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Original Article

Is it safe to give laparoscopic cholecystectomy (LC) treatment of acute cholecystitis in senile patients 3 months after percutaneous transhepatic gallbladder drainage (PTGD)? A case-control study

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Abstract: Background: PTGD combined with delay LC has been widely applied to elderly patients. Nevertheless, there are only few data available on delay LC after PTGD. We present a case-control study to evaluate the safety and efficacy of delay LC after PTGD 3 months later for acute cholecystitis. Methods: Data of elderly patients underwent LC for cholecystitis were prospectively collected in our hospital. From July 2014 to January 2016, 36 patients who underwent PTGD combined delay LC (group I) were compared with a prospective cohort of 50 patients who underwent emergency LC (group II) during the same period. The general condition, operative time, rate of common bile duct injury, intraoperative blood loss, rate of conversion to open surgery, postoperative anal exhaust time, postoperative hospital stay, and postoperative complications of patients were compared in the two groups. Results: The operative time of group I was significantly longer than that of group II (78.61 ± 23.87 min vs 67.70 ± 18.63 min P = 0.021), the conversion rate of group I was significantly higher than that of group II (P = 0.033). Intraoperative bleeding of the patients in group I was significantly higher than that in group II (P = 0.029). And the postoperative anal exhaust time and postoperative hospital stay of group I were significantly shorter than those of group II (14.02 ± 4.36 hours vs 16.44 ± 4.78 hours, P = 0.020; 4.83 ± 3.07 days vs 6.12 ± 2.56 days, P = 0.039). The postoperative complication rate of group I was significantly lower than that of group II (3 cases vs 14 cases, P = 0.024). Conclusion: Our study suggests delay LC after PTGD (3 months later) reduced postoperative hospital stay and the occurrence of postoperative complications, but increased the difficulties of operation.

Keywords: Percutaneous transhepatic gallbladder drainage, elder, laparoscopic cholecystectomy

Introduction

Laparoscopic cholecystectomy (LC) has been the golden standard of therapy for cholecystitis with cystic calculus because of its minimally invasive characteristic [1-4]. Meanwhile, with the intensifying of an aging society, incidence of acute cholecystitis increases progressively. At present, cholecystitis with cystic calculus accounts for a large proportion of elderly patients with acute cholecystitis (AC) [5, 6]. Elderly patients often have cardiopulmonary insufficiency, hypertension and diabetes, and therefore, they have high operative risks and suffer longer operation time, with a higher conversion rate and easier occurrence of complications in the perioperative period [7-10].

PTGD has been widely applied to elderly patients since its high safety and validity that have been well documented. For example, PTGD has been demonstrated to be able to reduce the complications in the perioperative period and shorten the length of hospital stay [11-15]. However, there are only few studies on the time of delay LC after PTGD. Some studies have shown the benefit of early intervention, while others showed delayed surgery could reduce the conversion rate and postoperative hospital stay [12, 16-22]. When is the best timing for LC after PTGD? Does longer waiting time of LC after PTGD mean more beneficial for patents' recovery and higher operation safety? The purpose of this study was to compare surgical outputs of the elderly treated with LC (within 72

hours of admission to hospital) vs delay LC after PTGD (3 months later).

