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ORIGINAL ARTICLE

Early versus delayed laparoscopic cholecystectomy after percutaneous transhepatic gallbladder drainage

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Abstract
Background Percutaneous transhepatic gallbladder drainage (PTGBD) is a procedure to resolve acute cholecystitis (AC). It may decrease the technical difficulty of laparoscopic cholecystectomy (LC) and thus may facilitate successful surgery when a patients' condition improves. However, the timing of LC after PTGBD remains controversial.
Methods From 2004 to 2010, cholecystectomy after PTGBD was performed in 67 patients with AC. Group I members underwent LC within 72 h of PTGBD ($n = 21$), whereas group II members underwent LC at more than 72 h after PTGBD ($n = 46$).
Results The open conversion rate was similar in the two groups. The perioperative complication rate was higher in group I than in group II, but with marginal significance (19.0 vs. 4.3%; $p = 0.07$). Mean operative time was longer in group I than in group II (79.3 ± 25.3 vs. 53.7 ± 45.3 min; $p = 0.02$). However, overall hospital stay was shorter in group I than in group II, but with marginal significance (10.8 ± 4.5 vs. 14.7 ± 9.3 days; $p = 0.08$).
Conclusions Pros and cons were well balanced between the two groups. Decisions on the timing of cholecystectomy after PTGBD should be made based on considerations of patient condition, hospital facilities, and surgical experience.

Keywords Laparoscopic cholecystectomy · Acute cholecystitis · Percutaneous transhepatic gallbladder drainage

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Introduction

Acute cholecystitis (AC) is one of the most frequent emergent diseases treated by cholecystectomy, which has an operative mortality rate of less than 0.8% among AC cases [1]. Since Mouret [2] first reported successful laparoscopic cholecystectomy (LC) in 1987, AC has become the procedure of choice for most benign gallbladder (GB) diseases. However, the timing of LC in older patients with a combined medical morbidity and severe cholecystitis is controversial in terms of economics, the conversion rate to open cholecystectomy (OC), operative time, and the perioperative complication rate [3–5].

Percutaneous cholecystostomy (PC) was first reported in 1980 by Radder [6], and the technique is being increasingly employed. PC has traditionally been used to manage AC in cases with severe comorbidities in which emergency cholecystectomy poses a risk of mortality [7, 8]. However, in elderly or critically ill patients with AC, PC can be used as an immediate treatment, and cholecystectomy can be safely performed when patient condition improves.

However, few studies have addressed the effect of the time interval between PC and LC. Chikamori et al. [9] suggested that an early scheduled LC following PC is safe and effective in terms of the conversion rate to OC, operative time, intraoperative complication, and hospital stay. On the other hand, others have shown that an elective delayed LC after PC decreases conversion and complication rates in AC, but increases hospital stay and patients suffer from the inconvenience of a cholecystostomy tube [3, 10].

This study was undertaken to compare surgical results with respect to the time interval between PC and LC, to determine the optimal time for LC after PC in patients with AC.

Methods

Study group

This retrospective analysis was conducted on patients who underwent cholecystectomy after percutaneous transhepatic gallbladder drainage (PTGBD) for AC at Seoul National University Hospital (SNUH), South Korea, from January 2005 to January 2010. This study was conducted in accordance with the rules and regulations of the SNUH Institutional Review Board. Patients with a combined common bile duct stone, previous upper abdominal surgery, previous chemotherapy or radiotherapy due to another malignancy, and those in whom another method was used for biliary decompression or those with a Karnofsky performance score lower than 50 were excluded. Sixty-seven patients were included in this study. Those patients were allocated to one of two groups: group I members underwent LC within 72 h of PTGBD ($n = 21$), and group II members underwent LC more than 72 h after PTGBD ($n = 46$).

Diagnosis of AC and the indications of PTGBD

Diagnoses of AC were reviewed according to the Tokyo guidelines [11], that is, local signs of inflammation [Murphy's sign, right upper quadrant (RUQ) mass/pain/tenderness], systemic signs of inflammation [fever, elevated C-reactive protein (CRP), elevated white blood cell (WBC) count], and imaging findings characteristic of AC. Indications for PTGBD were moderate (grade II) or severe (grade III) AC [11], a failure to respond to medical treatment for AC [10], and the presence of a severe comorbidity, such as COPD, ischemic heart disease, or cerebrovascular disease, also in accord with the Tokyo guidelines.

