

Impact of Percutaneous Transhepatic Gallbladder Drainage on The outcome of Laparoscopic Cholecystectomy

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CONCLUSIONS: Preoperative PTGBD is correlated with an extended hospital stay after surgery and is an independent short-term prognostic factor in cholecystitis patients aged ≥ 65 years old.

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Key Words: Cholecystitis; Hospital Stay; Laparoscopic Cholecystectomy; Percutaneous Transhepatic Gallbladder Drainage (PTGBD)

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ABSTRACT

AIM: The recommended treatment for acute cholecystitis is early laparoscopic cholecystectomy (LC) within 72 hours after onset of symptoms. However, palliative treatment using percutaneous transhepatic gallbladder drainage (PTGBD) is often chosen for clinical and logistical reasons, including difficulty performing early surgery due to manpower constraints. The goal of this study was to investigate the clinical significance of PTGBD on the outcome of patients with cholecystitis in our hospital.

MATERIALS AND METHODS: Relationships between preoperative drainage status (treatment with or without PTGBD) and clinicopathologic factors were examined in 190 patients with cholecystitis who underwent LC. The short-term impact of preoperative drainage on prognosis was evaluated by univariate and multivariate analysis.

RESULTS: Preoperative PTGBD was performed in 24 patients (12.6%). The average period between PTGBD and LC was 21.0 days. Preoperative PTGBD had a significant correlation with operation time and length of stay (LOS) after surgery ($p < 0.0001$). In patients aged ≥ 65 , preoperative PTGBD was found to be a significant short-term prognostic factor in univariate analysis (LOS: 10.43 vs. 5.39 days, $p < 0.0001$) and multivariate analysis ($p = 0.0488$).

INTRODUCTION

The recommended treatment for acute cholecystitis is early laparoscopic cholecystectomy (LC) within 72 hours after onset of symptoms. However, conservative treatment using percutaneous transhepatic gallbladder drainage (PTGBD) is often chosen for clinical reasons or due to difficulty arranging an early operation because of manpower constraints. Previous studies have advocated early surgery for patients with cholecystitis because of the poor course after delayed surgery. However, an early operation may also be a contributory factor in conversion to laparotomy, and it is important that an appropriate quality of laparoscopic surgery is maintained^[1,2].

This study was designed to investigate the short-term prognostic significance of PTGBD in patients with cholecystitis who underwent LC in our hospital. Relationships between the preoperative drainage status and other clinicopathologic factors were also evaluated.

Table 1 Clinicopathologic data for patients in the PTGBD and control groups.

Item	PTGBD	Control	p-value
Number	24(12.6%)	166(77.4%)	---
Drainageoperation (days)	21.0±10.6	---	---
Sex	male 10, female 14	male 73, female 93	0.831
Age	73.0±2.9	62.0±1.1	< .0001 [†]
BMI	22.3 ± 0.8	23.2 ± 0.3	0.312
Comorbidity of diabetes	8 (33.3%)	23 (13.9%)	0.034 ^{a*}
Laparotomy history	9 (37.5%)	41(24.7%)	0.219 ^a
Preoperative WBC	10557 ± 658	11461± 250	0.2006
Preoperative CRP	3.24 ± 1.0	2.47 ± 0.4	0.464
Operation Time (min.)	176.6±12.2	119.9±4.6	< .0001 [†]
Blood loss (g)	74.0±13.8	27.0±5.2	0.0017 [†]
Conversion	2(8.3%)	3(1.8%)	0.121 ^a
Complication	5(20.8%)	8(4.8%)	< .01 ^{a*}
Operation to discharge (days)	9.67±0.8	5.22±0.31	< .0001 [†]

[†]Fisher test, * significant

PATIENTS AND METHODS

A total of 224 patients with cholecystitis underwent cholecystectomy at NaraCityHospital from April 2012 to October 2014. Cholecystitis was defined as a case with imaging findings on CT or US of gallbladder wall thickening or biliary sludge or abnormal findings in surrounding tissues, and any one of (i) right hypochondrium, epigastric pain/tenderness, or presence of a Murphy sign, (ii) body temperature $\geq 37^{\circ}\text{C}$, or (iii) leukocytosis and elevated CRP. Clinicopathologic findings were obtained retrospectively from hospital records. Thirteen patients diagnosed with gallbladder cancer or gallbladder polyp and 21 who underwent surgery while still asymptomatic were excluded from the study.

