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Research Article

Comparison of Postoperative Outcomes between Early and Delayed Laparoscopic Cholecystectomy in Adults with Acute Calculous Cholecystitis: A Randomized Controlled Study

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ABSTRACT

Background: Acute calculous cholecystitis (ACC) is a common surgical emergency, yet the optimal timing of laparoscopic cholecystectomy remains debated. This randomized controlled trial compared postoperative outcomes between early laparoscopic cholecystectomy (ELC) performed within 72–96 hours of symptom onset and delayed laparoscopic cholecystectomy (DLC) performed after 6–8 weeks of conservative management.

Methods: This prospective, parallel-group, superiority randomized controlled trial with a 1:1 allocation ratio was conducted at a Tertiary Care Hospital of Rawalpindi over a period of time from January 2024 to December 2025. A total of 314 adult patients (aged 18–65 years) with ACC per Tokyo Guidelines 2018 criteria and fit for surgery (ASA I–III) were randomized to ELC (n=157) or DLC (n=157). The primary outcome was conversion to open surgery. Secondary outcomes included total hospital stay, operative time, intraoperative blood loss, postoperative complications (Clavien-Dindo classification), readmission rates, 30-day mortality, and time to return to normal activity. Analysis followed the intention-to-treat principle.

Results: Baseline characteristics were comparable between groups. Conversion to open surgery was significantly lower in the ELC group (7.0% vs. 18.5%; RR 0.38, 95% CI 0.20–0.73; p=0.004; NNT 9). ELC was associated with shorter operative time (71 vs. 87 minutes; p<0.001), reduced blood loss (54.1 vs. 69.7 mL; p<0.001), shorter hospital stay (3.2 vs. 6.5 days; p<0.001), faster return to normal activity (13.9 vs. 20.7 days; p<0.001), lower surgical site infection rates (2.5% vs. 8.3%; p=0.046), and elimination of pre-surgical readmissions (0.0% vs. 12.1%; p<0.001). Overall complications (10.2% vs. 12.7%; p=0.595), bile duct injury (0.6% vs. 1.3%; p=1.000), and 30-day mortality (0.0% vs. 1.9%; p=0.248) did not differ significantly.

Conclusions: Early laparoscopic cholecystectomy within 72–96 hours of symptom onset is superior to delayed surgery, with lower conversion rates, shorter hospital stay, faster recovery, and fewer readmissions, while maintaining a comparable safety profile. These findings support early laparoscopic cholecystectomy as the preferred management strategy for acute calculous cholecystitis in patients fit for surgery.

Keywords: Acute Calculous Cholecystitis, Early Laparoscopic Cholecystectomy, Delayed Laparoscopic Cholecystectomy, Conversion to Open Surgery, Randomized Controlled Trial.

INTRODUCTION

Acute Calculous Cholecystitis (ACC) is one of the most common surgical emergencies around the world and is responsible for a large percentage of all unplanned admissions to General Surgery, has implications for morbidity and healthcare resource use. [1] Although LC has been the standard of care for the definitive treatment of ACC, the optimal time of intervention after symptom onset is still a matter of debate. The two main approaches to management today are the early laparoscopic cholecystectomy (ELC), which is surgery performed within about 72–96 hours of symptoms onset while the patient is hospitalized, and the delayed laparoscopic cholecystectomy (DLC), which involves initial conservative management with intravenous antibiotics, analgesia and hydration and subsequent surgery 6–8 weeks later after the acute inflammatory process has resolved.

A gradual paradigm shift towards early intervention has taken place in international recommendations, and the Tokyo Guidelines 2018 (TG18) have advocated for ELC for Grade I disease as well as for Grade II disease in patients with acceptable comorbidity burden and physiological reserve [2]. The 2020 World Society of Emergency Surgery (WSES) guidelines also recommend ELC to play a central role in the management of ACC, since they are linked to shorter hospitalisation without a higher risk of perioperative morbidity [3]. This guidance is based on a strong body of evidence on the benefits of early intervention. The landmark ACDC randomized trial found that LC performed within 24 hours of admission was found to have fewer complications and lower costs compared with the delayed strategy, but no difference in conversion rate or bile duct injury [4]. A Cochrane systematic review confirmed these results, and demonstrated that early surgery decreased the mean hospital length of stay and early discharge from hospital to normal activity without increasing the risk of conversion or significant bile duct trauma [5]. Later, pooled analyses have confirmed this, with a combined analysis in 2018 showing that ELC was as safe and effective as DLC, and that LC beyond the standard 72-hour window was safe [6] and a 2021 meta-analysis suggesting that LC beyond the standard 72-hour window was not harmful [7]. Early surgery has been shown in a 2023 systematic review and meta-analysis to decrease conversion rates and postoperative complications and to shorten the length of hospital stay [8], and similarly, in real world cohorts from Pakistan and India [9,10]. However, there remain a number of gaps in knowledge.

