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Editorial Board Member of World Journal of Gastrointestinal Surgery, Andrea Cavallaro, MD, PhD, Doctor, Research Assistant Professor, Researcher, Department of Surgery and Medical Surgical Specialties, University of Catania, Catania 95123, Italy. and reacavallaro@tiscali.it

# **AIMS AND SCOPE**

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WJGS mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal surgery and covering a wide range of topics including biliary tract surgical procedures, biliopancreatic diversion, colectomy, esophagectomy, esophagostomy, pancreas transplantation, and pancreatectomy, etc.

# **INDEXING/ABSTRACTING**

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ORIGINAL ARTICLE

# **Retrospective Study** Effect of surgical timing on postoperative outcomes in patients with acute cholecystitis after delayed percutaneous transhepatic gallbladder drainage

# Wei Gao, Jun Zheng, Ji-Gang Bai, Zhao Han

| <b>Specialty type:</b> Gastroenterology and hepatology                     | Wei Gao, Department of Hepatobiliary Surgery, Hanzhong Central Hospital, Hanzhong 723000, Shaanxi Province, China                              |
|--|--|
| <b>Provenance and peer review:</b><br>Unsolicited article; Externally peer | <b>Jun Zheng</b> , Department of Hepatobiliary Surgery, The First Affiliated Hospital of Chongqing Medical University, Chongqing 400000, China |
| reviewed.  | Ji-Gang Bai, Department of Hepatobiliary Surgery. The First Affiliated Hospital of Xi'an   |
| Peer-review model: Single blind  | Jiaotong University, Xi'an 710061, Shaanxi Province, China   |
| Peer-review report's classification  | Zhao Han, Department of General Surgery, No. 215 Hospital of Shaanxi Nuclear Industry,   |
| Scientific Quality: Grade C, Grade   | Xianyang 712000, Shaanxi Province, China   |
| C, Grade D   | Corresponding author: Zhao Han, MD, Professor, Department of General Surgery, No. 215  |
| Novelty: Grade B, Grade B, Grade   | Hospital of Shaanxi Nuclear Industry, No. 35 Weiyang West Road, Qindu District, Xianyang   |
| D  | 712000, Shaanxi Province, China. hanzhao_004@163.com   |
| Creativity or Innovation: Grade B,   |  |
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| Scientific Significance: Grade B,  | Abstract   |
| Grade B, Grade C   | BACKGROUND   |
| <b>P-Reviewer:</b> Cai Q; Park YS;   | To date, the optimal timing for percutaneous transhepatic gallbladder drainage   |
| Shiryajev YN   | (PTGBD), particularly for patients who have missed the optimal window for  |
| Received: Intry 10, 2024   | onset) has not been determined.  |
| <b>Revised:</b> August 27, 2024  |  |
| Accented: September 9, 2024  | AIM  |
| Published online: November 27  | To study the effects of LC timing on outcomes of grade II/III acute cholecystitis  |
| 2024   | (AC) in patients with delayed PIGBD.   |
| <b>Processing time:</b> 112 Days and 3.3                                   | METHODS  |
| Hours  | Data of patients diagnosed with Tokyo Guidelines 2018 grade II or III AC who   |
|  | underwent delayed PTGBD followed by LC at a single hospital between 2018 and   |
|  | 2022 were retrospectively studied. According to the interval between gallbladder   |
|  | drainage and cholecystectomy, the patients were divided into early and delayed   |
|  | LC groups. Outcomes including surgery time, postoperative complications and  |

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two groups using *t*- and  $\chi^2$  tests.

hospital stay, and patient satisfaction were analyzed and compared between the

Gao W et al. Influence of GBD surgery on the timing of surgery

#### RESULTS

There were no significant differences between the two groups in intraoperative blood loss, postoperative abdominal drainage tube placement time, pain index, or total disease duration (all P > 0.05). Compared with those of the early LC group, the delayed group showed significant decreases in the length of procedure (surgery time), conversion rate to open surgery, degree of adhesions, surgical complications, postoperative hospital stay, and total treatment costs, and increased patient satisfaction despite a longer interval before PTGBD (all P < 0.05).

#### CONCLUSION

For patients with grade II/III AC with delayed PTGBD, LC should be performed 2 weeks after PTGBD to decrease postoperative complications and hospital stays and improve patient satisfaction.