Of the remaining 190 patients, 24 first received PTGBD as conservative treatment and then underwent LC after reduction of inflammation. The other 166 patients underwent LC without PTGBD and were used as a control group. Relationships between drainage status (that is, use of PTGBD) and other clinicopathologic factors were examined, and the prognostic impact of PTGBD was evaluated by univariate and multivariate analysis. Length of stay (LOS) after surgery was used as an index of short-term prognosis. The 190 patients were also divided into subgroups according to age to investigate the relationship between clinicopathologic factors and short-term prognosis of patients aged ≥ 65 years old.

Statistical analysis and graphing were performed with JMP 7.0.1 (SAS Institute Inc., Tokyo). Continuous data are expressed as the median or mean, depending on the data distributions. A chi-square test and t-test (or Fisher test) were used for univariate comparisons. Differences in LOS were compared by a Wilcoxon test, using the date of LC as the starting point. Multivariate analysis of prognostic factors related to LOS was performed using a Cox proportional hazard model with variables that were significant prognostic factors in univariate Wilcoxon analysis. $P < 0.05$ was considered to indicate significance in all analyses.

RESULTS

PTGBD was performed for 24 patients (12.6%) with cholecystitis as conservative treatment to control inflammation before LC. The mean period from PTGBD to surgery was 21.0 days. The clinicopathologic features in the PTGBD and control groups are listed in Table 1. There were significant differences in age, diabetes as a comorbidity, operation time, blood loss, complications and LOS after surgery ($p < 0.05$), but not in the rate of conversion to laparotomy or degree of inflammation.

Five of the 24 patients who underwent PTGBD developed

complications, but no cases had organ or space surgical site infection (SSI). The complications were intraoperative bile duct injury in 1 patient, postoperative bile spillage in 1 patient, and incisional SSI in 3 patients. The rate of incisional SSI was significantly higher in the PTGBD group (12.5% vs. 1.8%, $p = 0.015$) (Figure 1).

In the investigation of relationships between clinicopathologic factors and PTGBD status in the subgroup aged ≥ 65 years old, age was found to be an insignificant factor. In multivariate analysis in all patients, age was the only significant short-term prognostic factor (data not shown). In an analysis of patients aged ≥ 65 years old, preoperative PTGBD was a significant short-term prognostic factor in univariate analysis (LOS: 10.43 vs. 5.39 days, $p < 0.0001$), in addition to age, operation time, blood loss, and rate of conversion to laparotomy. Preoperative PTGBD and age remained as independent prognostic factors in multivariate analysis (Table 2).

DISCUSSION

Appropriate treatment of cholecystitis depends on the degree of local inflammation and damage to surrounding organs. Patients who do not receive definitive treatment with cholecystectomy during initial hospitalization have gallstone- or surgery-related 90-day and 1-year readmission rates of 29% and 35%, respectively^[3]. The 2013 Guidelines for Acute Cholangitis/Cholecystitis (ver. 2)^[4] recommend early cholecystectomy in initial hospitalization as therapy for acute cholecystitis, depending on the severity. LC is the suggested procedure in cases of mild severity, while the procedural choice is indicated to depend on the ability of the endoscopic surgical team in cases of moderate severity.

At our hospital, early surgery is not always possible because of a shortage of surgeons and equipment. In such cases, conservative treatment with PTGBD is performed first and surgery is delayed until improvement of inflammation. This approach is supported by studies showing that early surgery may be a contributory factor for conversion to laparotomy; therefore, preoperative PTGBD reduces inflammation and the risk of conversion to laparotomy^[1,2]. This background prompted us to investigate the impact of PTGBD on the outcome of LC for patients with cholecystitis in our hospital.

The indication for gallbladder drainage is moderate or severe cholecystitis, based on the severity criteria in the guidelines. Gallbladder drainage is a common and useful treatment in cases for which early surgery cannot be performed due to a high surgical risk, manpower and equipment constraints, or a patient declining surgery. A high surgical risk may be present in a case of severe cholecystitis, in which the top priority is to improve organ damage, but gallbladder drainage is also required as causal treatment. In such cases, an early

Table 2 Univariate and multivariate analyses of short-term prognostic factors in patients aged ≥ 65 years old.

