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Comparison of laparoscopic cholecystectomy and delayed laparoscopic cholecystectomy in aged acute calculous cholecystitis: a cohort study

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Abstract

Background In elderly patients with calculous acute cholecystitis, the risk of emergency surgery is high, and percutaneous cholecystostomy tube drainage (PC) combined with delayed laparoscopic cholecystectomy (DLC) may be a good choice. We retrospectively compared laparoscopic cholecystectomy (LC) to DLC after PC to determine which is the better treatment strategy.

Method We performed a retrospective cohort analysis of 752 patients with acute calculous cholecystitis. Patients with the following conditions were included: (1) age > 65 years old; (2) patients with a grade 2 or 3 severity of cholecystitis according to the 2013 Tokyo Guidelines (TG13); (3) the surgeons who performed the LC were professors or associate professors and (4) the DLC was performed in our hospital after PC. Patients who missed their 30-day follow-up; were diagnosed with bile duct stones, cholangitis or gallstone pancreatitis or were pregnant were excluded from the study. A total of 51 of 314 patients who underwent LC and 73 of 438 patients who underwent PC + DLC were assessed. PC + DLC and LC patients were matched by cholecystitis severity grade according to the TG13, and the National Surgical Quality Improvement Program (NSQIP) calculator was used to predict mortality ($n = 21$/group). Preoperative characteristics and postoperative outcomes were analysed.

Results Compared to the matched LC group, the DLC group had less intraoperative bleeding (42.2 vs 75.3 mL, $p = 0.014$), shorter hospital stays (4.9 vs 7.4 days, $p = 0.010$) and lower rates of type A bile duct injury (4.8% vs 14.3%, $p = 0.035$) and type D (0 vs 9.5%, $p = 0.002$) according to Strasberg classification, residual stones (4.8 vs 14.3%, $p = 0.035$) and gastrointestinal organ injury (0 vs 3.6%, $p < 0.001$). Patients in the DLC group had lower incidences of ICU admission and death and a significantly lower incidence of repeat surgery.

Conclusion In elderly patients treated for acute calculous cholecystitis, the 30-day mortality and complication rates were lower for PC + DLC than for LC. However, the total hospitalisation time was significantly prolonged and the costs were significantly higher for PC + DLC.

Keywords Acute calculous cholecystitis · Percutaneous cholecystostomy tube drainage · Laparoscopic cholecystectomy · Delayed laparoscopic cholecystectomy · NSQIP · TG13

Acute calculous cholecystitis is a common emergency disease for which cholecystectomy (CCY) has long been considered the most effective management [1–3]. In elderly patients with acute cholecystitis, the risk of emergency surgery is high [4], and a surgical approach including percutaneous cholecystostomy tube drainage (PC) combined with delayed laparoscopic cholecystectomy (DLC) may therefore be a good choice [5–7]. However, the current surgical effect of PC + DLC remains controversial. The purpose of this study was to investigate whether DLC after PC has an advantage over LC and determine its effect on postoperative survival in elderly patients.

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Method

Patients

In this study, we collected a total of 752 patients who were diagnosed with acute calculous cholecystitis and underwent LC (314) or PC + DLC (438) from January 2010 to January 2018 in Shengjing Hospital affiliated with China Medical University, Liaoning, China. The inclusion criteria for the study were as follows: (1) age > 65 years old; (2) patients with a cholecystitis severity of grade 2 or 3 according to the 2013 Tokyo Guidelines (TG13); (3) the surgeons who performed the LC were professors or associate professors and (4) the DLC was performed in our hospital after PC. The exclusion criteria included the following: (1) pregnant women; (2) a diagnosis of bile duct stones, cholangitis or gallstone pancreatitis and (3) missing 30-day follow-up. The severity of cholecystitis was diagnosed according to the TG13 as follows: 1 = healthy patient or mild inflammatory changes in the gallbladder; 2 = systemic inflammatory response or marked local inflammation and 3 = associated with dysfunction of any organs/systems [8, 9]. A total of 124 patients were included in the study, including 51 in the LC group and 73 in the PC + DLC group (Figs. 1, 2).

