

Re-Evaluating the Role of Delayed Cholecystectomy: Safety and Timing in the Management of Acute Cholecystitis

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Abstract

Background: Early laparoscopic cholecystectomy (LC) is the standard treatment for acute cholecystitis (AC) to reduce hospital stay and costs, but optimal timing remains debated due to severe complications like bile duct injury (BDI). Delayed LC (DLC) after conservative management or drainage provides a safer alternative with lower postoperative complications and BDI rates

Materials and Methods: This narrative review analyzed literature from PubMed and Embase (1990–October 2025). Surgical timing was categorized by inflammation phases: Early (<7 days), Intermediate (7 days to 6 weeks), and Delayed (>6 weeks). Evidence from RCTs, meta-analyses, and registries was evaluated, with a focus on BDI risks, surgeon experience, and hospital readiness. Limitations include potential selection bias and lack of formal quality assessment.

Results: Under optimal conditions, early LC reduced hospital stay and costs but was associated with higher postoperative complication rates (up to 26.7%). BDI rates peaked at 2.8% when operating between days 4–7, and open conversion rates reached 21%–28.6% in Grade I/II cases. Conversely, delayed LC after drainage mitigated these risks; one study reported zero conversions in the delayed group, and a meta-analysis showed a significantly higher BDI risk (HR 6.07) with early intervention.

Conclusion: Choosing between early and delayed LC must be individualized, prioritizing patient safety over economic benefits. While early LC is preferred under optimal conditions, it requires high expertise. In resource-variable settings, delayed LC serves as an essential, safer alternative that aligns with international guidelines.

Keywords: Acute cholecystitis, Cholecystectomy, Delayed cholecystectomy, Early cholecystectomy, Laparoscopic cholecystectomy, Safe cholecystectomy

INTRODUCTION

Currently, early laparoscopic cholecystectomy (LC) is the standard treatment for acute cholecystitis (AC) due to its proven ability to reduce total hospital stay and average costs.¹ However, the decision to proceed must weigh these benefits against the risk of bile duct injury (BDI), a critical complication that increases long-term mortality by 8.8%.² The key clinical dilemma lies in the gap between current guideline recommendations for early intervention and real-world clinical practice, where factors such as patient comorbidities, hospital readiness, and surgical expertise significantly influence outcomes.

MATERIALS AND METHODS

This study is a narrative review of the literature, identifying relevant articles through searches of PubMed and Embase for studies published from 1990 to October 2025. The search strategically combined terms such as “early versus delayed cholecystectomy” and “surgical outcomes of acute cholecystitis” to selectively review surgical outcomes, cost-effectiveness, and complication rates. Surgical timing was categorized into three distinct groups based on the underlying pathophysiologic evolution of gallbladder inflammation: The Early Phase (< 7 days), characterized by interstitial edema and easier dissection planes; the Intermediate Phase (7 days to 6 weeks), marked

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by subacute fibroblastic proliferation and dense, vascularized adhesions; and the Delayed Phase (> 6 weeks), where inflammation has matured or resolved. Evidence from randomized controlled trials (RCTs), meta-analyses, and large-scale registry studies was interpreted with a focus on both statistical significance and clinical relevance, particularly regarding the risk of bile duct injury (BDI) and the impact of surgeon experience and hospital readiness. As a non-systematic narrative review, a key limitation of this study is the potential for selection bias and the lack of a formal quality assessment for all included evidence, which may influence the generalizability of the findings.

Bile duct injury and acute cholecystitis

Nuzzo et al.³ reported the incidence of BDI following LC as 0.3%. They found that the incidence of BDI in the group with gallbladder inflammation was 0.56%, which was statistically significantly higher than in the group without inflammation. Furthermore, among the BDI group, 52.3% underwent LC for gallbladder inflammation, and 46.8% were described as easy surgeries.

Importance of the experience for LC in acute cholecystitis

Nuzzo et al.³ found that, when comparing the incidence of BDI with the surgeon's experience in LC, fewer than 150 cases over three years were associated with a BDI incidence of 0.86%. This incidence decreased significantly to 0.19% when the surgeon had more than 250 cases over three years. From this study, the researchers concluded that gallbladder inflammation is an important risk factor for BDI; therefore, experience with more than 250 cases over three years is required to reduce the risk of BDI. However, the author found that the proportion of patients with gallbladder inflammation and BDI was higher when the surgeon had more than 250 cases in 3 years. The researchers therefore recommended performing the surgery

with caution, even for surgeons with extensive experience.