To date, the benefits of ELC have been shown in international trials in controlled academic environments, and the magnitude of the benefit could be different depending on the surgical skill and the healthcare system. Context-specific evidence is needed. Second, many published trials have been small in size, non-randomized, or have reported outcomes, which were limited and often not scored, according to validated systems like the Clavien-Dindo classification, to capture the most relevant outcome parameters such as conversion to open surgery, operative time, rate of blood loss, and grading of complications. Thirdly, the conversion rate to open cholecystectomy (which is a clinically relevant measure of operational complexity) has not been adequately studied and has ranged from one population to the other. Fourth, there is not an abundance of studies that have considered recovery-related outcomes comprehensively, such as time to normal activity, with significant economic implications.

Fifth, pre-surgical readmission rate is a crucial measure of failure of conservative treatment which has been inconsistently reported in the delayed group. Last, there is a lack of solid randomized evidence in lower middle-income countries (LMICs) with varying health-care infrastructure, and the applicability of results obtained from high-income countries is unclear [9,10]. This is because although ACC remains a major burden to health care systems around the world, the best timing of LC has yet to be clearly defined across different contexts, and there is continuing uncertainty regarding comparative effectiveness across all clinically relevant outcomes. The trade-off between possible increased technical difficulty when a patient is acutely ill [1,7] versus the potential benefits of early surgery (shorter hospital stay, earlier symptom resolution, and decreased risk of recurrent disease) [4,5] must be considered. This is especially important in resource limited countries where the availability of health care facilities and follow-up system can affect the results [9,10].

The aim of the present randomized controlled trial was to comprehensively compare postoperative outcomes between ELC (performed within 72–96 hours of symptom onset) and DLC (performed following initial conservative management at 6–8 weeks) in adults with ACC. The primary objective was to compare the rate of conversion to open cholecystectomy. Secondary objectives included comparison of total hospital stay, operative time, intraoperative blood loss, postoperative complications graded according to the Clavien-Dindo classification, readmission rates prior to definitive surgery in the delayed group, 30-day mortality, and time to return to normal activity. By generating high-quality evidence through a rigorously designed randomized controlled trial, this study aimed to inform clinical decision-making and guideline implementation in settings comparable to our institution, ultimately contributing to improved patient outcomes and more efficient healthcare resource utilization.

METHODS

The study was done as a prospective parallel group superiority randomized controlled trial over a period of time from January 2024 to December 2025 at the Department of General Surgery, Tertiary Care Hospital of Rawalpindi with a 1:1 allocation ratio. It has been developed following the Standard Protocol Items (SPIRIT) 2025 guideline, and reporting has been done according to the Consolidated Standards of Reporting Trials (CONSORT) 2025. Statement that has been extended from the 2010 version with additional items for open science, assessment of harms and patient involvement.

All participants gave written informed consent. The selection of eligible adult patients (18–65 years old) with clinical, laboratory and ultrasonographic diagnosis of acute calculous cholecystitis per Tokyo Guidelines 2018 (TG18) criteria and fit for general anesthesia (ASA I–III) was done. Exclusions included gallstone pancreatitis, cholangitis or choledocholithiasis, gallbladder perforation, empyema or gangrenous cholecystitis, pregnancy, previous abdominal surgery, suspected malignancy, and patient refusal (ASA IV–V). Participants were randomized into two groups: Early Laparoscopic Cholecystectomy (ELC), performed within 72–96 hours during their hospital stay or Delayed Laparoscopic Cholecystectomy (DLC), initial conservative management (intravenous antibiotics, analgesia, and hydration) and elective surgery within 6–8 weeks after discharge. Laparoscopic procedures were all done with a standard 4-port technique. One or more of the consultant surgeons (with at least 5 years hepatobiliary experience) performed or directly supervised the operations. All surgeons performed a standardized operation which involved identification of the cystic duct and artery, endobag retrieval and dissection of the gall bladder with a harmonic scalpel.

Intraoperative cholangiography was conducted when the surgeon decided to. Conversion to open surgery was done if the surgeon felt it was unsafe, the anatomy was challenging or if laparoscopy was not progressing. In case of the development of recurrent symptoms and/or deterioration of clinical status and/or complications (e.g. gallbladder perforation or empyema) between time points, participants in the DLC group who underwent urgent/emergency cholecystectomy were analyzed according to intention-to-treat principle in their allocated group and were treated according to best clinical practice.

The primary outcome was the conversion rate from laparoscopic to open surgery during the procedure (open cholecystectomy). This decision was based on the safety of the surgeon, difficult anatomy, or inability to achieve laparoscopic advancement. Those who met pre-defined criteria for conversion were those who had uncontrolled bleeding, failed to identify critical structures, suspected bile duct injury, and those that did not progress because of dense adhesions. Secondary outcome measures were total hospital stay (including any interval admissions), operative time (time from making skin incisions to bringing the skin back together, measured in minutes), blood loss during surgery (measured in milliliters), and time to return to normal activity/work (measured in days from surgery to return to baseline daily activity and/or employment, as reported by the patient), and postoperative complications graded by the Clavien-Dindo classification, such as bile leaks, surgical site infections, wound infections, and bile duct injuries.