Key Words: Acute cholecystitis; Percutaneous transhepatic gallbladder drainage; Laparoscopic cholecystectomy; Surgical timing; Postoperative outcomes

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Core Tip: Previous studies have proposed that percutaneous transhepatic gallbladder drainage (PTGBD) should be performed as early as possible in patients with moderate-to-severe acute cholecystitis (AC). However, to date, no consensus has been reached on the optimal timing for PTGBD, particularly for patients who have missed the 72-hour emergency laparoscopic cholecystectomy (LC) window. This study assessed the effects of different operation times on postoperative outcomes of patients with grade II or III AC with delayed PTGBD (time from symptom onset to PTGBD exceeding 7 days). Our results suggest that LC should be performed 2 weeks after PTGBD.

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# INTRODUCTION

Acute cholecystitis (AC) is a common acute abdominal disease in the field of general surgery. It is usually caused by inflammation of the gallbladder wall caused by the stimulation or entrapment of gallstones in the gallbladder duct or bacterial infection. AC occurs rapidly and is associated with severe symptoms. If left untreated, complications such as gallbladder necrosis, gallbladder perforation, and sepsis may occur; in severe cases, AC can be life-threatening[1-3]. According to the Tokyo Guidelines 2018 (TG18), emergency laparoscopic cholecystectomy (LC) is an important early treatment option for AC[4]. However, for patients with moderate-to-severe AC, because of the increased difficulty of surgery and postoperative complications, and the fact that such patients often are of advanced age, have underlying diseases, and are in poor general condition, conservative treatment can be administered first. Treatment may include the administration of antibiotics or percutaneous transhepatic gallbladder drainage (PTGBD) to control infection before patients undergo elective surgery[5-7].

Although studies show that PTGBD should be performed as early as possible in patients with moderate-to-severe AC [8-11], there is no consensus on the optimal timing for PTGBD. In clinical practice, patients, particularly those referred from grassroots hospitals, will commonly seek medical attention after undergoing conservative drug treatment for more than 1 week with poor efficacy. These patients miss the optimal 72-hour emergency LC window and the possibility of undergoing early PTGBD. To date, few studies have considered the effect of delayed PTGBD on subsequent LC procedures.

Therefore, the present study investigated the effects of different operation times on the postoperative outcomes of patients with grade II or III AC with delayed PTGBD (time from symptom onset to PTGBD exceeding 7 days).

## MATERIALS AND METHODS

#### Ethical approval

This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of No. 215 Hospital of Shaanxi Nuclear Industry (No: 2024-011).

#### Patient selection

This retrospective study was conducted between January 2018 and December 2022. The data of all patients diagnosed with TG18 grade II or III[12] AC who underwent delayed PTGBD followed by LC at the No. 215 Hospital of Shaanxi



Nuclear Industry, were assessed.

The exclusion criteria were as follows: (1) History of upper abdominal surgery; (2) Obstructive jaundice caused by malignant diseases; (3) Pregnancy or lactation; (4) Undergoing medication treatment, such as oral anti-tuberculosis and anti-tumor drugs; and (5) Incomplete clinical data.

Finally, 68 patients were included and divided into two groups: (1) Early LC group (n = 32), for patients in whom the interval between PTGBD and LC was less than 2 weeks; and (2) Delayed LC group (n = 36), for patients in whom the interval between PTGBD and LC exceeded 2 weeks.

#### PTGBD technique

Preoperatively, patients were prohibited from eating and drinking for 12 hours and administered anti-infection, antispasmodic, and analgesic medications. Moreover, any internal environment disorders were correctified and appropriate strategies were used to manage blood pressure and blood glucose levels.