Data from a Thai study by Noppakunsomboon et al.⁴ investigated the outcomes of early LC in AC grade I versus grade II among surgeons with more than 50 LC cases per year. They found a minor BDI rate of 3.8% with no difference between grade I and II. The open conversion rate was 21%, attributable to dense intra-abdominal adhesions (63.6%), inflammation (50%), contamination (36.3%), and bleeding during surgery (22.7%).

While surgical volume serves as a useful proxy for experience, contemporary surgical standards emphasize that “high experience” must also incorporate individual outcome metrics and the mastery of safety protocols. Beyond achieving specific case volumes, a high-experience surgeon is defined by clinical judgment⁵ and consistent proficiency in avoiding complications, particularly in maintaining low individual bile duct injury (BDI) rates. Although no standardized individual BDI rate is currently established in the literature to define high experience, the focus remains on the surgeon's ability to recognize when intraoperative difficulties⁵—such as dense adhesions, scarring, or bleeding—necessitate ‘bailout’ strategies^{6,7}, including open conversion or subtotal cholecystectomy, to prioritize patient safety over the goal of laparoscopic completion.

Role of delayed LC in acute cholecystitis

The definition of early LC in the Tokyo guideline 2018¹ and the World Society of Emergency Surgery 2020⁸ refers to surgery performed within or equal to 7 days of hospital admission or within 10 days of symptom onset⁸. Delayed LC means surgery performed at least 6 weeks after the first day of symptoms (**Figure 1**). Surgery performed between 7 days and 6 weeks is considered intermediate LC based on the pathophysiology of inflammation and does not align with the definition of delayed LC in the aforementioned data.

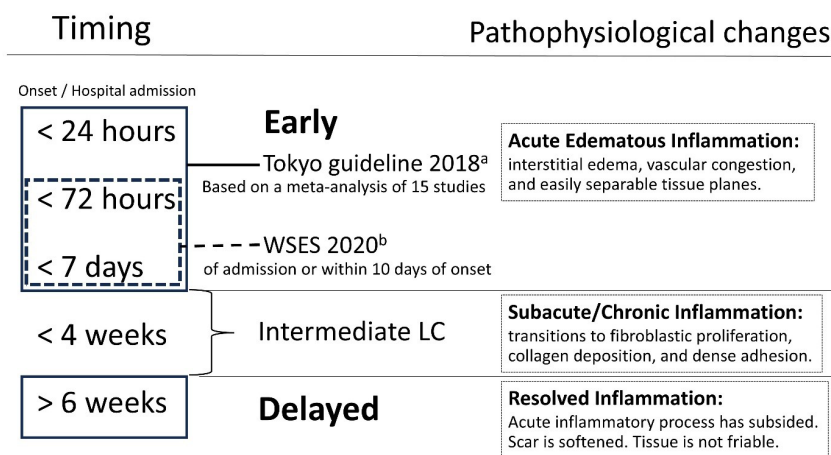


Figure 1 Definitions of early and delayed cholecystectomy

Note: a = Reference 1, b = Reference 8

Lo et al.⁹ reported a prospective RCT in 1998 comparing early (< 72 hours) and delayed (8-12 weeks) LC in AC. They found that the early LC group had a statistically significantly shorter total hospital stay and recuperation period before returning to work compared to the delayed LC group. This included a lower complication rate in the early LC group than in the delayed LC group (13% vs. 29%; $p = 0.07$). However, the delayed group had a statistically significantly shorter postoperative hospital stay (4 and 3 days, respectively, $p = 0.04$) (**Table 1**). The researchers therefore concluded that early LC should be recommended within 72 hours of hospital admission and performed by an experienced surgeon, as it offers benefits in terms of both surgical outcomes and costs.

while no BDI was found in the delayed LC group. The benefit of early LC reported by the authors in this study was a statistically significantly shorter total hospital stay in the early LC group compared to the delayed LC group (4.1 and 10.1 days, respectively) (**Table 2**). Nevertheless, the authors concluded that early LC is safe and should be recommended for AC patients, as it reduces hospital length of stay.