Methods

General information

This study was approved by the Ethical Committee of Wenzhou Central Hospital, The Dingli Clinical Institute of Wenzhou Medical University and informed consent has been signed. Elderly patients who underwent surgery were identified from a prospectively maintained database in Wenzhou Central Hospital. The whole study was performed based on the guidelines and principles of the Declaration of Helsinki [23]. From July 2014 to Jan 2016, a total of 683 patients were admitted to our department because of their clinical radiographic, and laboratory findings of calculous cholecystitis. AC was diagnosed by the clinical criteria including local (Murphy sign or right upper quadrant pain) and systemic signs of inflammation (fever, elevated C-reactive protein, or elevated leukocytes count) in addition to image findings. LC was performed on 86 elderly patients (all ≥ 65 years old) with AC. PTGD and delay LC treatment was defined as the presence of either one of these conditions: 1) patients refused emergency surgery; 2) patients with severe acute left heart failure (ALHF); 3) patients with acute respiratory failure;4) patients with history ofstroke; and 5) patients with hypoproteinemia. A total of 36 patients were operated through the LC (3 months following PTGD, Group I). Meanwhile, a prospective cohort of 50 patients underwent emergency LC (Group II). The interventions were provided by the same group of surgeons (an experienced medical team with more than 10 years of clinical and surgical experience). The group I contained 16 males and 20 females, with a mean age of 73.80 ± 5.80 years. The group II contained 27 males and 23 females, with a mean age of 73.06 ± 5.09 years. The diagnostic criteria were based on the revised Tokyo guidelines 2012 [24].

Inclusion Criteria: (1) patients ≥ 65 years old; (2) patients with previous history of cholecystitis; (3) B-mode ultrasound and CT findings of AC; (4) patients with cholecystitis and gall stone.

Exclusion criteria: (1) patients with blood coagulation dysfunction; (2) patients with cirrhosis; (3) Image findings suggested common bile duct expansion, and common bile duct calculi cannot be completely ruled out; (4) patients with hypohepatia, ALT ≥ 50; (5) patients with general peritonitis and suspected perforation of gallbladder; (6) patients who chose open cholecystectomy; (7) patients with a history of upper abdominal surgery.

On admission, the onset period in patients ranged from 1 d to 5 d. All the patients had upper abdominal pain or right upper abdominal pain. Among the total 86 patients in this study, 63 cases had fever, 51 cases had shoulder and back radiating pain and all patients exhibited right upper abdominal tenderness by physical examination. A total of 52 cases showed positive Murphy's sign. Gallbladder swelling and wall thickening were found using abdominal CT scan.

PTGD and delay LC treatment

PTGD was performed by interventional ultrasound physicians under ultrasound guidance. Under 2% lidocaine local anesthesia, a puncture needle (Angiotech Company, Denmark) was advanced insert into the gallbladder. After dilating the track, a 6Fr~12Fr drainage catheter (One step Drainage Catheter Set With Safety string Lock, BIOTEQUE Company, Taiwan) was positioned with its tip into the gallbladder, then pull out the guide wire and fixed the drainage tube. Clinical improvement after PTGBD was defined as meeting all three criteria: (1) Symptom relief; (2) body temperature < 37.5°C during 48 h period; (3) resolution of leukocytosis [25]. After achieving symptomatic relief, the patient was discharged from the hospital with drainage tube. Patients were given LC after 3 months after PTGD. Delay LC was performed using a 4 ports method. The decisions to convert to open cholecystectomy and use abdominal drains were made according to the clinical factors including poor control of intraoperative bleeding, the difficulty of dissection, and adhesions of the Calot triangle.

Emergency LC

After being admitted to the hospital, the patient underwent emergency LC. It was started with 4 trocars insertion. When complete dissection was not possible to achieve, open cholecystectomy was done. Drainage tube was placed in

Table 1. The baseline characteristics of the patients in Group I and Group II

Variables	Delay LC (n = 36)	Emergency LC (n = 50)	T value/χ^2 value	*P* value
AGE (year)	73.80 ± 5.80	73.06 ± 5.09	0.624[a]	0.379
Body mass index	25.58 ± 3.64	26.80 ± 3.42	1.578[a]	0.650
Gender (M/F)	16/20	27/23	0.764[b]	0.382
Time of onset (d)	2.64 ± 1.03	2.22 ± 1.04	1.822[a]	0.970
Leukocytes counts (× 10^9/L)	15.41 ± 3.43	14.36 ± 3.61	1.341[a]	0.790
CRP(mg/L)	81.06 ± 42.15	92.72 ± 47.7	1.160[a]	0.458
Temperature ≥ 38°C	13/23	24/26	1.207[b]	0.272
CT gallbladder wall thickness ≥ 4 mm	13/23	12/38	1.489[b]	0.222
Hypertension	23/13	28/22	2.132[b]	0.463
Diabetes	11/25	14/36	0.066[b]	0.797
Atrial fibrillation	8/28	12/38	0.037[b]	0.847
COPD	11/25	12/38	0.459[b]	0.498

Note: a, the t value of a group t test; b, the statistical values of a chi-square test. CRP, C-reactive protein; CT, computerized tomography; COPD, Chronic obstructive pulmonary disease.