PTGBD at our hospital is performed using the Seldinger puncture technique under ultrasonographic guidance. The technique is performed as follows. (1) The patient is placed in a supine position with no pillow, and ultrasonography is conducted on the gallbladder area. The puncture point is determined between the 7th and 8th ribs on the right side; (2) The puncture area is routinely disinfected and draped, and local infiltration anesthesia is administered using lidocaine (2%); (3) A 3.0-4.0 mm incision is made at the puncture point. Under ultrasonographic guidance, a puncture needle is inserted to enter the gallbladder through the middle and upper one-third of the gallbladder bed; (4) The outflow of bile is observed, followed by insertion of the guide wire along the puncture needle which is subsequently retrieved; (5) The skin expander is used to expand the skin and intercostal muscles, and a 12-French pigtail drainage tube is inserted along the guide wire; (6) The guide wire is removed and ultrasound is conducted to confirm that the tail of the drainage tube is located inside the gallbladder; (7) The drainage tube is secured in place using silk thread; the area is then wrapped in sterile patches, and the tube is connected to a sterile drainage bag; and (8) Postoperatively, bile is extracted for bacterial culture and drug sensitivity testing. Patients are monitored for abdominal changes/symptoms, bile drainage volume and color, and to ensure that the drainage tube remains unobstructed and well secured.

Secondary surveys of the gallbladder using ultrasound or computed tomography are performed in cases in which postoperative abdominal pain, high fever, and a continuous increase in white blood cell count exceed 24 hours.

## LC technique

All patients undergo a comprehensive preoperative examination to rule out surgical contraindications. The preoperative measures are the same as that for PTGBD. All patients undergo tracheal intubation under general anesthesia. The threehole method is used for LC, and the specific steps are as follows. (1) The area is prepared with conventional disinfection and placement of sterile drapes; (2) A small incision is made at the navel followed by a 1-cm incision to separate the tissue; (3) A puncture needle is inserted to establish a carboxy peritoneum with a pressure of 12 mmHg, and a laparoscope is inserted; (4) Laparoscopic exploration of the abdominal cavity is conducted focusing on the gallbladder triangle, gallbladder, and liver adhesions; (5) Subsequently, under laparoscopic guidance, a 10-mm diameter trocar is inserted into the main operating hole (hole B), 1 cm below the xiphoid process, and a 5-mm diameter trocar is inserted into the auxiliary operating hole (hole C) 3-5 cm below the junction of the midline of the right clavicle and rib arch; (6) The gallbladder triangle is fully exposed, and non-absorbable ligation clamps are used to close and cut the cystic artery and duct. The gallbladder is peeled from its bed, excised, and a drainage tube is placed in the gallbladder bed; (7) The abdominal carbon dioxide is released, and the incision is sutured. When dense adhesions around the neck of the gallbladder cause difficulty in dissecting the gallbladder triangle or when intraoperative damage to blood vessels leads to uncontrollable bleeding, timely conversion to open surgery is performed; and (8) Postoperative treatment includes routine fluid replacement and antibacterial therapy. The time to removal of the drainage tube is determined based on the amount and color of the drainage and bedside ultrasound results.

#### **Outcome measures**

The surgical time, intraoperative blood loss, degree of adhesion, conversion to open surgery rate, abdominal drainage tube placement time, pain index, postoperative complications, postoperative hospital stay, total disease duration, total treatment cost, and patient satisfaction were compared between the two patient groups.

## Quality control

PTGBD and LC were performed by senior surgeons with comparable operational experience who are ranked as deputy chief physicians or above. The determination of the degree of gallbladder adhesion during LC is subjective; there is currently no quantitative evaluation method to measure adhesion. To minimize the subjective impact for this study, we referred to "tight adhesion between the gallbladder triangle and surrounding tissues" as documented in surgical records as 'severe adhesion' and referred to other amounts as 'mild adhesion'.

#### Statistical analysis

Statistical analyses were conducted using SPSS software (version 22.0; SPSS, Inc., Chicago, IL, United States). LC operative time, intraoperative blood loss, number of complications, and other measurement data are expressed as means  $\pm$  SD and were analyzed using a twotail paired Student's *t*-test. The conversion rate to open surgery, degree of adhesions, and other count data are expressed as *n* (%) and were analyzed using the  $\chi^2$  test. Statistical significance was set at *P* < 0.05.

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# RESULTS

#### **Baseline characteristics**

There were no significant differences in demographics or preoperative clinical features between the two groups (all P > 0.05; Table 1).

#### Indications and complications of PTGBD

PTGBD tubes were successfully placed under ultrasound guidance in all 68 patients, with a puncture success rate of 100% (Figure 1). Among them, 49 patients experienced significant relief from abdominal pain 3-6 hours after the procedure, while the remaining 19 patients experienced partial relief.