Matching procedure

The LC group and the PC + DLC group were matched 1:1 according to the National Surgical Quality Improvement Program (NSQIP) calculation for 30-day mortality. For general surgery, the 2019 NSQIP included 18 indicators to evaluate postoperative prognoses. Patients within the LC patient group and the PC + DLC patient group with similar predictions for mortality were identified and paired. If two patients' predicted mortality results differed by more than 5%, the two patients were included in a matched group. Based on this method, 38 patients were included in each of the groups (LC group and PC + DLC group). According to the TG13 classification,

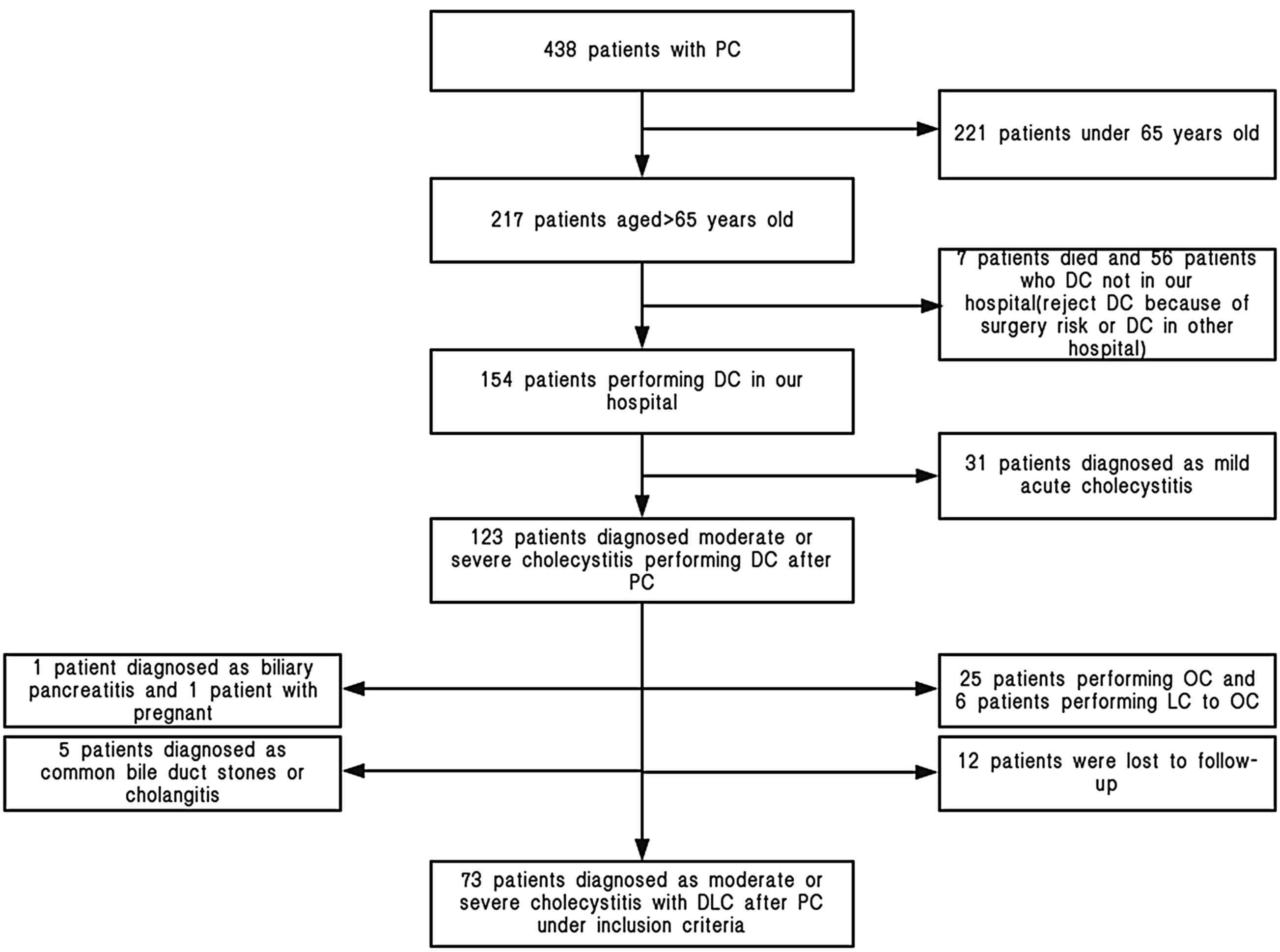

Fig. 1 Patients in the PC + DLC group

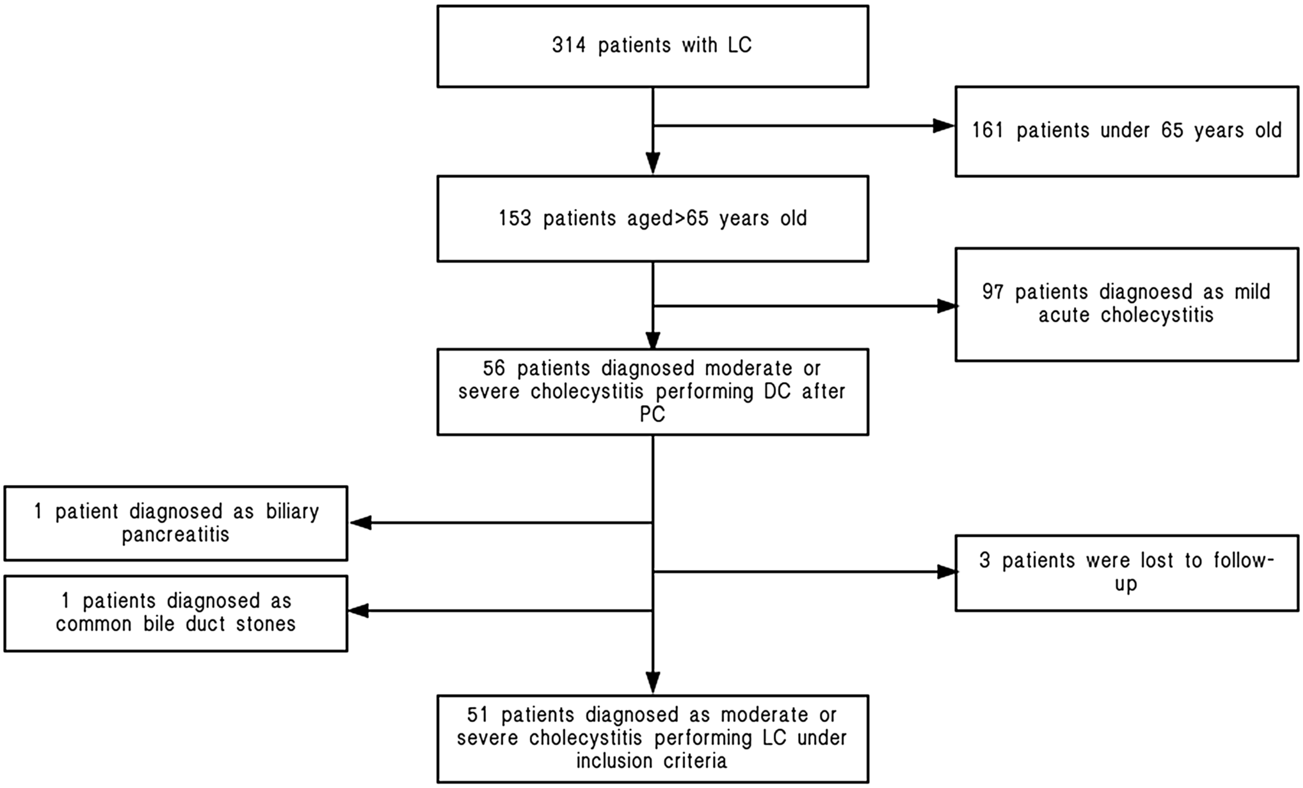

Fig. 2 Patients in LC group

patients with different grades of gallbladder severity were excluded. Finally, 42 patients were included in the matching group, with 21 patients in each group.