Ozkardes et al.¹¹ reported a prospective RCT in 2014 that compared early (< 24 hours) and delayed LC (6-8 weeks) in 60 AC patients. They found that the early LC group had a significantly higher rate of intraoperative and postoperative complications than the delayed LC group (26.7% vs 0%; $p = 0.002$). Of the eight patients with complications, two were due to BDI or bile leakage, and

Table 1 Comparison of the outcomes of early LC and delayed LC⁹

	Early group	Delayed group	<i>p</i> -value
Postoperative pain score	2.3	2.7	0.275
Postoperative stay (days)	4	3	0.046
Total hospital stay (days)	6	11	< 0.001
Total recuperation period (days)	12	19	< 0.001
Duration of loss of working capacity (days)	15	26	0.017

Kolla et al.¹⁰ reported a prospective RCT in 2004 comparing early (< 24 hours) and delayed (6-12 weeks) LC in AC. They found that the early LC group had a significantly greater blood loss. Furthermore, they had more complications, though this difference was not statistically significant. However, in the early LC group with complications, two out of four cases were due to BDI,

one was due to bleeding. However, the early LC group had a statistically significantly shorter total hospital stay than the delayed LC group (5.2 vs 7.8 days; $p = 0.04$). No difference was found in operative time or open conversion rate (**Table 3**). Based on the above data, the authors concluded that although early LC has more intraoperative and postoperative complications than delayed LC, early LC

Table 2 Outcomes of early LC and delayed LC from the study by Kolla et al.¹⁰

	Early group	Delayed group	<i>p</i> -value
Blood loss (mL)	228.5	114.5	0.006
Postoperative stay (days)	3.2	2.3	0.161
Total hospital stay (days)	4.1	10.1	0.023
Conversion rate (%)	25	25	0.540
Complications (%)	20	15	0.456

Table 3 Outcomes of early LC and delayed LC from the study by Ozkardes et al.¹¹

	Early group	Delayed group	<i>p</i> -value
Operative time (min)	67.0	71.3	0.202
Hospitalization duration (days)	5.20	7.80	0.040
Intraoperative, postoperative complications (%)	26.70	0.00	0.002
Open conversion (%)	13.30	0.00	0.112
Cost (Turkish Lira)	2,500.97	3,713.47	0.030

should be recommended for AC due to the shorter hospital stay and lower costs in the early LC group.

From the aforementioned RCT data, early LC for AC is associated with a shorter total hospital stay than delayed LC across all studies, leading to reduced treatment costs. However, it cannot be concluded that early LC is safer, given the rate of intraoperative complications, particularly the higher incidence of BDI reported in some studies in the early LC group.^{10,11}

Okamoto et al.¹ reported the results of a meta-analysis of 15 RCTs in AC to determine the optimal timing for LC. Four key factors were considered: (1) BDI; (2) operative time; (3) total hospital stay; and (4) medical costs.

(1) The comparison between early LC (< 72 hours) and a delayed LC of six weeks in BDI found that the early group had an odds ratio for BDI of 1.38 (95% CI: 0.21-8.95). Another comparison between early LC (< 1 week) and a delayed LC of six weeks found that the early LC group had an odds ratio for BDI of 0.77 (95% CI: 0.18-3.26). No statistically significant difference was found in either time period.

(2) The comparison between early LC (< 72 hours and one week) and delayed LC of six weeks found that the operative time in the early LC groups showed a tendency to be shorter than the delayed LC group with mean differences of 8.95, 95% CI: -3.17-19.18 and 6.92, 95% CI: -0.26-14.09, respectively. However, no statistically significant difference was found in either time period.

(3) The comparison between early LC (72 hours and one week) and delayed LC of six weeks found that the early LC groups had statistically significantly shorter total hospital stays than the delayed LC of six weeks with mean differences of -3.43, 95% CI: -4.97-1.89, and -3.31, 95% CI: -4.62-2.00, respectively.

(4) The comparison between early LC (< 72 hours) and delayed LC of six weeks found that the early LC group had a statistically significantly lower overall medical cost

than the delayed LC group with a standard mean difference of -1.42, 95% CI: -2.32 to -0.52).