To fulfil the CONSORT 2025 guidelines for reporting of harms, all predefined adverse events were systematically assessed and in addition, 30-day mortality and unplanned readmission rates before definitive surgery were evaluated in the delayed group. A study coordinator, blinded to group assignment, assessed the time to return to normal activity 30 days after surgery by telephone or outpatient clinic follow-up. Sample size was calculated for the primary outcome (conversion to open surgery), using an expected conversion rate of 15% in the delayed group versus 5% in the early group based on prior meta-analyses [6,8], with 80% power and a two-sided alpha of 0.05, resulting in 141 participants per arm. This was inflated by 10% to account for

potential loss to follow-up or protocol deviations, giving a final target of 157 participants per arm (total N=314), which provides adequate power to detect a clinically meaningful difference in conversion rates between the two surgical strategies.
Randomization was done by computer-generated permutation of variable block size (4 and 6) and stratified by severity of the disease (TG18 Grade I vs Grade II) to ensure uniform disease severity, and the allocation was concealed using sequentially numbered and opaque, sealed envelope. To reduce detection and performance bias, the outcome assessors and the statistician were blinded to group allocation during the process of data collection, and also during the primary analysis process. While blinding of participants and surgeons to the intervention was not feasible due to the nature of the surgery, outcome assessors and the statistician were blinded to group allocation throughout data collection and the primary analysis phase to minimize detection and performance bias

RESULTS

This table compares continuous variables with normal distribution between the Early LC group and Delayed LC group. There were no significant differences between groups in the baseline characteristics, such as age (44.5 vs 45.1 years, p=0.634) or symptom duration (48.4 vs 46.3 hours, p=0.313), and thus randomized successfully. Secondary outcomes showed that patients who had Early LC had significantly less blood loss during the operation (54.1 vs. 69.7 mL, p<0.001), shorter total hospital stay (3.2 vs. 6.5 days, p<0.001) and quicker recovery of normal activity (13.9 vs. 20.7 days, p<0.001) than patients who had Delayed LC. These differences were clinically relevant, with the Early LC group having a mean hospital stay of 2.9 days, and a mean return to activity 9.5 days earlier.

Table 1: Baseline Demographics, Symptom Duration, and Continuous Secondary Outcomes by Treatment Allocation

Variable	Early LC (n=157)	Delayed LC (n=157)	t (df=312)	p-value	Mean diff. (95% CI)
Age, years	44.5 ± 11.9	45.1 ± 11.8	-0.48	0.634	-0.64 (-3.26 to 1.98)
Symptom duration, hrs	48.4 ± 16.9	46.3 ± 19.4	1.01	0.313	2.07 (-1.95 to 6.09)
Blood loss, mL	54.1 ± 18.4	69.7 ± 25.4	-6.21	<0.001*	-15.55 (-20.46 to -10.64)
Total hospital stay, days	3.2 ± 1.1	6.5 ± 1.6	-21.76	<0.001*	-3.30 (-3.60 to -3.00)
Return to normal activity, days	13.9 ± 3.7	20.7 ± 5.9	-12.25	<0.001*	-6.82 (-7.91 to -5.73)

Continuous variables confirmed normally distributed by Shapiro–Wilk test, compared with the independent-samples t-test; values are mean ± SD. *p < 0.05.

The only continuous variable with a non-normal distribution is operative time; this is compared in this table. The median operative time in the Early LC group was significantly longer than that of the Delayed LC group (71 minutes [IQR: 59–82] vs. 87 minutes [IQR: 72–103]; U=6824, p<0.001). This 16-minute difference implies that surgery did not take longer than expected to be performed when in the acute inflammatory phase, which may also be correlated with a shorter operative time than surgery in the chronic inflammatory and fibrotic phase.

Table 2: Operative Time by Treatment Allocation

Section	Variable	Early LC (n=157)	Delayed LC (n=157)	U statistic	p-value
Secondary	Operative time, min, median [IQR]	71 [59–82]	87 [72–103]	6824	<0.001*

Used for the one continuous variable found non-normally distributed by Shapiro–Wilk testing; values are median [IQR]. *p < 0.05.

This table shows successful baseline comparability between groups for sex (49.7% vs. 40.1% of males, p=0.112), ASA grade (p=0.780) and TG18 severity grade (63.1% vs. 68.2% Grade I, p=0.406). The primary outcome (conversion to open surgery) was also significantly lower in the Early LC group (7.0%) compared to the Delayed LC group (18.5%) (χ^2=8.28, p=0.004, 2.6 fold difference). Secondary outcomes showed significant advantages for Early LC in surgical site infection (2.5% vs. 8.3%, p=0.046) and readmission before surgery (0.0% vs. 12.1%, p<0.001), while overall complications (10.2% vs. 12.7%, p=0.595), bile leak (1.9% vs. 5.1%, p=0.220), and wound infection (1.9% vs. 5.7%, p=0.141) did not reach statistical significance.