Statistical analysis

All statistical analyses were performed using IBM SPSS software (version 19.0; Armonk, NY, USA). Data with a normal distribution are expressed as $\chi \pm s$ and were compared using *t* tests. The sample rate was compared using the Chi-square test or Fisher's exact test. The significance of the results was set at the 5% level. The discharge date of the deceased patient was based on the date of death. Kaplan–Meier curves were generated in GraphPad Prism (version 8, GraphPad Software, La Jolla, CA) and compared using the Mantel–Cox log-rank test. Significance was set at $\alpha = 0.05$.

All data collection has been approved by the IRB.

Results

Patient characteristics

Overall, TG grades were higher in patients in the PC + DLC group than in those in the LC group (2.5 ± 0.5 vs 2.3 ± 0.4, $p < 0.001$), and a higher NSQIP predicted 30-day mortality (19.3 vs 12.1%, $p < 0.001$, and 15.2 vs 12.9, $p = 0.272$, respectively). Parameters that were significantly different between the PC + DLC group and the LC group based on the NSQIP surgical risk calculator input variable included the following: age, disseminated cancer, hypertension requiring medication, dyspnoea, congestive heart failure within 30 days days and insulin use ($p < 0.05$). After matching, the PC + DLC group and the LC group had similar predicted 30-day mortality rates (15.2 vs 12.9%, $p = 0.272$) and acute cholecystitis severity (2.4 vs 2.4, $p = 0.809$). The matched PC + DLC group had a higher rate of COPD (33 vs 28%, $p = 0.519$) and a higher rate of congestive heart failure within 30 days (28.6 vs 23.8%, $p = 0.496$), although these differences were not significant. Significant differences between the two groups that were eliminated by the matching method included TG13 grade, age, creatinine, disseminated cancer, hypertension requiring medication, dyspnoea, current smoker within 1 year, dialysis and insulin use (Table 1).

Operative and postoperative data

All patients in the PC group underwent DLC when cholecystectomy is indicated, and the interval between PC and DLC was 1–769 days, with an average of 113 days. All patients