Table 2. Results of operation in the two groups

Variables	Delay LC (n = 36)	Emergency LC (n = 50)	T value/χ^2 value	*p* value
Operative time (min)	78.61 ± 23.87	67.70 ± 18.63	2.351[a]	0.021
Common bile duct injury	1/35	0/50	1.405[b]	0.236
Conversion to open surgery	5/31	1/49	4.558[b]	0.033
Intraoperative bleeding ≥ 50 ml	15/21	10/40	4.765[b]	0.029
Postoperative anal exhaust time (h)	14.02 ± 4.36	16.44 ± 4.78	2.367[a]	0.020
Postoperative hospital stay (d)	4.83 ± 3.07	6.12 ± 2.56	2.090[a]	0.039
Postoperative Complications	3/33	14/36	5.104[b]	0.024
Bile leakage	0/36	1/49	0.728[b]	0.393
Pneumonia	1/35	6/44	2.381[b]	0.123
Intraperitoneal hemorrhage	1/35	0/50	1.405[b]	0.236
Respiratory failure	0/36	4/46	3.020[b]	0.082
Heart failure	1/35	2/48	0.093[b]	0.761
Stroke	0/36	1/49	0.728[b]	0.393

Note: a, the t value of a group t test; b, the statistical values of a chi-square test.

the gallbladder bed after surgery in every patients. When there was no liquid outflow, tube was removed.

Outcomes

We compared the general condition, operative time, rate of common bile duct injury, intraoperative blood loss, rate of conversion to open surgery, postoperative anal exhaust time, postoperative hospital stay, and postoperative complications of patients in 2 groups.

Statistical analysis

All data were analyzed using the professional statistics software SPSS 17.0 (SPSS Inc., Chicago, IL, USA). Continuous data were expressed as mean ± standard deviation (SD) and further analyzed by *t* test or Mann-Whiney *U* test. Categorical data in the study were tested using χ^2 test. The values of $P < 0.05$ were considered statistically significant in our study.

Results

General conditions of patients

The basic characteristics of the patients are shown in **Table 1**. The differences in age, gender, BMI, time of onset, leukocyte counts, CRP, body temperature (°C), and CT gallbladder wall thickness were not statistically significant between the group I and group II (all $P > 0.05$).

This difference in patients with internal diseases between the two groups was not statistically significant. PTGD was technically successful in all patients; PTGBD-related adverse events did not occur.

Comparison of surgery results for delay LC (group I) and emergency LC (group II)

Comparison of surgery results are shown in **Table 2**. The operative time of group I was significantly longer than that of group II (78.61 ± 23.87 min vs 67.70 ± 18.63 min P = 0.021). Bile duct injury during LC did not occur in group I, but occurred in 1 patients in group II without significant difference (P = 0.236). The conversion rate of group I was significantly higher than that of group II (P = 0.033). Intraoperative bleeding of the patients in group I was significantly more than that in group II (P = 0.029). And the postoperative anal exhaust time and postoperative hospital stay of group I were significantly shorter than those of group II (14.02 ± 4.36 hours vs 16.44 ± 4.78 hours, P = 0.020; 4.83 ± 3.07 days vs 6.12 ± 2.56 days, P = 0.039). There were no deaths reported in the two groups.