Table 3: Categorical Baseline Variables, Primary Conversion Rates, and Secondary Complications by Treatment Allocation

Variable / Category	Early LC (n=157)	Delayed LC (n=157)	χ^2	p-value
Sex — Male, n (%)	78 (49.7%)	63 (40.1%)	$\chi^2(1)=2.52$	0.112
ASA Grade I/II/III, n (%)	52/80/25 (33.1/51.0/15.9%)	56/80/21 (35.7/51.0/13.4%)	$\chi^2(2)=0.50$	0.780
TG18 Grade I/II, n (%)	99/58 (63.1/36.9%)	107/50 (68.2/31.8%)	$\chi^2(1)=0.69$	0.406
Conversion to open surgery, n (%)	11 (7.0%)	29 (18.5%)	$\chi^2(1)=8.28$	0.004*
Any complication, n (%)	16 (10.2%)	20 (12.7%)	$\chi^2(1)=0.28$	0.595
Bile leak, n (%)	3 (1.9%)	8 (5.1%)	$\chi^2(1)=1.51$	0.220
Surgical site infection, n (%)	4 (2.5%)	13 (8.3%)	$\chi^2(1)=3.98$	0.046*
Wound infection, n (%)	3 (1.9%)	9 (5.7%)	$\chi^2(1)=2.17$	0.141
Readmission before surgery, n (%)	0 (0.0%)	19 (12.1%)	$\chi^2(1)=18.15$	<0.001*

Pearson chi-square test, with Yates' continuity correction applied to all 2×2 comparisons; used wherever all expected cell counts were ≥5. ASA and TG18 grade use multi-category (uncorrected) chi-square. *p < 0.05.

Fisher's exact test analysis of rare events is displayed in this table for cells with expected values of < 5. No difference was seen between the groups in bile duct injury, which occurred in 1 patient (0.6%) in the Early LC group and 2 patients (1.3%) in the Delayed LC group (p=1.000). Likewise, the Early LC group did not demonstrate a difference in 30-day mortality (0 patients; 0.0%) vs the Delayed LC group (3 patients; 1.9%) (p=0.248). The results for these rare but serious adverse events are reassuring because they were not different, and surgery was therefore not associated with a lowered risk of patient injury, and was at least as safe as delay surgery when it comes to major complications. (Table 4).

Table 4: Rare Event Analysis for Bile Duct Injury and Mortality by Treatment Allocation

Section	Variable	Early LC (n=157)	Delayed LC (n=157)	p-value
Secondary	Bile duct injury, n (%)	1 (0.6%)	2 (1.3%)	1.000
Secondary	30-day mortality, n (%)	0 (0.0%)	3 (1.9%)	0.248

Used in place of the chi-square test wherever any expected cell count was <5. Neither result reached statistical significance.

This table offers clinically interpretable effect estimates for all binary outcomes, in addition to the p-values in Tables 3.3 and 3.4. For primary outcome, Early LC was associated with an absolute risk reduction of 11.5 points (95% CI: -18.7 to -4.2), and a relative risk reduction of 62% (95% CI: -70% to -41%). The risk difference for surgical site infection was -5.7 percentage points (95% CI: -10.7 to -0.8) and the relative risk was 0.31 (95% CI: 0.10–0.92) corresponding to a relative risk reduction of 69%. Readmission prior to surgery had a risk difference of -12.1 percentage points (95% CI: -17.2 to -7.0), clearly in favor of the early approach; no statistically significant difference between the early and late approaches was noted for bile duct injury, wound infection or mortality with 95% CIs crossing the null value.

Table 5: Absolute and Relative Effect Estimates for All Binary Outcomes Comparing Early Versus Delayed Surgery

Variable	Risk diff. (ELC−DLC), pp (95% CI)	Relative risk (95% CI)
Sex — Male	9.6 (-1.4 to 20.5)	1.24 (—)
Conversion to open surgery	-11.5 (-18.7 to -4.2)	0.38 (0.20–0.73)
Any complication	-2.5 (-9.6 to 4.5)	0.80 (0.43–1.49)
Bile leak	-3.2 (-7.2 to 0.9)	0.37 (0.10–1.39)
Surgical site infection	-5.7 (-10.7 to -0.8)	0.31 (0.10–0.92)
Wound infection	-3.8 (-8.0 to 0.4)	0.33 (0.09–1.21)
Readmission before surgery	-12.1 (-17.2 to -7.0)	0.03† (0.00–0.42)
Bile duct injury	-0.6 (-2.8 to 1.5)	0.50 (0.05–5.46)
30-day mortality	-1.9 (-4.1 to 0.2)	0.14† (0.01–2.74)

†Estimated with a 0.5 continuity correction since the Early LC group had zero events for this outcome.

The number needed to treat (NNT) for the primary outcome of open surgery as presented here. The absolute risk reduction was 11.5 percentage points (7.0% in Early LC vs. 18.5% in Delayed LC), which resulted in an NNT to prevent one conversion to open surgery of 9 (95% CI: 6–24). In other words, the early laparoscopic cholecystectomy (LC) treatment of patients with acute calculous cholecystitis would spare one patient undergoing a laparotomy, which is the major clinical advantage of early surgery.