There was no significant difference between the early and delayed LC groups in PTGBD indications such as septic shock and gallbladder perforation (all P > 0.05; Table 2). There was no significant difference between the two groups in PTGBD-related complications such as catheter detachment and bile leakage (all P > 0.05; Table 3). One patient in the early LC group presented with minor bleeding complications (50 mL), which were controlled with coagulation drugs and intravenous infusion. No PTGBD-related deaths occurred in either group.

#### Postoperative outcomes

There were no significant differences between the early and delayed LC groups in intraoperative blood loss, postoperative abdominal drainage tube placement time, pain index, or total disease duration (all P > 0.05). Compared with the early LC group, the delayed LC group showed a significant decrease in LC operative time, conversion rate to open surgery, degree of adhesions, surgical complications, postoperative hospital stay, and total treatment costs, and increased patient satisfaction despite a longer PTGBD tube placement time (all P < 0.05) (Table 4).

# DISCUSSION

LC is the current standard surgical method for AC[13-15]. Compared with open cholecystectomy, LC has no significant differences in surgical time and mortality rate; however, the recovery time of patients after LC is significantly reduced[16-19]. Regarding the timing of LC, studies have shown that compared with delayed LC, early LC (performed within 72 hours after admission) has a significantly lower mortality rate and incidence of complications such as bile leakage and wound infections[20]. The 2018 Tokyo Guidelines recommend that LC be performed within 72 h of symptom onset[4].

However, with the aging of the population and increasing prevalence of chronic diseases such as diabetes, coronary heart disease, chronic heart failure, and chronic obstructive pulmonary disease, some patients with these comorbidities and high-risk factors cannot tolerate emergency LC. Affected patients have a mortality rate of up to 35%[21] and a relatively high incidence of postoperative complications such as biliary tract injury and biliary fistula[22-25]. PTGBD technology was developed to alleviate general systemic symptoms and reduce complications[26-28]. Clinical studies have shown that PTGBD can improve symptoms safely during the critical period. After the general condition of the patient improves, surgery can be performed to remove the gallbladder. At this point, the surgical risk is significantly reduced [29]. In the present study, the collected data were from patients with TG18 grade II or III AC unable to undergo emergency LC owing to high-risk factors who underwent PTGBD, with a time interval between symptom onset and PTGBD exceeding 7 days. After the patients' general conditions improved, LC was performed.

Currently, there is no consensus on the optimal timing of LC after PTGBD, and there are few reports on the impact of the timing of PTGBD on subsequent LC outcomes. Previous studies have shown that compared with delayed surgery, early surgery (PTGBD to LC two interval < 72 hours) may lead to increased intraoperative blood loss, prolonged surgical time, and increased complications[30,31]. Inoue *et al*[32] showed that compared with patients with a PTGBD to LC interval of  $\geq$  9 days, patients with an interval of < 9 days had a significant increase in complications (35.7 *vs* 7.6%; *P* = 0.006). Jung and Park[33] conducted a comparative study with groups based on PTGBD to LC intervals of < 10 days or  $\geq$  10 days and obtained similar results. Altieri *et al*[34] compared the effectiveness of cholecystectomy with PTGBD to LC surgery intervals of < 8 weeks and  $\geq$  8 weeks and found that patients in the early group had more complications and longer hospital stays.

However, not all studies have shown that a longer interval between PTGBD and LC leads to better outcomes. Sakamoto *et al*[35] divided patients into groups based on the interval between PTGBD and LC procedures and analyzed the results using restricted cubic spline curves. They found that compared with patients with a 10-day interval, patients with a PTGBD to LC interval of  $\leq$  6 days or  $\geq$  27 days had a higher mortality rate and incidence of complications. Compared with patients with a 15-day interval, patients with a PTGBD to LC interval of  $\leq$  10 days or  $\geq$  19 days had longer hospital stays.

Based on previous studies and in particular Sakamoto *et al*'s mathematical model[35], we adopted 14 days as the cutoff point for the PTGBD to LC interval and divided patients into an early LC group (< 14 days) and a delayed LC group ( $\geq$  14 days). There were no significant differences in the indications for or complications of PTGBD catheterization between the two groups. Consistent with previous results, our research indicated that compared with patients in the early LC group, patients in the delayed LC group showed a significant decrease in LC operative time, conversion rate to open surgery, degree of adhesions, surgical complications, postoperative hospital stay, and total treatment costs, and higher patient satisfaction despite a longer PTGBD tube placement time (all P < 0.05).