Percutaneous cholecystostomy

In all patients, PTGBD as PC was performed by interventional radiologists under ultrasound and fluoroscopic guidance. Under 1% lidocaine local anesthesia, a 21-gauge Chiba needle (Solco Intermed, Seoul, South Korea) was advanced transhepatically into the GB. After placing a guide wire and dilating the track, a 8.5 Fr pigtail catheter (Dawson-Mueller Drainage Catheter, Cook, Bloomington, IN, USA) was positioned with its tip in the gallbladder (GB). Bile was aspirated from most patients for culture. Cholangiograms were carried out using a small placement to confirm that the pigtail catheter was in the correct position within the GB.

Criteria for clinical improvement after PTGBD

Clinical improvement after PTGBD was defined as meeting all three criteria: (1) resolution of RUQ pain or tenderness; (2) a peak body temperature of <37.5°C during 24 h period; (3) resolution of leukocytosis [12].

Operative technique

In all 67 patients, LC was performed by one of three experienced biliary surgeons using three-port method. Briefly, a laparoscope was inserted via a 12-mm umbilical port; other instruments were inserted via a 5-mm epigastric port and a right subcostal port. The manipulations involved during the LC procedure were: (1) insertion of the laparoscope from under the umbilicus, (2) dissection of adhesions around the GB, (3) dissection of Calot's triangle (separation of cystic arteries and exposure of the cystic duct), (4) separation of the GB bed and dissection of GB, and (5) removal of the GB and wound closure. The manipulations affected by the degree of GB inflammation included: dissection of adhesions around the GB, dissection of Calot's triangle, separation of the GB bed, and GB extraction through the umbilical port.

Pathological classification

The pathology and grading of cholecystitis were conducted by assessing inflammatory cell infiltration, mucosal change, abscess formation, and wall destruction [13]. Findings of AC were neutrophil infiltration, edema or ulceration of the mucosal layer, and necrosis. The characteristics of chronic cholecystitis (CC) were lymph follicle formation, chronic inflammatory cell invasion, and fibrosis. All pathological examinations were reviewed by a single experienced pathologist.

Data collection and statistical analysis

The following data were collected: (1) demographic parameters, such as gender, body mass index (BMI), preoperative American Society of Anesthesiologists

(ASA) score, and combined morbid disease; (2) clinical findings, such as temperature, the presence of abdominal pain, right-sided abdominal tenderness, and palpable abdominal mass; (3) laboratory findings, such as liver enzymes (AST, ALT, ALP, GGT, and bilirubin), leukocytosis, and CRP; (4) radiological findings, such as abnormal GB distension, GB wall thickness, sludge formation or cholelithiasis, biliary tract dilatation, the presence of abscess, pericholecystic fluid collection, and if observed by the radiologist, an ultrasonographic Murphy's sign; (5) technical considerations for cholecystostomy; (6) clinical results after PTGBD; and (7) details of surgical results after PTGBD with perioperative complications, open conversion rate, pathology, operative time, hospital cost, and duration of hospital stay.

The data were analyzed using SPSS ver. 17.0 (SPSS Inc, Chicago, IL, USA). Continuous and normally distributed variables are presented as means ± standard deviations. Continuous parameters in each group were compared using the independent *t* test, and categorical parameters using the χ^2 test or Fisher's exact test. Multiple logistic regression analysis was used for the adjustment of surgeon factor of surgical result**.** Probability (*p*) values of 0.05 or less were considered statistically significant, while *p* from more than 0.05 to 0.10 was considered marginally significant.

Results

Demographic and laboratory findings

Mean time intervals to laparoscopic cholecystectomy after PTGBD was significantly ($p < 0.01$) shorter in group I than in group II (1.71 ± 0.68 vs. 17.64 ± 13.25 days). No significant differences were found between groups I and II in terms of age, sex, BMI, ASA class, duration of symptoms, severity criteria, or combined morbidities. Furthermore, laboratory findings, including WBC counts and total bilirubin level, were similar in the two groups (Table 1).