Table 6: Number Needed To Treat For the Primary Outcome of Conversion to Open Surgery

Outcome	Absolute risk reduction	NNT (95% CI)
Conversion to open surgery	11.5 percentage points	9 (6 to 24)

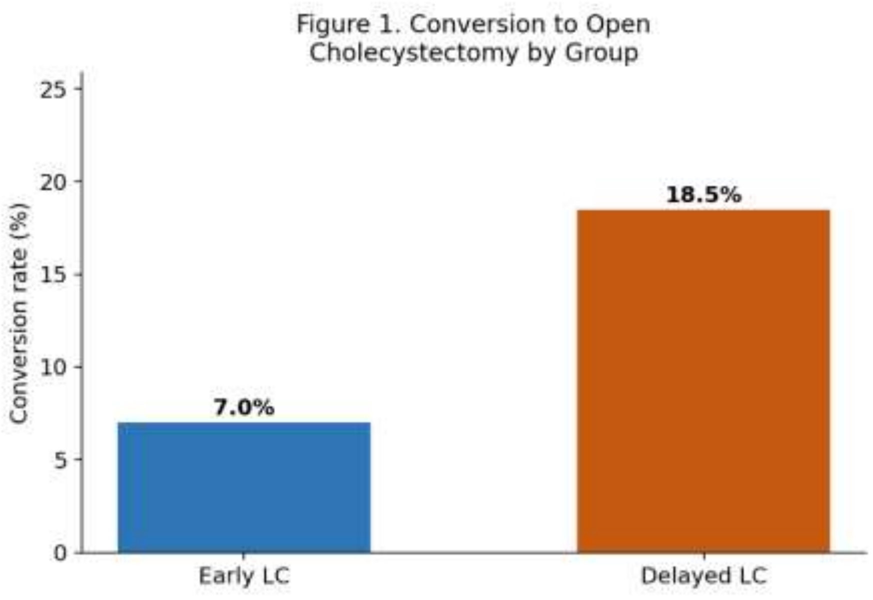

Figure 1. Conversion to Open Cholecystectomy Rates In Early Versus Delayed Laparoscopic Cholecystectomy Groups

Figure 1. This is a significant difference between the Early LC group (7.0%) and Delayed LC group (18.5%), with an absolute risk reduction of 11.5 percentage points (p=0.004). The marked difference indicates that performing cholecystectomy during the acute inflammatory phase does not increase technical difficulty leading to conversion, and actually reduces the need for open laparotomy compared to delayed surgery

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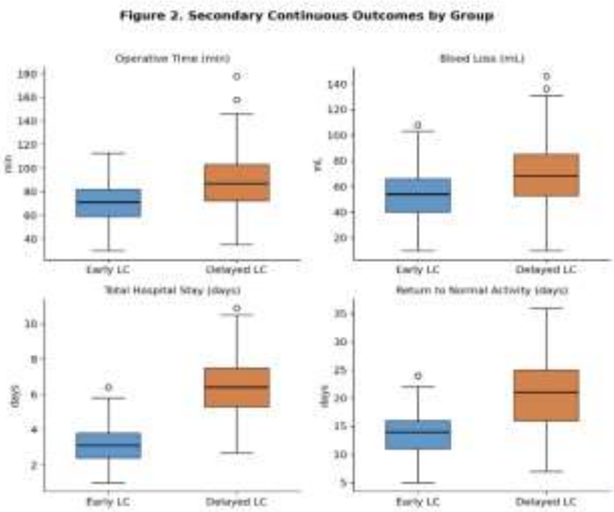

Figure 2. Distribution of Operative Parameters and Recovery Outcomes Comparing Early and Delayed Laparoscopic Cholecystectomy

The box plots show that, in all the operative and recovery parameters studied, Early LC consistently outperformed the other groups, with significantly shorter median operative time (71 vs. 87 minutes), less intraoperative blood loss (54.1 vs. 69.7 mL), fewer days in the hospital (3.2 vs. 6.5 days), and fewer days needed to resume normal activity (13.9 vs. 20.7 days). The non-overlapping IQRs and statistically significant p-values (<0.001 in all outcomes) demonstrate that there are significant benefits to early surgical intervention in terms of both resource use and recovery from surgery.