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| Table 1 Baseline characteristics of the two groups before percutaneous transhepatic gallbladder drainage, mean ± SD |                                 |                                   |         |
|---|---------------------------------|-----------------------------------|---------|
| Variables   | Early LC group ( <i>n</i> = 32) | Delayed LC group ( <i>n</i> = 36) | P value |
| Sex (male/female)   | 18/14                           | 20/16                             | 0.954   |
| Age (years)   | $65.4 \pm 15.2$                 | $62.1 \pm 17.3$                   | 0.823   |
| BMI (kg/m <sup>2</sup> )  | $25.26 \pm 4.28$                | 24.36 ± 3.19                      | 0.428   |
| Etiology (with/without stone)   | 30/2                            | 35/1                              | 0.486   |
| Grade of AC (II/III)  | 14/18                           | 23/13                             | 0.096   |
| CCI (< 4/≥ 4)   | 15/17                           | 14/22                             | 0.506   |
| ASA-PS class (< 3/≥ 3)  | 12/20                           | 16/20                             | 0.561   |
| Time from symptom onset to PTGBD (days)   | $8.9 \pm 1.1$                   | 9.2 ± 1.3                         | 0.748   |

PTGBD: Percutaneous transhepatic gallbladder drainage; LC: Laparoscopic cholecystectomy; BMI: Body Mass Index; CCI: Charlson Comorbidity Index; ASA-PS: American Society of Anesthesiologists Physical Status.

| Table 2 Indications for percutaneous transhepatic gallbladder drainage catheterization in the patient groups, n (%) |                |                  |                |
|---|----------------|------------------|----------------|
| Indications   | Early LC group | Delayed LC group | <i>P</i> value |
| Septic shock  | 14 (43.8)      | 12 (33)          | 0.378          |
| Gallbladder perforation   | 10 (31.3)      | 11 (30.6)        | 0.951          |
| Progressive abdominal pain  | 5 (15.6)       | 8 (22.2)         | 0.490          |
| Persistent high fever   | 2 (6.3)        | 3 (8.3)          | 0.743          |
| Sepsis  | 1 (3.1)        | 2 (5.6)          | 0.626          |
| Cardiovascular dysfunction  | 5 (15.6)       | 7 (19.4)         | 0.680          |
| Neurological dysfunction  | 0 (0)          | 1 (2.7)          | 0.342          |
| Respiratory dysfunction   | 6 (18.8)       | 11 (30.6)        | 0.262          |
| Liver or kidney dysfunction   | 8 (25)         | 5 (13.0)         | 0.245          |
| Coagulation disorders   | 1 (3.1)        | 0 (0)            | 0.285          |
|   |                |                  |                |

LC: Laparoscopic cholecystectomy.

| Table 3 Percutaneous transhepatic gallbladder drainage catheterization complications in the patient groups, <i>n</i> (%) |                |                  |                |
|--|----------------|------------------|----------------|
| Complications  | Early LC group | Delayed LC group | <i>P</i> value |
| Catheter detachment  | 2 (6.3)        | 1 (2.8)          | 0.486          |
| Bile leakage   | 2 (6.3)        | 2 (5.6)          | 0.903          |
| Biliary peritonitis  | 1 (3.1)        | 1 (2.8)          | 0.933          |
| Infection  | 0 (0.0)        | 1 (2.8)          | 0.342          |
| Hemorrhage   | 1 (3.1)        | 0 (0.0)          | 0.285          |

LC: Laparoscopic cholecystectomy.