Table 1 Patient characteristics at the time of first admission

Patient characteristics	LC $n=51$	PC + DLC $n=73$	p	Matched LC $n=21$	Matched PC + DLC $n=21$	p
INR	1.1 ± 0.1	1.1 ± 0.2	0.110	1.1 ± 0.1	1.1 ± 0.1	0.547
ASA	2.9 ± 0.3	3.0 ± 0.4	0.126	3.0 ± 0.3	3.1 ± 0.3	0.823
Age	69 ± 2	70 ± 3	< 0.001	69 ± 3	70 ± 4	0.894
Male	22 (43.1%)	28 (38.4%)	0.192	7 (33.3%)	9 (42.9%)	0.246
Temperature (°C)	37.5 ± 0.5	37.6 ± 0.6	0.535	37.5 ± 0.5	37.6 ± 0.5	0.824
TG13	2.3 ± 0.4	2.5 ± 0.5	< 0.001	2.4 ± 0.5	2.4 ± 0.5	0.809
White blood cell count (× 10^9 cells/L)	13.1 ± 2.4	13.8 ± 2.7	0.168	12.3 ± 2.5	12.4 ± 2.8	0.295
COPD	12 (23.5%)	20 (27.4%)	0.331	6 (28.6%)	7 (33.3%)	0.519
Ascites	2 (3.9%)	4(5.5%)	0.429	2 (9.5%)	1 (4.8%)	0.240
Systemic sepsis within 48 h	19 (39.2%)	25(32.9%)	0.174	6 (28.6%)	8 (38.1%)	0.353
Creatinine (mg/dL)	1.6 ± (0.4)	1.8 ± (0.5)	0.035	1.8 ± 0.3	1.8 ± 0.4	0.742
Disseminated cancer	1 (1.7%)	5 (5.8%)	0.011	1 (4.8%)	2 (9.5%)	0.240
Diabetes	13 (22.5%)	24 (31.7%)	0.072	5 (23.8)	7 (33.3)	0.189
Hypertension requiring medication	11 (21.5%)	29 (35.6%)	< 0.001	5 (23.8)	7 (33.3)	0.189
Congestive heart failure within 30 days	6 (12.4%)	21 (26.0%)	< 0.001	5 (23.8%)	6 (28.6%)	0.496
Dyspnoea	12 (18.2%)	23 (27.9%)	< 0.048	10 (47.6%)	8 (38.1%)	0.309
Current smoker within 1 year	15 (26.5%)	15 (21.2%)	0.029	7 (33.3%)	6 (28.6%)	0.519
Dialysis	0	2 (2.9%)	0.016	0	0	> 0.99
Acute renal failure	1 (1.7%)	3 (4.8%)	0.183	1 (4.8%)	1 (4.8%)	> 0.99
BMI	28 ± 6	27 ± 5	0.107	30.7 ± 2.7	29.9 ± 3.6	0.170
Insulin	4 (7.4%)	10 (14.4%)	0.040	3 (14.3%)	3 (14.3%)	> 0.99
Hypoglycaemic agents	8 (14.9%)	13 (17.3%)	0.537	6 (28.6%)	5 (23.8%)	0.496
Cerebrovascular diseases	14 (21.5%)	23 (32.7%)	0.329	8 (38.1%)	8 (38.1%)	> 0.99

Quantitative data are expressed as normal ± standard error of the mean and were compared using Student's *t* test

Qualitative data are expressed as *n* (%) and were compared using the Chi-square test or Fisher's exact test

LC laparoscopic cholecystectomy, *PC* percutaneous cholecystostomy, *DLC* delayed laparoscopic cholecystectomy, *INR* International normalised ratio, *COPD* chronic obstructive pulmonary disease, *BMI* Body Mass Index

performing LC were placed in abdominal drainage tube during surgery. And 17 patients (81.0%) in the DLC group were placed in abdominal drainage tube during surgery. Compared to the LC group, the DLC group had shorter operative time, abdominal drainage tube removal time and less Intraoperative bleeding, the statistical results of which were significantly different in matched group (Table 2).

Complications

Compared to the matched LC group, the DLC group had lower rates of congestive heart failure (0 vs 4.8%, $p=0.042$), pleural effusion (9.5% vs 28.6%, $p=0.001$), type A bile duct injury (4.8% vs 14.3%, $p=0.035$) and type D (0 vs 9.5%, $p=0.002$) according to Strasberg classification [10] and gastrointestinal organ injury (0 vs 9.5%, $p=0.002$). There were 2 patients with gastrointestinal organ injury in the LC group, and all of these patients underwent reoperation. A comparison of the matched DLC and CCY groups revealed that the rate of residual stones was significantly higher (4.8% vs 14.3%, $p=0.035$) in the latter. All patients with residual stones underwent endoscopic treatment, and all of these patients were cured. There was no significant difference in stroke, pulmonary

Table 2 Comparison of operative and postoperative data between the two study groups

Outcomes	Matched DLC $n=21$	Matched LC $n=21$	p
Operative time(min)	72 ± 24	118 ± 32	0.036
Intraoperative bleeding (ml)	42.2 ± 22.0	75.3 ± 46.8	0.014
Drainage tube removal time (days)	5.4 ± 4.1	10.1 ± 9.0	< 0.001

Drainage tube removal time is the time from intraoperative abdominal drainage tube insertion to removal