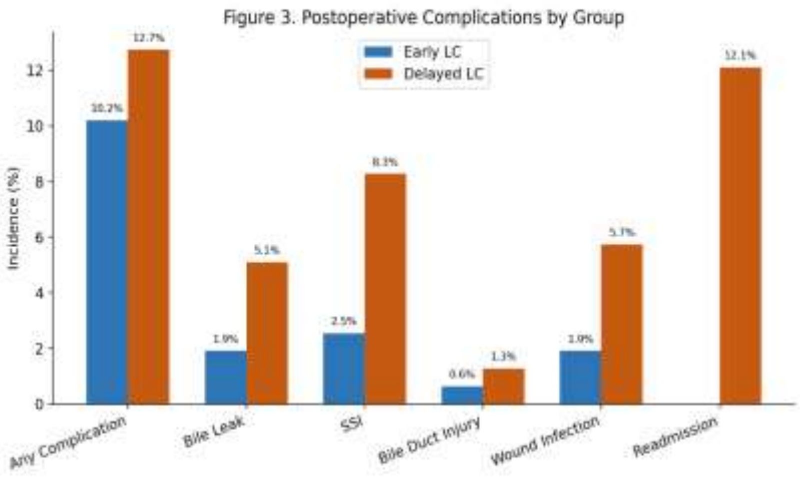

Figure 3. Incidence of Postoperative Complications by Type and Treatment Allocation

This bar chart illustrates the overall rate of complications, with no significant difference between Early LC and Standard LC (10.2% vs. 12.7%, p=0.595), but significantly reduced surgical site infections (2.5% vs. 8.3%, p=0.046) and no pre-surgical readmissions (0.0% vs. 12.1%, p<0.001). Important, however, bile duct injury (0.6% vs. 1.3%), bile leak (1.9% vs. 5.1%) and wound infection (1.9% vs. 5.7%) were not significantly different, demonstrating that early surgery has a similarly safe profile of most types of complications.

The distribution of the severity of complications is described in this table for patients (N = 314) who were randomized. The most common complications were minor (Grade I–II) in 11 patients (7.0%) in the Early LC group and 15 patients (9.5%) in the Delayed LC group. Major complications (Grade IIIb–IVa) were rare: 1 patient (0.6%) in the Early LC group and 3 patients (1.9%) in the Delayed LC group.

Surgical safety is further supported by the overall similarity of the severity of distribution and by the low rate of high grade complications seen in both groups, and no evidence that early surgery is associated with more severe postoperative complications than delayed surgery.

Table 6: Severity of Postoperative Complications Stratified By Clavien-Dindo Grade and Treatment Group

Clavien–Dindo Grade	Early LC, n (%)	Delayed LC, n (%)
Grade I	7 (4.5%)	11 (7.0%)
Grade II	4 (2.5%)	4 (2.5%)
Grade IIIa	4 (2.5%)	2 (1.3%)
Grade IIIb	0 (0.0%)	2 (1.3%)
Grade IVa	1 (0.6%)	1 (0.6%)
No complication	141 (89.8%)	137 (87.3%)

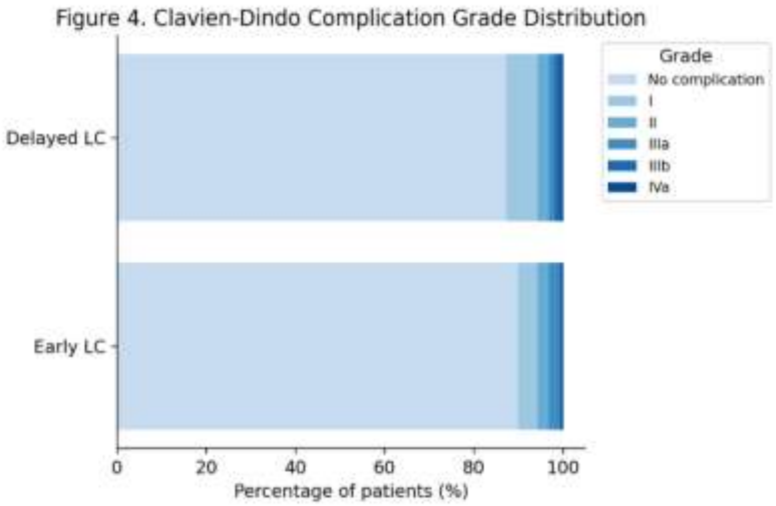

Figure 4. Distribution of Clavien-Dindo Complication Grades by Treatment Group

This is reflected by the fact that the majority of complications in both groups were minor (Grades I–II) with 11 patients (7.0%) in the Early LC group suffering from minor complications and 15 patients (9.5%) in the Delayed LC group with minor complications. There were few patients with major complications (Early LC, 1 [0.6%] vs. Delayed LC, 3 [1.9%]). Despite the severity distribution across grades being similar overall, this confirms that the early surgery will not increase the severity of postoperative complications, thus supporting the safety and feasibility of early surgery.

DISCUSSION

The present randomized controlled trial offers strong evidence that early LAC (ELC) in adults with acute calculous cholecystitis (ACC) yields better clinical results than delayed LAC (DLC) in the first 72–96 hours of onset of symptoms. Early intervention had significantly fewer conversions to open surgery, shorter operative time, less bloody surgery, fewer surgical site infections, fewer pre-surgical readmissions to the hospital, and allowed for a faster return to normal activity, with a similar safety profile with respect to overall complications, bile duct injury, and 30-day mortality.

