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ORIGINAL ARTICLE

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급성담낭염으로 경피적 담낭배액술을 시행한 환자에서 담낭절제술 시행의 적절한 시기

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Timing of Cholecystectomy after Percutaneous Cholecystostomy for Acute Cholecystitis

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Background/Aims: Laparoscopic cholecystectomy is the standard treatment for acute cholecystitis. Percutaneous cholecystostomy is an alternative treatment to resolve acute inflammation in patients with severe comorbidities. The purpose of this study is to determine the optimal timing of laparoscopic cholecystectomy after percutaneous cholecystostomy for the patients with acute cholecystitis.
Methods: This retrospective study was conducted in patients who underwent cholecystectomy after percutaneous cholecystostomy from January 2010 through November 2014. Seventy-four patients were included in this study. The patients were divided into two groups by the operation timing. Group I patients underwent cholecystectomy within 10 days after percutaneous cholecystostomy (n=30) and group II patients underwent cholecystectomy at more than 10 days after percutaneous cholecystostomy (n=44).
Results: There was no significant difference between groups in conversion rate to open surgery, operation time, perioperative complications rate, and days of hospital stay after operation. However, complications related to cholecystostomy such as catheter dislodgement occurred significantly more often in group II than group I (group I:group II=0%:18.2%; p=0.013).
Conclusions: Timing of laparoscopic cholecystectomy after percutaneous cholecystostomy did not influence postoperative outcomes. However, late surgery caused more complications related to cholecystostomy than early surgery. Therefore, early laparoscopic cholecystectomy should be considered over late surgery after percutaneous cholecystostomy insertion. **(Korean J Gastroenterol 2015;66:209-214)**

Key Words: Acute cholecystitis; Laparoscopic cholecystectomy; Cholecystostomy

INTRODUCTION

Acute cholecystitis (AC) is one of the most commonly encountered diseases in surgical practice and cholecystectomy is the standard treatment for AC. Laparoscopic cholecystectomy (LC) was first performed in 1987 by Mouret.[1] In the early days of laparoscopic surgery, LC was contraindicated for AC due to the difficulty of the surgical technique and frequent complications. However, postoperative outcomes have improved through accumulated experience in laparoscopic surgery and improvements in laparoscopic instruments. A meta-analysis of 10 prospective randomized trials concluded that patients who had emergency LC had a shorter hospital stay and similar frequency of complications com-

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pared to those who underwent open cholecystectomy (OC).[2] LC is currently accepted as a gold standard treatment for AC and is regarded as a safe and effective treatment option.[3,4]

Although LC is performed routinely as an emergent treatment option of AC, postoperative complications are still of major concern. Morbidity rates after LC in elderly patients with high surgical risk are reported to be between 14% and 46%.[5]

Percutaneous cholecystostomy (PC) using ultrasonography guidance was first described by Radder[6] in early 1980s. PC is a minimally invasive technique that can be performed safely under local anesthesia. Therefore, it is an alternative treatment for AC in elderly patients with high surgical risk[7,8] and considered a bridging procedure for surgical treatment.[9,10] However, optimal timing of LC after PC remains unclear. Updated Tokyo Guidelines for the Management of Acute Cholangitis and Cholecystitis (TG13) recommends delayed cholecystectomy at three months after PC insertion for the patients with severe grade cholecystitis.[11] Conversely, several studies reported early cholecystectomy after PC insertion was also safe and had some advantages in comparison with later operation.[12,13] Therefore, in this study, our interest is the optimal timing of LC after PC through the analysis of differences in complication rates and rate of conversion to OC according to timing of LC after PC.