From a meta-analysis report by Pisano et al. In 2020,⁸ the early LC group was found to have a shorter total hospital stay than the delayed LC group, with an average difference of 4 days, and to return to work an average of 9 days sooner. No difference was found in terms of the mortality rate or open conversion rate. However, two RCT studies that were not included in the 2018 meta-analysis by Okamoto et al. will be discussed next.

While some studies, such as the one by Mustafa et al.¹², report a statistically significant increase in bile duct injury (BDI) for early LC—finding a 10.5% rate compared to 0% in the delayed group ($p < 0.05$) (Table 4), these results are often viewed as outliers in the broader literature. For instance, a meta-analysis of 15 randomized controlled trials found no statistically significant difference in BDI rates between early and delayed approaches. However, a critical distinction must be made between statistical significance and clinical concern. While large-scale data may not always reach a p-value threshold for BDI due to the fortunately low frequency of the event, the devastating impact of a single injury on patient mortality and quality of life remains a primary clinical concern for the operating surgeon. Therefore, while high BDI rates in isolated studies such as Mustafa et al. may not reflect the standardized outcomes of high-volume centers, they serve as a cautionary “real-world” reminder of the risks associated with severe inflammation and variable surgical expertise.

Early LC has been widely accepted as the standard for AC due to its clear benefits, including a shorter total hospital stay and lower medical costs compared with delayed LC. The benchmark for the incidence of BDI is between 0.3% and 0.5%. RCTs with a high rate of BDI are often excluded from meta-analyses because the quality of surgery is considered below standard. Thus, the data on surgical complications are not sufficiently weighted to outweigh the benefits mentioned above.

Table 4 Outcomes of early LC and delayed LC from the study by Mustafa et al.¹²

	Early group	Delayed group	p-value
Operative time (min)	112.25	154.94	< 0.05
Blood loss (mL)	26	75	< 0.05
Bile duct injury (%)	10.50	0.00	< 0.05
Pain score (VAS)	2.98	2.43	0.67

VAS: visual analogue score

Limitations and safety of early LC in acute cholecystitis

The relationship between the timing of LC and the severity of acute cholecystitis (AC) is a critical factor in determining surgical success and patient safety. Endo et al.¹³ reported an international, multicenter, retrospective observational study that was representative of real-world practice, as it was conducted in 155 hospitals across Japan and Taiwan. The study involved 5,329 AC patients who were divided into groups based on the treatment received: (A) primary cholecystectomy; (B) delayed LC after percutaneous gallbladder drainage (PTGBD); (C) PTGBD alone; and (D) medical treatment alone. The group with the highest mortality rate was the PTGBD alone at 9.8%, and the lowest was the delayed LC after PTGBD group at 0.6% (**Table 5**). However, a key finding was that the AC grade III group treated with primary cholecystectomy had a high mortality rate of 4.13%. After analyzing the factors that affected the mortality rate (multivariate analysis), they found that patients with any of the three negative predictive factors had a mortality rate increase from 0% to 9.3%. The negative predictive factors were jaundice, neurological dysfunction, and respiratory dysfunction. Although the study by Endo et al.¹³ demonstrated that bile duct injury (BDI) rates were not significantly different between early LC and delayed LC after PTGBD, it is worth noting that the highest rate of BDI was found in the early LC group between days four and seven (2.8%) (**Table 6**). Notably, even though this study was conducted in training institutions where surgeries were performed exclusively by surgeons specializing in hepato-pancreato-biliary surgery, the peak BDI rate was still 2.8% in the early LC group during that specific four- to seven-day window. Their analysis further found that conversion rates to open surgery were

5.9% for primary cholecystectomy (Group A) and 8.3% for cholecystectomy after drainage (Group B). In addition, they observed a trend toward reduced operative time and blood loss in the early LC group, with the shortest operative times specifically recorded for patients undergoing surgery within zero to three days of admission