Table 3 Comparison of complications between the two study groups

Complication	Matched DLC $n=21$	Matched LC $n=21$	p
Stroke	1 (4.8%)	2 (9.5%)	0.240
Congestive heart failure	0	1 (4.8%)	0.042
Pleural effusion	2 (9.5%)	7 (28.6%)	0.001
Pulmonary embolism	1 (4.8%)	1 (4.8%)	> 0.99
Residual stones	1 (4.8%)	3 (14.3%)	0.035
Renal insufficiency	1 (4.8%)	2 (9.5%)	0.240
Gastrointestinal organ injury	0	2 (9.5%)	0.002
Incision infection	2 (9.5%)	1 (4.8%)	0.240
Bile duct injury (Strasberg classification)	1 (4.8%)	5 (23.9%)	< 0.001
Type A	1 (4.8%)	3 (14.3%)	0.035
Type D	0	2 (9.5%)	0.002

Type A injury Bile leak from a minor duct still in continuity with the common bile duct

Type D injury Lateral injury to extrahepatic bile ducts

Table 4 Comparison of serious complications between the two study groups

Serious complications	Matched DLC $n=21$	Matched LC $n=21$	p
Admission for ICU	1 (4.8%)	7 (33.3%)	< 0.001
Death	0	3 (14.3%)	< 0.001
Return to surgery	1 (4.8%)	5 (23.8%)	< 0.001

embolism, renal insufficiency and incision infection between the matched groups (Table 3).

Serious complications

Patients in the DLC group had a lower incidences of ICU admission, death and return to surgery ($p<0.001$). Patients with gastrointestinal organ injury were included in the return to surgery group, and the remaining patients were re-hospitalised due to partial LC. Patients who underwent endoscopic treatment were not included in the return to surgery group (Table 4).

Hospital stay and 30-day mortality

There were significant differences in hospitalisation times and mortality rates between the matched and unmatched groups. Compared with the LC group, the patients in both matched and unmatched DLC groups had lower predicted mortality and shorter hospital stays ($p<0.05$), and the length of hospital stay did not count the time prior to admission for PC (Table 5). Compared with first admission, after PC, the predicted 30-day mortality was significantly lower (15.2 vs 6.3%, $p<0.001$). In DLC group, the observed mortality rates were lower and observed hospital stay shorter compared with LC group in both matched and unmatched groups. In the LC group, the observed mortality rates were similar with predicted mortality. However, in the DLC group observed mortality rates were lower than its predicted mortality rates. And the observed hospital stay were longer than predicted hospital stay in the two groups (Figs. 3, 4). In the matched groups, compared with LC patients, patients in the PC + DLC group had longer total hospitalisations (9.5 ± 3.6 vs 13.2 ± 4.1 days, $p<0.001$) and higher total costs (8142 ± 664 vs $12{,}105 \pm 2548$ dollars, $p<0.001$) (Table 6).

Discussion

Laparoscopic cholecystectomy (LC) is the treatment of choice for acute cholecystitis; however, it is associated with higher morbidity and mortality in high-risk populations [11–13]. Percutaneous cholecystostomy tube drainage (PC) combined with delayed laparoscopic cholecystectomy (DLC) provides a safer alternative treatment; however, the incidence and safety of it are still unknown.

Table 5 Predicted and observed 30-day mortality and hospital stays in matched and unmatched patients who underwent DLC and LC

Outcome	Analysis	DLC	LC	p
Predicted mortality (%)	Unmatched	6.8 ± 3.5	9.0 ± 4.5	$p=0.026$
	Matched	6.3 ± 2.9	11.2 ± 5.4	$P=0.043$
Observed mortality (%)	Unmatched	1 (1.4%)	5 (9.8%)	$p<0.001$
	Matched	0	3 (14.3%)	$p<0.001$
Predicted hospital stay (days)	Unmatched	3.3 ± 2.2	3.9 ± 2.7	$p=0.196$
	Matched	2.7 ± 1.4	4.0 ± 2.6	$p<0.001$
Observed hospital stay (days)	Unmatched	6.2 ± 2.8	9.5 ± 3.6	$p=0.041$
	Matched	4.9 ± 2.4	7.4 ± 5.1	$P=0.010$