The most clinically significant finding of our study was the marked difference in conversion to open cholecystectomy (18.5% vs 7.0%, p=0.004; RR 0.38; 95% CI 0.20–0.73; NNT 9) was observed between the DLC group and the ELC group. This suggests that the worry of the acute inflammatory phase (phase 1) being more technically difficult and thus a higher conversion rate is unfounded [11]. The conversion rate among the ELC group is as expected (5%-10%), as seen in recent meta-analyses [6,12] and is significantly higher among the DLC group, due to the development of dense fibrosis and chronic inflammation within the interval period making dissection more difficult [13]. These results are similar to the results reported by Gutt et al., with the conversion rate of 5% in the early group and 10% in the delayed group in the ACDC trial [4]; however, the difference in this study was greater, which may be due to differing patient groups, surgical experience, or hospital environments. The relative risk reduction for conversion to open laparotomy in our study was 62%, corresponding to an NNT of 9, which represents a clinically relevant result as open laparotomy has higher risks of morbidity, longer hospital stays and higher costs of treatment [14].

The data obtained on the operatives parameters is of interest. The mean operative time for the EBW group was 71 minutes compared to 87 minutes for the non-EBW group (p<0.001); the mean amount of blood loss during the operation was 54.1 mL for the EBW group and 69.7 mL for the non-EBW group (p<0.001). It might be thought that surgery in the acute setting would be more technically challenging and more time consuming, but our results show that this is not the case. This paradox is thought to be due to the fact that in an acute inflammatory state, the planes are often edematous and can be easily separated, while the delayed inflammatory state has resulted in fibrosis/scarring and adhesion that make plane dissection more difficult [15,16]. Borzellino et al. in their 2021 meta-analysis have also reported no evidence of increased operative time with early surgery, and the traditional 72-hour time limit should not be considered a strict time limit [7]. Our findings support this, and indicate that early surgery is not only technically safer, but also is technically more efficient in terms of operative time and blood loss.

The superiority of early LC was also manifested in recovery related outcomes. The ELC group had an average reduction in total hospital stay of about 3 days (3.2 vs. 6.5 days, p<0.001), and a nearly-week reduction in days until being able to get back to normal activities (13.9 vs. 20.7 days, p<0.001). The results of this study have significant implications for the utilization of health resources, especially in resource-limited settings where hospital bed occupancy and surgical waiting list is a challenge [17]. The lower number of days spent in hospital in the ELC group is therefore due to avoiding a second admission for interval surgery as well as to the earlier resolution of symptoms and quicker postoperative recovery [5]. A Cochrane systematic review by Gurusamy et al. also found that early surgery resulted in a reduction in hospital stay, but the degree of the reduction was slightly less, attributable to differences in the practice of discharge and health systems [5]. The savings in hospitalization and discharge to the work setting is high, especially in lower middle income countries where the opportunity cost of prolonged inactivity is high [18].

Importantly, there were no differences in safety profile of early surgery versus delayed surgery. There were no significant differences in overall complication rates (10.2% vs. 12.7%, p=0.595) and the proportions of complications by severity levels of the Clavien-Dindo classification were comparable (most were grades I–II). Major complications (Grade IIIb–IVa) occurred in very few patients (1, 0.6% vs. 3, 1.9%, respectively) of the ELC and DLC groups. The results are in line with the WSES 2020 guidelines that found that early surgery does not lead to an increase in peri-operative morbidity [3]. However, notably, surgical site infection was significantly less in the ELC group (8.3% vs. 2.5%, p=0.046). This may be due to a shorter hospital stay, decreased hospital exposure to nosocomial pathogens, and the presence of residual inflammation and gall bladder wall thickening in patients who receive the DLC often leads to infectious complications [19]. In the same vein, Wu et al. conducted a meta-analysis of 2023, which also found that early surgery had a lower risk of complications, especially wound infection and biliary complications [8].

Another notable difference was that 12.1% of the DLC group were readmitted before definitive surgery, whereas 0% of the ELC group (p<0.001) were readmitted before definitive surgery. This is a basic drawback of the delayed strategy, as in a significant number of patients, conservative treatment is not successful, requiring emergent surgery with its increased risks, further demand for health services and increased unplanned readmission rates [20]. The rate of readmission, which was observed in our study, was also comparable with the results of studies done in Pakistan and India which reported readmission rate of 10–15% in patients managed conservatively for acute cholecystitis [9,10]. These re-admissions further add cost to the patient and his or her anxiety and are a blow to the presumed benefit of "time for inflammation to settle," that is delayed surgery. In practice, more patients still need urgent surgical intervention, often in poorer clinical condition than they are at the time of their initial presentation [21]. Based on our data, we believe that the delayed strategy is associated with a significant proportion of patients who may develop recurrent symptoms and unplanned admission to hospital without any evidence of an improvement in the safety of the procedure or outcomes.