Conversely, other studies highlight that increased disease severity often leads to more challenging procedures and higher complication rates during the early phase. In a systematic review, Nassar et al.¹⁴ reported that while early LC is preferred, it carries a higher risk of open conversion and BDI in cases of complicated AC, with overall conversion rates of 15.7% for early LC and 6.4% for delayed LC. This increased difficulty in moderate cases was echoed by Noppakunsomboon et al.⁴, who observed that Grade II AC patients had a 28.6% conversion rate compared with 9.5% for Grade I, along with higher estimated blood loss. Furthermore, Bourgouin et al.¹⁵ used a scoring system showing that, for high-risk patients, delayed LC significantly reduced serious operative events and resulted in a 0.0% conversion rate, compared with 16.7% with early intervention. However, database research by Altieri et al.¹⁶ indicated that early LC (within 72 hours) is associated with a lower conversion rate of 7.5% compared to 13.8% for late interventions. These varied outcomes emphasize that while early surgery is optimal for many, patient-specific factors and disease severity must guide timing to avoid adverse outcomes.

AC patients planned for conservative treatment followed by delayed LC had a 6.8%¹⁷ chance of failing conservative treatment. The management guidelines for this scenario were divided into emergency cholecystectomy

Table 5 Comparison of 30-day mortality rates stratified by treatment from a study by Endo et al.¹³

30-day mortality	1° cholecystectomy	DLC after PTGBD	PTGBD alone	Medical treatment alone
Grade I	0.25%	0.50%	4.76%	1.34%
Grade II	0.37%	0.00%	4.30%	1.68%
Grade III	4.13%	0.79%	13.46%	5.93%
Overall 90-day mortality	0.8%	0.6%	9.8%	3.4%

DLC: delayed laparoscopic cholecystectomy; PTGBD: percutaneous transhepatic gallbladder drainage

Table 6 Rate of bile duct injury stratified by the timing of cholecystectomy¹³

	Primary cholecystectomy						Delayed cholecystectomy after PTGBD					
Day	0-3	4-7	8-30	>31	Total	<i>p</i> -value	4-7	8-30	>31	Total	<i>p</i> -value	
BDI (%)	1.1	2.8	1.5	0.7	1.2	0.199	0.8	0.8	2.1	1.3	0.405	

BDI: bile duct injury; PTGBD: percutaneous transhepatic gallbladder drainage

and PTGBD, followed by delayed LC. A meta-analysis by Nassar et al.¹⁴ in 2022 compared early LC with delayed LC after PTGBD in 216,926 patients from RCTs and observational studies. No difference in mortality rate was found between the two groups (hazard ratio [HR] = 1.3, 95% CI: 0.60-2.83). However, the postoperative complication rate in the early LC group was significantly higher than in the delayed LC group after PTGBD (HR = 2.88, 95% CI: 1.78-4.65). Importantly, the BDI rate in the early LC group was significantly higher than that in the delayed LC after PTGBD group (HR = 6.07, 95% CI: 1.67-21.99). The early LC group was also found to have a longer post-op hospital stay than delayed LC after PTGBD, with an average difference of 1 day. Nevertheless, the total hospital stay for the early LC group was statistically significantly shorter than that for the delayed LC group after PTGBD, with an average difference of 6.6 days, which aligns with data from all other studies.

While PTGBD is widely adopted in clinical practice, advanced endoscopic techniques—specifically endoscopic ultrasound-guided gallbladder drainage (EUS-GBD) and endoscopic transpapillary gallbladder drainage (ETP-GBD)—have emerged as viable alternatives for high-risk surgical candidates. Systematic reviews indicate that EUS-GBD achieves technical and clinical success rates comparable to PTGBD. Notably, when using cautery-enhanced lumen-apposing metal stents (LAMS), EUS-GBD is superior to PTGBD in terms of safety and long-term efficacy.¹⁸ Research shows EUS-LAMS significantly reduces adverse events (19.0% vs. 45.2%; $p = 0.0006$), recurrent cholecystitis (2.0% vs. 6.8%; $p = 0.02$), and hospital readmissions (7.3% vs. 37.1%; $p = 0.03$)¹⁹ (**Table 7**). Conversely, ETP-GBD, while associated with lower mortality and reintervention rates than PT-GBD, typically yields lower technical success. Consequently, EUS-GBD with LAMS is increasingly preferred over percutaneous

drainage in specialized centers for patients requiring definitive non-surgical management.