Comparison of postoperative complications for delay LC (group I) and emergency LC (group II)

There was one case of pneumonia, one case of intraperitoneal hemorrhage and one case of heart failure in group I, the rate of postoperative complications was 8.33%. There were six cases of pneumonia, one case of bile leakage, four cases of respiratory failure, two cases of heart failure and one case of stroke in group II, the rate of postoperative complications was 28.00%. The postoperative complication rate of group I was significantly lower than that of group II.

Discussion

Some studies have pointed out that delayed LC after PTGD has lower difficulty compared with emergency LC, with obviously shortened time of operation and less bleeding [10, 26]. According to our data, delayed LC after PTGD was more difficult to perform than emergency LC. It had significantly longer operation time, more bleeding and more conversion rate than emergency LC. This may be related to the following situations: in delayed LC, we found that atrophic changes usually occurred in gall bladder and there was evident synechia of calot's triangle and tissues, which increased difficulties for dissection. Due to continuous stimulus of PTGD tube on gall bladder, inflammation was not absorbed obviously 3 months after PTGD, and subacute changes occurred, leading to a relatively difficulty in resecting the gall bladder. In our study groups, five patients were given conversion operation because of difficult dissection and an unclear anatomy of Calot triangle. On the contrary, most patients of the emergency LC group were in the "golden 72 h" and most tissues were in edema, which offered a clear view of dissection, resulting in a high success rate of operations [13, 27]. Only one patient received conversion operation.

In our study, the delay LC group had shorter postoperative anal exhaust time, fewer days of postoperative hospital stay and fewer postoperative complications than the emergency LC group, which may be related to physiological conditions of patients and poor preparation of emergency LC group. Elderly patients often have some internal diseases, such as diabetes, hypertension, COPD, and heart disease. If the blood glucose and the blood pressure in an elderly patient cannot be controlled well before the operation, the conditions of the patient, including the blood glucose and blood pressure might be worse due to the operational stress and the inflammatory reactions. These critical pathological changes might even lead to serious postoperative complications, such as infections in respiratory system and cardiopulmonary dysfunction [28]. Delayed LC, or known as LC at selective periods, has adequate time for preparation and assessment before the operation, thus having far fewer complications after the operation compared with the emergency LC group. Therefore, the emergency LC group shall pay attention to pulmonary infection, cardiac failure and other postoperative complications. Controlling liquid infusion speed and total liquid amount as well as real-time monitoring of cardio-pulmonary functions maybe important. Data of the emergency LC group showed that it had 6 cases of pulmonary infection, 2 cases of ARDS and 2 cases of 1-type respiratory failure, to which much attention needs to be paid. Airway management in the perioperative period and activities in early period after the operation may be beneficial for reducing pulmonary infection.

It is still controversial on the time of delay of LC after PTGD. Some researchers have suggested that at least four weeks after PTGD are required to perform LC to ensure the safety [29]. Our research demonstrated that delayed LC performed 3 months after PTGD contributed significantly longer operation time and higher conversion rate than the emergency LC group. This was exactly the opposite of our expectation. Taken together, delayed LC performed 3 months after PTGD is more difficult and close attention needs to be paid to the operation safety. Of course, these clinical discoveries still need further verifications based on randomized controlled trials.

Finally, this study has several limitations. First, it was a case-control study, which was performed based on the guidelines of the Declaration of Helsinki. Patients were provided with detailed information about the opinion of emergency LC and PTGD + delay LC. Possible complications were also explained; some patients insisted on emergency LC and others preferred to have PTGD + delay LC. Under these circumstances, the patient preference was followed. Furthermore, collecting a good quality of data needs a large randomized controlled trial. Second, owing to ethical considerations, we did not compare delay LC (3 months after PTGD) with open cholecystectomy.

Conclusions

Nowadays, PTGD combined with LC has become the therapy of choice for the elderly with acute cholecystitis. Although PTGD is easy-to-operate, safe and delay LC could reduce the occurrence of postoperative pneumonia and heart cerebrovascular accident, LC 3 months after PTGD will increase operation difficulties and conversion to laparotomy, and surgeons should pay attention to operation safety.

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Disclosure of conflict of interest

None.

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