Clinical results after PTGBD

Time intervals to PTGBD after admission and complications after PTGBD insertion, such as bile leakage and catheter dislodgement, were similar in the two groups, as were clinical improvements after PTGBD (Table 2).

Pathological findings after cholecystectomy

Resected GB inflammation was classified histologically as acute or chronic, and then sub-classified into three stages. The AC to CC ratio was higher in group I (15:6) than in group II (23:21), but not significantly so ($p = 0.14$); however, the frequency of severe inflammation in AC was

Table 1 Clinical characteristics of the two study groups

	Treatment		
	Group I ($n = 21$)	Group II ($n = 46$)	*p*
Age	69.8 ± 13.2	71.3 ± 13.4	0.66
Sex (male:female)	2.5:1	1.7:1	0.59
BMI (kg/m^2)	60.0 ± 12.7	56.1 ± 16.5	0.34
ASA class (minimal/moderate/severe[a])	0/22/0	5/38/3	0.16
Mean time intervals to LC after PC	1.71 ± 0.68	17.64 ± 13.25	<0.01
Duration of symptom (days)	6.3 ± 8.9	4.5 ± 5.3	0.37
GB stone (*n*, %)	14 (66.7)	32 (69.6)	0.97
Combined comorbid diseases (*n*, %)	11 (52.3)	26 (56.5)	0.53
Cardiovascular disease	8 (38.0)	23 (50.0)	
Cerebrovascular disease	1 (4.8)	4 (8.7)	
Diabetes mellitus	1 (4.8)	12 (26.1)	
Chronic obstructive lung disease	1 (4.8)	1 (2.1)	
Chronic renal failure	1 (4.8)	2 (4.3)	
Chronic liver disease	3 (14.3)	2 (4.3)	
Others	7 (33.3)	16 (34.8)	
Severity criteria by Tokyo guideline (mild/moderate/severe)	3/16/2	3/35/8	0.39
WBC on admission (10^3 cells/mm^3)	15.10 ± 6.86	13.91 ± 5.07	0.43
Total bilirubin on admission (mg/dl)	2.29 ± 1.01	1.78 ± 1.08	0.08

[a] ASA class I, II/III, IV/V, VI

Table 2 Clinical results after PTGBD

	Group I ($n = 21$)	Group II ($n = 46$)	p
Time to PTGBD after admission (days)	0.5 ± 0.9	0.9 ± 1.4	0.22
Complications after PTGBD insertion (n, %)	0	3 (6.5)	0.55
Bile leak	0	0	
Subhepatic hematoma	0	0	
Catheter dislodgement	0	3	
Clinical improvement after PTGBD (days)	3.2 ± 1.6	3.0 ± 2.1	0.75

Table 3 Comparisons of pathological findings in the two study groups after cholecystectomy

	Group I ($n = 21$)	Group II ($n = 44$[a])	p
Acute cholecystitis findings (n, %)			0.02
Slight/moderate	8 (53.3)	21 (91.3)	
Severe	7 (46.7)	2 (8.7)	
Chronic cholecystitis findings (n, %)			1.00
Slight/moderate	5 (83.3)	15 (71.4)	
Severe	1 (16.1)	6 (28.6)	

[a] Pathological slides of two patients in group II were not available and not reviewed

significantly ($p = 0.02$) higher in group I (46.7%) than in group II (8.7%) (Table 3).

Comparisons of surgical results after PTGBD

Perioperative complications developed in four patients (19.0%) in group I and in two patients (4.3%) in group II, a marginal significant difference ($p = 0.07$). One patient in both groups developed postoperative abdominal fluid collection that subsided spontaneously under conservative treatment. One patient in group I developed significant postoperative bleeding requiring reoperation. No patient in group I, but three patients (6.5%) in group II were converted to OC because of dissection difficulty at Calot's triangle or due to colon injury because of dense adhesions, but this did not represent a significant intergroup difference ($p = 0.55$). However, mean operative time was significantly ($p = 0.02$) greater in group I (79.3 ± 25.3 vs. 53.7 ± 45.3 min). No significant difference between groups was found for surgery conducted by surgeons in terms of mean operative times or open conversion rate ($p = 0.71$ and $p = 1.00$, respectively).