SUBJECTS AND METHODS

1. Patients

This retrospective study was conducted in patients who were diagnosed and treated with AC at Wonkwang University Hospital (Iksan, Korea) between January 2010 and November 2014. Five hundred eighteen patients underwent surgery for AC during study period, and among these patients, 74 patients who underwent cholecystectomy after PC insertion were enrolled in this study. These patients were divided into the following two groups by operation timing. Group I patients underwent cholecystectomy within 10 days after PC insertion (n=30) and group II patients underwent cholecystectomy at more than 10 days after PC insertion (n=44). Age, sex, white blood cell (WBC) counts on admission, presence of gallbladder stone, American Society of Anesthesiologist (ASA) score, and severity grade of cholecystitis were reviewed. The severity grade of cholecystitis was based on TG13.[14] Mild grade was defined as AC in a healthy patient with no organ dysfunction and mild inflammatory changes in the gallbladder, making cholecystectomy a safe and low-risk operative procedure. Moderate grade was defined as AC associated with any one of the following conditions: elevated WBC count ($>18{,}000/mm^3$), palpable tender mass in the right upper abdominal quadrant, duration of complaints >72 hours, marked local inflammation. Severe grade was AC associated with dysfunction of any one of the following organs or systems: cardiovascular, neurological, respiratory, renal, hepatic, hematological dysfunction. This study was approved by the institutional review board of Wonkwang University Hospital (WKUH 201510-HRE-095).

2. Treatment protocol

The diagnosis of AC was based on a combination of clinical findings, laboratory data, and radiologic findings, including ultrasonography or CT. Patients who had no contraindications to emergent surgery underwent LC immediately. If the patients were taking anticoagulants (e.g., aspirin, warfarin) that might cause bleeding during surgery or were at high surgical risk due to co-morbid conditions, the PC was inserted instead of urgent cholecystectomy. Patients over 70 years old underwent PC insertion before surgery to evaluate occult comorbidities that are frequent in the elderly. After PC insertion, the patients were started on fluid resuscitation, analgesics, and intravenous antibiotics. During conservative management, we performed multidisciplinary pre-operative tests such as echocardiography and pulmonary function test for perioperative risk evaluation. If the patient's condition was stabilized and perioperative risk evaluation and management were completed, LC was performed. In patients who needed a long period of conservative management and perioperative risk evaluation, the treatment and work-up period before surgery was usually over 10 days after PC insertion. Therefore we compared postoperative results by dividing the patients into early and late operation group on the basis of the 10th day after PC insertion.

3. Percutaneous cholecystostomy

PC was performed by interventional radiologists under ultrasound guidance. A trans-hepatic approach was performed for all included patients because of the relatively low risk of bile leakage. Bile samples were obtained and sent for gram staining and culture study.

4. Surgical technique

LC was performed by two experienced hepatobiliary surgeons using a three-trocar technique. The 12-mm laparoscope port was inserted in the infraumbilical region, and carbon dioxide gas injected into the intraperitoneal cavity to maintain an intra-abdominal pressure of 10-12 mmHg. Another two trocars (5 mm) were inserted in the epigastric area and the right subcostal area.

5. Statistical analysis

Statistical analysis was performed using PASW Statistics software ver. 18.0 (IBM Co., Armonk, NY, USA). χ^2 and Fisher's exact tests were employed for categorical parameters, and independent t-test for continuous parameters. Null hypotheses of no difference were rejected if p-values were less than 0.05.

RESULTS

1. Clinical characteristics

There was no significant difference in clinical characteristics between groups including preoperative ASA score (Table 1). Most of the patients had comorbid conditions, with hypertension the most common comorbidity. There was no significant difference in comorbid conditions and anticoagulant use between groups (Table 1).

2. Complications associated with percutaneous cholecystostomy insertion

Median time to cholecystectomy after PC insertion was 6 days (range, 2-10 days) in group I and 23 days (range, 11-38 days) in group II. Significantly more complications associated with PC insertion occurred in group II (18.2%) than in group I (0%) (p=0.013; Table 2). Catheter related complications developed in eight patients in the delayed group at median 17.5 days (range, 13-27 days) after PC insertion. The most com-

Table 1. Clinical Characteristics

Characteristic	Group I (n=30)	Group II (n=44)	p-value
Age (yr)	67.9±16.4	69.17±11.4	0.703
Sex (male:female)	17:13	27:17	0.686
WBC count on admission (/mm^3)	14,696±5,207	14,090±465	0.670
Gallbladder stone	27 (90.0)	37 (84.1)	0.465
ASA score			0.825
I	3 (10.0)	5 (11.4)	
II	15 (50.0)	23 (52.3)	
III	12 (40.0)	15 (34.1)	
IV	0 (0)	1 (2.3)	
Comorbid disease			0.482
None	5 (16.7)	4 (9.1)	
Hypertension	18 (60.0)	23 (52.3)	
Diabetes mellitus	10 (33.3)	8 (18.2)	
Congestive heart failure	1 (3.3)	2 (4.5)	
Ischemic heart disease	3 (10.0)	6 (13.6)	
Malignant disease	4 (13.3)	4 (9.1)	
Liver cirrhosis	1 (3.3)	0 (0)	
Others	7 (23.3)	9 (20.5)	
Taking anticoagulants	22 (73.3)	28 (63.6)	0.454
Severity criteria[a]			0.949
Mild	18 (60.0)	27 (61.4)	
Moderate	11 (36.7)	15 (34.1)	
Severe	1 (3.3)	2 (4.5)	