	Number	Univariate analysis ^κ		Multivariate analysis [#]
		From Operation to Discharge (days)	p-value	p-value
Age (y.o.)	≥ 70 73	6.96	<.0001*	0.0135*
	<70 27	5.07		
Sex	Male 43	6.42	0.223	---
	Female 57	6.47		
Comorbidity; diabetes	Absent 77	6.68	0.894	---
	Present 22	5.82		
BMI	≥ 22 49	5.88	0.16	---
	<22 51	7.00		
Laparotomy History	Absent 75	6.27	0.578	---
	Present 24	7.17		
Pre-operative WBC ($\times 10^2/\mu\text{L}$)	≥ 100 73	6.14	0.833	---
	<100 27	6.88		
Pre-operative CRP	≥ 2.0 30	6.60	0.058	---
	<2.0 70	6.39		
Pre-treatment	None 48	5.29	0.058	---
	Done 52	7.52		
Drainage	None 79	5.39	0.0001*	0.0488*
	Done 21	10.43		
Operation time (min)	≥ 110 55	7.56	0.0034*	0.3159
	<110 45	5.09		
Blood loss (g)	≥ 30 28	9.20	<.0001*	0.5156
	<30 72	5.42		
Laparoscopic procedure	Complete 96	6.01	0.01*	0.1435
	Convert 4	17.00		

^κ Wilcoxon test; [#] Cox proportional hazard model; * significant.

operation may not be warranted and precedence must be given to reduction of jaundice or treatment of comorbidities. In our study, we found more diabetes cases in the PTGBD group than in the control group in an analysis of clinicopathologic features. This tendency may be related to the PTGBD cases being compromised hosts, but may also be because diabetic patients had to control their blood sugar before surgery. Koo *et al*^[5] suggested that the timing of surgery can be based on pathological findings: if the ambient gallbladder is edematous within 72 hours from onset, the gallbladder will be surgically separable from surrounding tissue; whereas if this situation is not present until more than 72 hours after onset, surgery may be difficult and drainage is a suitable option. Regarding manpower, early surgery depends on the availability of surgeons as a team, an accurate diagnosis from a primary-care clinician, and the availability of an anesthetist.

A survey by the Japan Society for Endoscopic Surgery (JSES)^[6] showed an increasing trend in facilities choosing early LC, with 35% of respondents choosing early surgery for all cases and 54% for some cases (Figure 2). However, LC can be difficult to complete because of the hardness, swelling and tendency to bleed of the gallbladder wall^[7]. Early LC in Japan has rates of conversion to laparotomy of 0-21.4% and complication rates of 8.4-10.3%, which are similar to those in elective surgery, but the average LOS of 4.4-8.9 days after early LC is significantly shorter than that after elective surgery^[8-16]. Similarly, in the current study, the rates of conversion to laparotomy after early LC were almost equivalent to those in patients who first underwent PTGBD. However, the preoperative PTGBD group had a higher risk for complications and a longer stay after surgery.

Biliary tract infection develops frequently after preoperative biliary tract drainage for obstruction of the biliary tree by cancer^[17,18], and biliary infection increases the frequency of SSI^[19]. In our study, there was a significantly higher rate of incisional SSI in the PTGBD group, but no significant differences for organ/space SSI, intraoperative biliary injury, and postoperative bile spillage. However, preoperative PTGBD was found to be a significant short-term prognostic factor. We do not postpone discharge of patients based on incisional SSI, and thus we are unable to determine if the presence of this complication

contributed to the elongation of the stay after surgery.

Drainage before surgery was also performed by ENBD/ENGBD or ERBD, but only PTGBD was a significant short-term prognostic factor in multivariate analysis. This may be because PTGBD is the only percutaneous method, with resident flora on the skin always being a risk for bacterial infection in percutaneous methods; or because PTGBD is the only method that affects the liver. Regardless, it seems that PTGBD is associated with prolongation of postoperative inflammatory reactions. However, the average period of 21.0 days between LC and PTGBD in this study seems to be appropriate based on previous studies. Thus, Kim *et al*^[20] found significantly reduced rates of conversion to laparotomy and complications after LC performed an average of 19.9 days after PTGBD; and Katagiri *et al*^[1] reported a 0% rate of conversion to laparotomy in LC performed 3 weeks after PTGBD in cases in which LC was not the first treatment choice for acute cholecystitis.

In conclusion, preoperative PTGBD was found to correlate with extension of hospital stay after LC and to be an independent short-term prognostic factor in cholecystitis in patients aged 65 or over.

CONFLICT OF INTEREST

None of the authors have a conflict of interest with regard to the work in the manuscript.

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