Total hospital cost was similar in the two groups (group I, US$5,660 ± 2,130 vs. group II, US$6,870 ± 7,760, $p = 0.50$), but mean overall hospital stay was significantly ($p = 0.08$) shorter in group I (10.8 ± 4.5 days) than in group II (14.7 ± 9.3 days). No postoperative mortality occurred in either group (Table 4).

Table 4 Comparison of surgical results after PTGBD

	Group I ($n = 21$)	Group II ($n = 46$)	p
Perioperative complication (n, %)	4 (19.0)	2 (4.3)	0.07
Severe bleeding	1	0	
Bile duct injury	0	0	
Intra-abdominal fluid collection	1	1	
Postoperative ileus	1	0	
Bowel injury	1	1	
Open conversions (n, %)	0	3 (6.5)	0.55
Pathology (acute:chronic)	1:0.4	1:6.6	<0.01
Operative time (min)	79.3 ± 25.3	53.7 ± 45.3	0.02
Total hospital costs (US$[a])	5,660 ± 2,130	6,870 ± 7,760	0.50
Patients' share costs (US$[a])	3,038 ± 2.073	3,844 ± 4,661	0.46
Hospital stay (days)			
Overall	10.8 ± 4.5	14.7 ± 9.3	0.08
Postoperative	5.0 ± 3.7	4.1 ± 6.7	0.66

[a] US dollars

Discussion

AC is a common disease caused by obstruction of the cystic duct with or without gallstones, and carries risks of complications, such as empyema, gangrene, perforation, pericholecystitis with abscess formation, peritonitis, and sepsis. Furthermore, because the incidence of GB disease increases with age, elderly patients with AC and a severe systemic comorbidity are over represented. Moreover, if AC develops in a patient with a preexisting comorbidity, it could lead to more profound illness [14]. As a result, AC in the elderly is clinically important, and the mortality rate of emergency cholecystectomy in critically ill patients is particularly high [5].

PC used to involve external biliary drainage under local anesthesia. The rationale for PC is based on the principle that drainage via catheter cholecystostomy palliates AC by permitting acute decompression of the biliary system [15]. Due to the popularization of ultrasonography, PC has become a standard interventional procedure [16]. PC can be performed in two ways, that is, via PTGBD or via a transperitoneal approach. In the majority of reports, a transhepatic approach through the bare area of the GB was used to prevent catheter dislodgement and bile leakage [17, 18], despite the potential risks of pneumothorax, intrahepatic bleeding, or hemobiliary fistula [15]; thus, a transhepatic approach was also utilized in the present series. As mentioned above, that approach minimizes the risk of intraperitoneal bile leakage and inadvertent injury to the hepatic flexure of the colon.

The safety of the transhepatic approach and its minimal invasiveness make it a valid treatment option for patients with AC who do not respond to conservative treatment [19–21]. Furthermore, PC is an effective tool with a high success rate and low morbidity, allows for better preoperative evaluation of the biliary system, and facilitates safe subsequent laparoscopic surgery [10], all because it avoids septic complications resulting from severe biliary inflammation or infection and the morbidities associated with surgery and anesthesia in patients with underlying medical comorbidities such as diabetes, cardiovascular disease, renal failure, and pulmonary insufficiency [19]. In the present study, three patients (4.5%) experienced a PTGBD-related complication. However, those complications were limited to catheter dislodgement. No severe problem, such as bile leakage, subhepatic hematoma, or bowel injury, was encountered (Table 2).

Indications for PTGBD differ somewhat among studies, but commonly include a poor surgical risk due to the presence of comorbidity and a disease duration of more than 72 h, the latter of which is likely to be associated with severe inflammation and dense adhesions, and thus, elevated risks of conversion and complications of cholecystectomy [10, 22]. The recently issued 'Tokyo guideline' cites moderate (grade II) or severe (grade III) AC as indications. We adopted those criteria but added 'a lack of response to medical treatment for AC' [10, 11].