Predicted mortality, NSQIP predicted 30-day mortality

Hospital stay before the time of the first PC admission was not counted

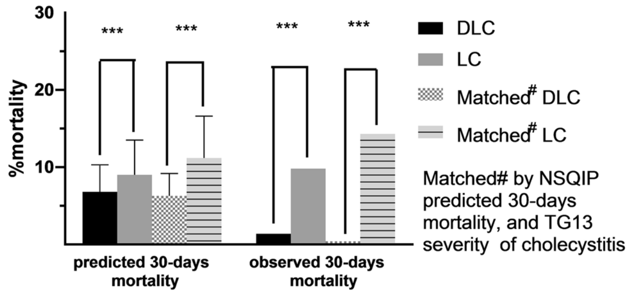

Fig. 3 Predicted and observed 30-day mortality following DLC and LC (***$p < 0.05$)

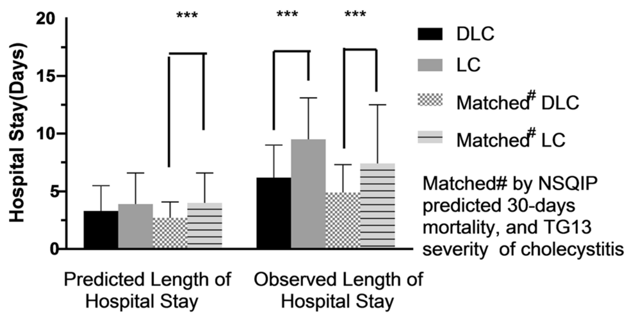

Fig. 4 Predicted and observed hospital stays following DLC and LC (***$p < 0.05$)

We matched the two included groups by NSQIP scores and TG13 scores to eliminate any differences in underlying disease status between the groups. When comparing patients with the same underlying disease and inflammatory status, the prognosis remained significantly different between the DLC group and the LC group. Our results showed that the postoperative complication rate and mortality were significantly lower in the DLC group than in the LC group. With regard for hospitalisation time, total hospital stays were longer and hospitalisation costs were significantly higher in the PC + DLC group than in the LC group. This finding is in line with the results of a prospective experiment performed by Özkardeş [7]. In contrast to our study, Özkardeş performed only conservative treatment in patients in the DLC group and considered LC a more favourable approach in the early stage of acute cholecystitis and their laparoscopic conversion rate suggested that there was no difference between the LC group and DLC group.

There has been controversy over the treatment of acute sever cholecystitis. An article from JAMA Surgery suggests that DLC has higher morbidity, mortality and costs than emergency laparoscopic cholecystectomy (ELC) [14]. And one 2010 meta-analysis based on safety and effectiveness found that there was no significant difference in the incidence of complication and OC conversion between ELC and DLC groups, but postoperative hospital stay of DLC was longer [15]. Kim et al. reported that in the comparison of LC, PC + ELC and PC + DLC for the treatment of complicated acute cholecystitis, PC + DLC had lower conversion rate and complication rate [5]. There were other studies suggesting that PC without DLC can be an effective treatment for patients with acute cholecystitis [16–21]. In Koetsu Inoue's univariate analysis of the timing of surgery for moderate cholecystitis, the risk of early LC was considered to be higher, and PC was viewed as a better choice [22]. Because our study subjects were limited to the treatment of patients with acute calculous cholecystitis, the efficacy of PC without a DLC in acalculous cholecystitis was not studied.