Values are presented as mean±SD or n (%).
Group I, patients underwent cholecystectomy within 10 days after percutaneous cholecystostomy insertion; group II, patients underwent cholecystectomy at more than 10 days after percutaneous cholecystostomy insertion.
WBC, white blood cell; ASA, American Society of Anesthesiologist.
[a]Updated Tokyo Guidelines for the Management of Acute Cholangitis and Cholecystitis (TG13) severity grading for acute cholecystitis.

mon catheter-related complication was catheter dislodgement (11.4%) and four of five patients with catheter dislodgement developed symptoms such as fever and abdominal pain. All patients with catheter dislodgement underwent tube cholangiography or computed tomography for evaluation, and the PC was re-inserted. Bleeding and bile leakage also occurred by accidental retraction of tube at 15 days and 20 days after PC insertion.

3. Postoperative outcomes

We compared surgical time, days of hospital stay after cholecystectomy, conversion rate to open surgery, and postoperative complications between two groups. The mean surgical time was 102.6±49.0 min in group I and 94.9±39.9 min in group II, and the mean hospital stay duration after cholecystectomy was 7.4±5.3 days in group I and 7.6±6.8 days in group II, not significantly different (Table 3). The conversion rate to OC was not significantly different between groups, 33.3% (10/30) in group I and 25.0% (11/44) in group II. The reasons for conversion to open surgery are described in Table 3. Difficulty in dissecting the Calot's triangle because of severe inflammation was the most common reason for conversion to open surgery. Postoperative complications occurred in two patients (6.7%) of group I and in six patients (13.6%) of group II, but the difference was not statistically significant (Table 3). Fluid collection around the surgical site was the most frequent complication (3/8). There were two cases of operation site bleeding and one case each of bile duct injury, postoperative embolism, and pseudomembranous colitis.

Table 2. Complications Associated with Percutaneous Cholecystostomy

Group I (n=30)	Group II (n=44)	p-value
0 (0%)	8 (18.2%) Tube obstruction, 1 Bleeding, 1 Bile leakage, 1 Tube dislodgement, 5	0.013

Group I, patients underwent cholecystectomy within 10 days after percutaneous cholecystostomy insertion; group II, patients underwent cholecystectomy at more than 10 days after percutaneous cholecystostomy insertion.

DISCUSSION

Tokyo Guidelines for the Management of Acute Cholangitis and Cholecystitis (TG07) published in January 2007 are widely used as international guidelines[15] and TG07 has been updated and published to TG13. According to TG13, early LC within 72 hours since the onset of symptoms is preferable to delayed cholecystectomy.[16] Early LC could solve the problem immediately, result in a shorter hospital stay and earlier return to daily activities.[17] However, although LC is widely performed as a safe emergency procedure for AC, several studies find that elderly patients undergoing emergency LC have high mortality and morbidity rates.[5,18] The incidence of gallstone disease increases with age,[19] and comorbid diseases are frequent in elderly patients. Therefore, LC is a challenging procedure for AC in elderly patients, especially those with comorbid diseases and high surgical risks.