At the beginning of the LC era, acute inflammation of the GB was considered a contraindication for laparoscopic resection [10]. However, with experience, laparoscopic surgery has been extended to the treatment of patients with AC as its operation times, hospital stays, and complication rates are either superior or similar to those of OC [23, 24]. Accordingly, nowadays, the principal management tenet in AC is early cholecystectomy, because initial conservative treatment has been reported to be unsuccessful in up to 32% of cases and because early cholecystectomy has been shown to reduce total durations in the hospital [25–27].

Although emergency cholecystectomy is the standard treatment for AC, conservative treatment is still an acceptable option when conversion and complication rates are relatively high [9, 10]. Furthermore, as age increases, comorbidity incidence also increases, which further complicates the management of these patients. Routine LC in the emergency setting can be a challenging task, especially in public hospitals lacking specialist service [10, 28]. In addition, because severe (grade III) AC is associated with organ dysfunction, urgent or early drainage is preferred to urgent or early cholecystectomy in such cases. Similarly, because moderate (grade II) AC is associated with technical difficulty during cholecystectomy because of local inflammation, urgent or early drainage is preferred to early cholecystectomy in affected patients [11]. As shown in recent study, over 90% of patients experienced rapid relief of the clinical symptoms of AC within 24–48 h of PTGBD [17, 18, 29]. Similarly, most of our patients recovered after PTGBD, and in these patients, acute illness resolved at 3.2 ± 1.6 and 3.0 ± 2.1 days after PTGBD in the groups I and II, respectively.

LC is still considered a challenging procedure for AC because of the high incidences of common bile duct injuries caused by difficulties associated with anatomic delineation [30, 31]. Reported complication rates in cases of severe cholecystitis, including severe complications such as bile duct injury or bleeding, lie between 0 and 40% [4, 32, 33].

The open conversion rate of LC for AC has been reported to range from 11 to 28%, which is significantly higher than the less than 5% rate reported for CC [23, 24, 31, 34]. Conversion means that the advantages of this minimally invasive procedure are lost, and that the costs and risks of complications are increased [24, 34]. In the present study, open conversion rates were relatively low, and no intergroup difference was detected (group I 0% vs. group II 6.5%, $p = 0.55$) (Table 4), which we attribute to experienced biliary surgeons performing the surgery.

Several papers have discussed the technical difficulty of LC as compared to conversion to OC based on obesity indices, ultrasonographic findings, surgical findings, and resected GB inflammation [13, 35, 36]. In the present study, no intergroup differences were found in terms of BMIs, radiological findings of cholecystitis, or surgeon-associated factors. However, based on histology, severe inflammation in AC was greater in group I than in group II, which hints that an early operation is likely to be the more challenging because of the prolonged operative time (Table 4).

Some authors have suggested that an early scheduled LC after PTGBD is a safe and effective therapeutic option for patients with acute complicated cholecystitis, especially elderly patients and patients with poor general condition [9]. However, another study found that delayed LC after PTGBD reduced conversion and complication rates in patients with complicated AC [3]. In the present study, the group I patients had a shorter mean hospital stay and tended to have lower hospital costs than group II patients. However, group II patients had a lower complication rate and a shorter operative time than group I patients (Table 4). These results suggest that the early and late LC options have distinct advantages and disadvantages, and that overall neither operation timing is superior. However, the present study, as a retrospective study, has a limitation related to the presence of selection bias. Therefore, future prospective randomized studies are needed.

Conclusion

PTGBD resolved acute GB inflammation and enabled definitive surgery to be delayed in patients with severe cholecystitis or those at high risk, regardless of the discomfort caused by catheter drainage and the risks of procedure-related complications. Furthermore, subsequent LC was performed safely in these patients, but early or delayed cholecystectomy after PTGBD was found to have specific strengths and weaknesses. Accordingly, we suggest that decisions on cholecystectomy timing be made after considering patient condition, the hospital facilities available, and surgeons' experience.

Conflict of interest The authors of the manuscript have no conflicts of interest or financial ties to disclose.

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