbation of gallbladder if the catheter was removed and another stone compromised the cystic duct patency. Another factor favoring not removing the catheter was to eliminate patients' dropouts of scheduled date of delayed cholecystectomy if the catheter was removed and complete resolution of symptoms occurred. PTGBD had the added advantage of allowing a route of biliary system imaging before delayed cholecystectomy to document the patency of the cystic and common bile duct. In four patients (5.3 %), cholangiography revealed common bile duct stones, which were successfully managed by endoscopic sphincterotomy with stone extraction through endoscopic retrograde cholangiopancreatography before the cholecystectomy. This reduced the risk of retained common bile duct stones or the need for perioperative cholangiography and common bile duct exploration.

Conclusion

In patients with grade II acute cholecystitis who presented to the hospital ≥72 h after the onset of symptoms, PTGBD and ELC are highly efficient in resolving cholecystitis sepsis. PTGBD followed by delayed laparoscopic cholecystectomy produces better outcomes with a lower conversion rate, fewer procedure-related complications, and shorter hospital stay than emergency laparoscopic cholecystectomy. Percutaneous drainage represents a valuable and effective tool with a high success rate and low morbidity to treat cholecystitis sepsis in a short period of time, allows for better preoperative evaluation of the biliary system, and facilitates further laparoscopic cholecystectomy.

Author Contribution Ahmed El-Gendi performed the surgeries, wrote the manuscript, and collected the data. Mohamed El-Shafei performed the intervention radiology procedures. Doaa Emara performed the diagnostic radiology, revised the manuscript, and analyzed the data.

Compliance with Ethical Standards The ethics committee and review board at our institute approved the study and treatment protocol. An informed consent was obtained from all patients who agreed to participate in this study.

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