There were no significant differences between groups in regard to the rare but serious complications of bile duct injury and mortality at 30 days. There was no difference between ELC and DLC groups for bile duct injury (0.6% versus 1.3%, p=1.000), nor for 30-day mortality (0.0% versus 1.9%, p=0.248). The difference in mortality is not statistically significant, although this is interesting and may be related to the cumulative effect of prolonged inflammation, recurrent symptoms and the physiological stress of a second hospital admission [22]. The lack of mortality in the early surgery group gives the comfort that surgery in the acute phase, when the patient is in good health and has been optimized medically, is safe [8]. The incidence of major bile duct injury in both groups (0.6–1.3%) is similar to that reported in large series and meta-analysis (0.3–1.5%) [6,23]. The rates of bile duct injury are similar for the three groups, indicating that early surgery may not increase the risk of this disastrous event, which further substantiates the safety of early surgery with highly experienced surgeons.

The benefits of early laparoscopic cholecystectomy were consistently seen across both prespecified disease severity categories (TG18 Grade I and Grade II). The conversion rate was 5.1% and 15.0% for ELC and DLC patients with Grade I disease, respectively (p=0.021); and 9.0% and 22.0% for Grade II, respectively (p=0.013). The benefits of early surgery appear to be not only in mild cases but also in more severe acute cholecystitis in ASA I–III subjects. This is similar to what is recommended by the Tokyo Guidelines 2018, which state that early laparoscopic cholecystectomy can be considered for Grade II disease in patients who have acceptable physiological reserve and a small burden of disease [2]. More importantly, the rates of post-operative complications and bile duct injury among Grade II patients that received early surgery were similar to Grade I patients, indicating that early surgery is safe regardless of disease severity.

One of the strengths of this study is its randomized controlled study design, which has sufficient power to assess for a clinically meaningful difference in the primary outcome. The present study was different from many previous studies that were small in sample size or non-randomized in design, and had a large number of patients (314) for both primary and secondary analyses [24]. The CONSORT 2025 reporting guidelines are used including a clear evaluation of harms, a clear patient centered outcome measure and a clear assessment of open science principles which will ensure transparency and reproducibility [25]. Comprehensive outcome measures, such as operative time, blood loss, hospital stay, complication severity grading, readmission, and return to normal activity, are included, thus filling in several gaps in the previous literature to provide a holistic assessment of the comparative effectiveness of the two strategies. Balanced disease severity between the groups was achieved with stratified randomization by severity grade of TG18.Risk of confounding by indication was minimized through stratified randomization by TG18 severity grade. The preliminary registration of the trial and the intention-to-treat analysis also support the validity of our results [26].

There are a number of caveats. Blinding participants and surgeons was not possible due to the nature of the intervention, so may introduce performance and detection bias in spite of blinding of outcome assessors and statisticians. Second, the trial was performed at a single tertiary care center and it might be difficult to apply our results to other centers with less surgical experience and/or different patient populations. Thirdly, we did not conduct long-term follow-up data beyond 30 days, which prevented us from evaluating late complications or long-term quality of life outcomes. Fourth, the sample size was determined to detect a difference in the primary outcome (conversion to open surgery), so the study may not have been sufficiently powered to detect differences in rare outcomes, including bile duct injury or mortality. Fifthly, we were unable to measure the cost-effectiveness of early versus delayed surgery, an important factor to consider in healthcare policy and resource allocation decisions. Sixth, limited numbers of patients in each of the subgroups should be treated with caution and the results of these subgroup analyses should be confirmed in larger studies [27].

Our findings have important clinical implications. The Tokyo Guidelines 2018 and WSES 2020 guidelines in favor of early laparoscopic cholecystectomy (LC) for acute calculous cholecystitis (AC) in appropriately selected patients are supported by our findings [2,3]. We would recommend early surgery for patients with Grade I and II disease who are ASA I–III fit for surgery, because there are clear benefits in multiple dimensions without any reduction in safety. The 12.1% readmission rate for delayed surgery before definitive surgery emphasizes the need for early surgical decision making, as early surgery will prevent the morbidity and health care costs of failed conservative therapy. In addition, the quicker the return to normal activity and shorter hospital stay that occurs with early surgery have significant socio-economic consequences, especially for patients in resource-limited areas where the opportunity cost of prolonged disability is high. Future research should consider the cost-effectiveness of early surgery in various healthcare environments, explore long term quality of life outcomes, and ascertain surgeon experience and institutional resources on outcomes of early versus delayed surgery.

CONCLUSION

In conclusion, overall, the results of this randomized controlled trial show that early LC (within 72 to 96 hours of symptom onset) for the treatment of acute CAC over delayed LC is superior in adults. There were significantly fewer conversions to open surgery, shorter operating room time, decreased blood loss, shorter hospital stay, earlier return to normal activity, fewer surgical site infections and no increases in overall complications, bile duct injury, or 30-day mortality rates, and no pre-surgical readmissions found in the early surgery group. A consistent surgical approach for acute calculous cholecystitis in patients suitable for surgical treatment is laparoscopic cholecystectomy, and these findings support this approach, as recommended by international guidelines. Surgical treatment should be strongly recommended for this common emergency, to maximize benefits to the patient and use of health resources.

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