Older patients are more likely to explore treatment options for acute calculous cholecystitis because of their older age and larger number of basic diseases. Some studies suggest that LC is completely feasible for the treatment of high-risk acute cholecystitis [23–26]. An article from Italy considered that cholecystectomy in patients over 80 years old is a relatively safe procedure with an acceptable risk of complications and hospital stay comparable to younger ones [26]. However, a meta-analysis in November 2018 considers, for elderly patients with acute cholecystitis, PC + DLC had lower postoperative complications, open cholecystitis rate and shorter operative time [6].There were also some studies that hold similar views [16–18, 20]; however, these studies did not examine whether PC + DLC or PC alone had different prognostic outcomes. Francesca et al.'s analysis of propensity scores in elderly patients with TG13 grade 3 cholecystitis demonstrates worse outcomes with cholecystostomy tube placement in a matched cohort of patients with grade III disease, with increased mortality, survival, length of stay, complications and readmissions after cholecystostomy tube placement [27]. In the severe patients with grade 3, the Tokyo guidelines recommend urgent gallbladder drainage with a cholecystostomy tube as initial treatment, followed

Table 6 Total hospital stay and total cost in the matched and unmatched groups

outcome	Analysis	PC + DLC	CCY	p
Total hospitalisation (days)	Matched	13.2 ± 4.1	9.5 ± 3.6	$p < 0.001$
	Unmatched	15.7 ± 5.4	7.4 ± 5.1	$p < 0.001$
Total cost (dollars)	Matched	12,105 ± 2548	8142 ± 664	$p < 0.001$
	Unmatched	13,597 ± 2916	7753 ± 890	$p < 0.001$

by antibiotics and delayed cholecystectomy [27]. Although several studies performed that TG13 has a guiding role in the diagnosis and treatment of different degrees of cholecystitis, more studies identifying target types of patients who can benefit from PC or DLC are essential [8, 28–30].

The significant differences observed in our study may be due to the screening of enrolled patients. In this study, elderly patients with grade 2 and grade 3 cholecystitis were selected as subjects. All patients in the DLC group underwent PC treatment and were matched by NSQIP and TG13 to reduce selection bias. The intraoperative outcomes of PC + DLC and CCY, postoperative complications, hospital stay and 30-day mortality were studied. The shortcoming is that no patients with conservative treatment + DLC were studied.

Our study also found that NSQIP predicted 30-day mortality, and the predicted mortality rates and hospital stay durations were not consistent with the observed mortality rates and hospital stay durations. However, many studies have confirmed the effectiveness of NSQIP [31, 32]. However, some studies do not approve the prediction results of NSQIP [32–38]. Corkum et al. studied the perioperative outcomes of the same patients in three large databases, including NSQIP, with significant differences [10]. A comparison of the Tokyo Guide and NSQIP on acute cholecystitis indicates ACS-NSQIP did not accurately predict complications or LOS and patient outcomes [38]. This is consistent with the findings of our study.

Limitations

There are several limitations associated with our study. First, in this study, we reduce selection bias by NSQIP to predict 30-day mortality and TG13 to assess the extent of gallbladder inflammation. However, as a retrospective, single-centre study, the possibility of unintentional selection bias could not be fully excluded. Indeed, although NSQIP is already a multi-validated surgical risk calculator, it dose not cover all the disease-related variables. Risk calculators cannot replace surgeon judgement, and experienced doctors will judge the appropriate surgical method.

Conclusion

For elderly patients with moderate to severe acute calculous cholecystitis, PC + DLC surgery can effectively reduce the incidence of postoperative complications and mortality. Moreover, compared with LC, PC + DLC had lower secondary surgery, residual stone and ICU occupancy rates. However, this type of surgery also requires higher costs and extends the total hospital stay. The results predicted by the NSQIP, a surgical risk calculator, did not match the observed mortality rates and hospitalisation times observed in this study. The patient information collected for the NSQIP was mostly obtained in Europe and the United States, and regional differences may be one source of bias in the predicted results. Confirming the optimal treatment options for elderly patients with severe cholecystitis will require a larger sample size of prospective studies.

Compliance with ethical standards

Disclosures Dr. Dengtian Lin, Shuodong Wu, Changwei Ke and Ying Fan have no conflicts of interest or financial ties to disclose.

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