We believe that the difference in postoperative outcomes between the two groups was a result of the different timing of the LC. The time between the onset of cholecystitis symptoms and LC was longer in the delayed LC group than the early LC group  $(31.2 \pm 6.7 vs 23.0 \pm 5.2 days)$ . After the pressure inside the gallbladder has been reduced, the infected bile has been drained, and medicinal treatment has been administered, the gallbladder enters a phase of inflammation resolution, and the degree of adhesion is reduced. Therefore, the difficulty of surgery is reduced, and as seen by findings of the present study, this resulted in the operating time, conversion rate to open surgery, and incidence of surgical complications being lower in the delayed LC group than those in the early LC group. In addition, owing to the shortened

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| Table 4 Surgical outcomes between the two groups of patients after PTGBD, mean ± SD |                                 |                                   |         |
|---|---------------------------------|-----------------------------------|---------|
| Outcome measures  | Early LC group ( <i>n</i> = 32) | Delayed LC group ( <i>n</i> = 36) | P value |
| LC surgery time (minute)  | 108.3 ± 14.2                    | 90.2 ± 12.2                       | < 0.001 |
| Intraoperative blood loss (mL)  | 15.4 ± 5.1                      | $16.0 \pm 4.3$                    | 0.474   |
| Operation (LC/ laparotomy)  | 21/11                           | 32/4                              | 0.021   |
| Degree of adhesions (mild/severe)   | 20/12                           | 33/3                              | 0.004   |
| Number of complications   | 9                               | 2                                 | 0.012   |
| Surgical site infection   | 3                               | 1                                 | 0.248   |
| Bile leakage  | 2                               | 1                                 | 0.486   |
| Hemorrhage  | 2                               | 0                                 | 0.128   |
| Pulmonary infection   | 1                               | 0                                 | 0.285   |
| Hyperamylasemia   | 1                               | 0                                 | 0.285   |
| Abdominal drainage tube placement time (day)  | $1.9 \pm 0.7$                   | $2.0 \pm 0.7$                     | 0.378   |
| Postoperative hospital stay   | $9.1 \pm 4.1$                   | $3.0 \pm 0.9$                     | < 0.001 |
| PTGBD drainage tube placement time (day)  | $10.8 \pm 1.6$                  | $19.8\pm4.0$                      | < 0.001 |
| Pain index (0-10)   | 3.3 ± 1.3                       | 3.7±1.1                           | 0.083   |
| Patient satisfaction (%)  | $80.5 \pm 11.5$                 | 85.3 ± 9.8                        | 0.028   |
| Total disease duration (day)  | 32.1 ± 5.3                      | 33.2 ± 5.1                        | 0.125   |
| Total treatment costs (Yuan)  | 23570.9 ± 4996.1                | 21144.7 ± 2065.5                  | 0.002   |

PTGBD: Percutaneous transhepatic gallbladder drainage; LC: Laparoscopic cholecystectomy.



Figure 1 Computed tomography of patients with acute cholecystitis after percutaneous transhepatic gallbladder drainage catheterization. The arrow shows the drainage tube inside the gallbladder.

postoperative hospitalization time, the total treatment cost of patients with delayed LC decreased and patient satisfaction improved.

If the interval between PTGBD and LC is too short, the Calot's triangle of the gallbladder will have increased inflammatory edema, and the boundary with the surrounding common bile duct, duodenum, and greater omentum will be blurred, easily leading to procedure-related injuries to the biliary and/or intestinal tract. However, if the interval is too long, stimulation of the drainage tube on the gallbladder mucosa and the persistent presence of stones can induce chronic inflammation, forming tough, dense adhesions with the surrounding tissues. Simultaneously, gallbladder atrophy can significantly increase the difficulty of secondary surgery.

This study had some potential limitations. First, the sample size was relatively small. Second, this was a single-center study; therefore, the results may have been affected by local conditions. More large-scale multicenter studies are required to confirm these findings.

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# CONCLUSION

In conclusion, we suggest that for patients with grade II or III AC and delayed PTGBD (time from symptom onset to PTGBD exceeding 7 days), LC should be performed 2 weeks after PTGBD. At this time, the difficulty of surgery decreased, the incidence of postoperative complications was low, and the patients' postoperative hospitalization time and total treatment cost were significantly reduced.

# FOOTNOTES

Author contributions: Gao W and Han Z contributed to the study conception and design; Gao W, Zheng J and Bai JG performed material preparation, data collection and analysis, and wrote the first draft of the manuscript; Han Z reviewed and revised the manuscript; all authors read and approved the final manuscript.

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Country of origin: China

ORCID number: Wei Gao 0009-0009-1670-6044; Zhao Han 0009-0007-3193-9984.

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