In TG13, optimal treatment for AC was categorized according to the severity grade of cholecystitis.[16] Early LC was pre-

Table 3. Postoperative Outcomes

	Group I (n=30)	Group II (n=44)	p-value
Operation time (min)	102.6±49.0	94.9±39.9	0.459
Hospital stay after operation (day)	7.4±5.3	7.6±6.8	0.910
Open conversion	10 (33.3)	11 (25.0)	0.435
Severe inflammation	8	10	
Severe bleeding	3	2	
Bile duct injury	1	0	
Postoperative complications[a]	2 (6.7)	6 (13.6)	0.343
Grade I	1	0	
Grade II	0	2	
Grade III	1	4	

Values are presented as mean±SD or n (%).
Group I, patients underwent cholecystectomy within 10 days after percutaneous cholecystostomy insertion; group II, patients underwent cholecystectomy at more than 10 days after percutaneous cholecystostomy insertion.
[a]Clavien-Dindo classification of surgical complications.

ferred for patients with mild cholecystitis (grade I). Early LC was recommended for patients with moderate cholecystitis (grade II) in experienced centers or if patients had severe local inflammation, early gallbladder drainage (percutaneous or surgical), because early cholecystectomy might be difficult and incurs a high risk of bile duct injury. Medical treatment with gallbladder drainage and delayed cholecystectomy were recommended. For patients with severe cholecystitis (grade III), urgent management of organ dysfunction and management of severe local inflammation by gallbladder drainage should be carried out. Delayed elective cholecystectomy should be performed when cholecystectomy was indicated.

PC using ultrasonographic guidance was first described by Radder[6] in the early 1980s. PC could be performed under local anesthesia, resolving acute inflammation through a minimally invasive procedure. Scheduled elective LC after PC insertion could provide more time to accurately assess the patient's comorbidity and to improve the patient's general condition. For these reasons, PC is thought a useful treatment method for AC, especially in elderly patients with high surgical risk. However, disagreement still exists regarding the optimal timing for LC after PC.

Cholecystectomy is often performed following PC after intervals of several days,[12,20] although performing a cholecystectomy over two weeks later is also common.[21] In general, early LC following PC is preferred when the patient's condition improves and the patient is confirmed to have no comorbid disease with high surgical risk. In TG13 management bundles for AC,[11] for patients with severe cholecystitis (grade III) with jaundice and poor general conditions, emergent gallbladder drainage with supportive care including antibiotics are considered initial therapy. For patients found to have gallbladder stones during biliary drainage, cholecystectomy is performed after three months, after the patients' general condition improved. However, because of lack of strong evidence, the optimal time for LC following PC insertion remains controversial.

Several studies compare postoperative outcome between early and late LC following PC insertion. Chikamori et al.[12] suggested that early scheduled LC following PC was a safe and effective treatment option for patients with AC. In their study, open conversion rate and surgery time was lower in patients who underwent early LC after PC (within seven days) than later. Conversely, Kim et al.[21] reported that delayed LC after PC (over 14 days) tended to decrease the rate of conversion to open laparotomy, with similar postoperative complication rate. Han et al.[13] reported that the complication rate was lower and surgical time was shorter in late LC group (over three days) but hospital stay duration was longer with a similar open conversion rate. They concluded that decisions on timing of LC following PC should be made based on considerations of patient condition, hospital facilities and surgical experience.

In this study, we inserted PC in the patients who were taking anticoagulant drugs or those who had high surgical risk due to comorbid conditions. After PC insertion, we determined the surgery timing after considering the half-life of the drugs and time necessary for evaluating surgical risks. Hence, we compared the results by dividing the patients into two groups on the basis of the 10th day, the minimal time for improving patient condition and evaluating surgical risk. There was no difference between groups in comorbid conditions that could affect surgical outcome. In this study, we compared the surgery time, hospital stay after cholecystectomy, conversion rate to open surgery, and perioperative complications between early and delayed groups to compare post-surgical outcome. There was no significant difference. However, catheter-related complications were significantly more frequent in the delayed group (18.2%) than in the early group (0%) (p=0.013). In the delayed group, median time to surgery after PC was 23 days. Maintaining a catheter over 20 days caused inconvenience in daily life, and catheter management was difficult for the patients, especially for the elderly. Catheter-related complications mainly occurred more than 10 days after PC insertion, causing patient complaints, longer hospital stay and higher cost. We suggest that early LC within 10 days after PC insertion is preferable if the patient condition improved and preoperative evaluation and management were completed.

However, there are several limitations to this study. This study was a retrospective study and included a small number of patients. Further reliable studies such as randomized controlled trials or large cohort will be needed.

In conclusion, the timing of LC after PC did not influence postoperative outcomes, but late LC could cause more catheter-related complications, resulting in longer hospital stay and costs. Therefore, early LC following PC insertion should be considered with priority over late LC.

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