Considerations for translating the study data into clinical practice include these aspects. All studies were conducted in hospitals with high readiness in equipment, operating rooms, and postoperative intensive care units, or in training institutions where surgeries were performed by specialists in hepato-pancreato-biliary surgery or highly experienced laparoscopic surgeons.^{1,8,13,20} Furthermore, patient selection and preparation were meticulous. The patient's clinical assessments, which included severity of inflammation, systemic organ failure, physical condition, and underlying diseases, were always considered. Thus, only when LC is performed strictly under all the above-mentioned conditions can a reduction in total hospital stay and medical cost be expected. There is no supporting data that postoperative complications or the BDI rate can be reduced. Moreover, the BDI rate in some reports is higher compared to delayed LC.^{10,11,13,14}

Ultimately, the selection of surgical timing should not be based solely on predefined intervals but on a comprehensive synthesis of patient-specific risks, the local surgical environment, and the institutional support structure. While early LC remains the gold standard under optimal conditions, the transition from acute edema to dense fibrosis during the intermediate phase and the potential for catastrophic bile duct injury require a nuanced approach that prioritizes patient safety over economic benefits. To assist clinicians in navigating this complexity, particularly in resource-limited settings, we propose a practical decision-making framework. This framework, presented in **Table 8**, categorizes recommendations based on the severity of inflammation, the presence of negative predictive factors, and the level of available surgical expertise, thereby bridging the gap between international guidelines and real-world clinical practice.

Table 7 Summary of Outcomes EUS-GBD versus PTGBD¹⁹

Outcomes	EUS-GBD (LAMS)	PTGBD	p-value
Technical success	95.9 %	99.6 %	0.1
Clinical success	91.0 %	94.8 %	0.1
Adverse events	19.0 %	45.2 %	0.0006
Recurrent cholecystitis	2.0 %	6.9 %	0.02

EUS-GBD: endoscopic ultrasonography guided gallbladder drainage, LAMS: lumen apposing metallic stent, PTGBD: percutaneous transhepatic gallbladder drainage

Table 8 Proposed decision framework for surgical timing

Clinical Scenario	Recommended Timing	Supporting Rationale
Ideal Conditions (Grade I/II AC, high-volume center, expert HPB surgeon)	Early LC (< 72 hrs)	Maximizes cost-efficiency and reduces total hospital stay
High-Risk Patient (Grade III AC, multiple comorbidities, jaundice/respiratory failure, ΔMS)	Initial PTGBD → Delayed LC	Significantly reduces mortality and postoperative complications compared to emergency surgery.
Limited Resources (Solo surgeon, no ICU backup, or lack of 24/7 laparoscopic equipment)	Delayed LC (6-12 weeks)	Prioritizes patient safety and avoids the high BDI rates seen in "standard" settings without expert support.
Failure of Conservative Treatment	Emergency LC vs. PTGBD	Requires immediate intervention; PTGBD is preferred if the surgical risk of BDI is deemed too high.

AC: acute cholecystitis, LC: laparoscopic cholecystectomy, ΔMS: mental status change, PTGBD: percutaneous transhepatic gallbladder drainage, ICU: intensive care unit, BDI: bile duct injury.

CONCLUSION

In light of the evidence reviewed, the decision between early and delayed LC for acute cholecystitis (AC) must be individualized and multifaceted. While our findings align with the Tokyo Guidelines 2018 (TG18) in recommending early LC as the preferred approach to reduce hospital stay and medical costs, this recommendation is predicated on “optimal conditions”. These conditions include a highly experienced surgical team, adequate hospital infrastructure (such as 24/7 operating room availability and intensive care support), and a patient profile that lacks severe systemic negative predictive factors. In real-world clinical practice, where surgical expertise and institutional resources may vary, clinicians should utilize a practical decision-making framework to balance the clear economic benefits of the early approach against the potentially catastrophic risk of bile duct injury (BDI). Delayed LC following conservative management or PTGBD remains an essential and safer alternative for high-risk patients or in settings where “safe cholecystectomy” criteria cannot be strictly met. This stratified approach ensures that surgical timing prioritizes patient safety and the avoidance of postoperative complications without significantly increasing mortality rates.

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