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Optimal timing for cholecystectomy following percutaneous cholecystostomy: insights from a multicenter retrospective cohort study

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Contributions

AP, CR, MM, JCT, SM, GP, RM, GC, VM, FC, GC, CS, FR, MY, and AR contributed in collecting and analyzing data. AP, CR, and RC contributed in writing the manuscript. AG, BC, and AL contributed in reviewing the literature data. AP, CR, VD, and RC supervised the project and collaborated in drafting the manuscript. All the authors approved the current version of the manuscript.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Abstract

Laparoscopic cholecystectomy is the standard of care for patients with acute cholecystitis. However, in high-risk surgical candidates who do not respond to conservative management, percutaneous cholecystostomy is recommended. When used as bridge therapy, the optimal timing for performing laparoscopic cholecystectomy as definitive treatment still remains uncertain. The primary outcome of this study was to assess the incidence of major perioperative complications, defined as Clavien–Dindo grade ≥ III. A retrospective, multicenter, observational cohort study was conducted across nine hospitals—seven in Italy and two in Colombia. We reviewed the medical records of all patients who underwent cholecystectomy following percutaneous cholecystostomy at the participating institutions between January 2020 and December 2024. Patients were stratified into two groups based on the 50th percentile (median) of the time interval between procedures, which was 59 days. Accordingly, the groups were defined as ≤ 59 days (approximately ≤ 8 weeks) and > 59 days (approximately > 8 weeks). A total of 123 patients were included in the study. The median age was 75.0 years, and the majority were male (56.1%). Logistic regression analysis showed that older age and an open surgical approach were significantly associated with a higher risk of major complications. The time interval between cholecystostomy and cholecystectomy was not significantly associated with the risk of major complications in any model. However, in the sensitivity analysis—after excluding outliers above the 95th percentile and below the 5th percentile—the incidence of major complications was 21.1% in the ≤ 8 weeks group versus 11.3% in the > 8 weeks group, without statistically significant differences ($p = 0.262$). The results of this study suggest that, within the observed range of intervals, no definitive advantage can be attributed to either earlier or delayed surgery based solely on timing. There remains a critical need for a rigorously designed, multicenter prospective study to determine the optimal timing of surgery based on clinically meaningful endpoints.

Keywords Laparoscopic cholecystectomy · Percutaneous cholecystostomy · Surgical risk · Optimal timing · Bridge to surgery · Postoperative complications

Introduction

Laparoscopic cholecystectomy is the standard of care for patients with acute cholecystitis. However, in high-risk surgical patients who do not respond to conservative management, percutaneous cholecystostomy is recommended [1]. Depending on the patient's clinical condition, cholecystostomy may serve either as definitive treatment or as a bridge to surgery. When used as a bridge therapy, the optimal timing for performing laparoscopic cholecystectomy as definitive management remains unclear [1]. Following percutaneous cholecystostomy, certain therapeutic goals should be met before considering cholecystectomy: (1) resolution of the infectious source and sepsis, (2) stabilization and optimization of comorbidities that initially contraindicated surgery, and (3) physical rehabilitation and prehabilitation in preparation for a subsequent procedure [1]. Using cholecystostomy as definitive treatment presents significant challenges, including the risk of recurrent disease and a potential decline in quality of life. Therefore, decisions must consider life expectancy, the anticipated difficulty of cholecystectomy, individual patient risks, and patient preferences to support a shared decision-making approach [2–5]. In this context, the objective of this study was to explore the optimal timing for performing laparoscopic cholecystectomy after percutaneous cholecystostomy

Materials and methods

Design study

A retrospective, multicenter, observational cohort study was conducted across nine hospitals—seven in Italy and two in Colombia. The Italian Society of Research in Surgery (SIRC) established a registry for patients who have undergone percutaneous cholecystostomy. This registry has been approved by the Institutional Ethics Committee approval of the University of Perugia (ID: 151.944-02/05/2024). The study was reported in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines [6]. We reviewed the medical records of all patients who underwent cholecystectomy following percutaneous cholecystostomy at the participating institutions between January 2020 and December 2024. Patients were excluded if data were missing regarding either the time interval between procedures or the occurrence of complications, which was our primary outcome. Eligible patients were categorized into two groups based on the median time between cholecystostomy and cholecystectomy. Patients were stratified into two groups based on the 50th percentile (median) of the time interval between procedures, which was 59 days. Accordingly, the groups were defined as ≤ 59 days (approximately ≤ 8 weeks) and > 59 days (approximately > 8 weeks). The following variables were collected and analyzed: patient demographics, American Society of Anesthesiologists (ASA) Physical Status classification, Charlson Comorbidity Index (CCI), severity of cholecystitis according to the Tokyo Guidelines 2018 (TG18), leukocyte count, surgical approach (laparoscopic, conversion to open, or primary open surgery), need for subtotal cholecystectomy, length of hospital stay, and the occurrence of major complications (defined as Clavien–Dindo grade ≥ III). Follow-up continued until either the first postoperative outpatient visitor in-hospital death, whichever occurred first.

Statistical analysis

A comprehensive analysis was conducted using demo graphic, clinical, and surgical variables. Categorical variables were summarized as percentages, while continuous variables were reported as medians with corresponding interquartile ranges (IQR). Bivariate analyses were per formed to assess differences according to the timing of cholecystectomy, using the Chi-squared test for categorical variables and the Mann–Whitney U test for continuous variables. The timing of cholecystectomy was categorized based on whether it occurred above or below the 50th percentile. To identify factors associated with major complications (defined as Clavien–Dindo grade ≥ III), a binary logistic regression model was employed. We generated several models: one without interactions, one including an interaction between ASA and time to surgery, another including an interaction between the Charlson Comorbidity Index and time to surgery, and a final model treating time as a continuous variable. The percentage of missing data was 1.9% for ASA classification and 13% for the Charlson Comorbidity Index; these values were imputed using multiple imputation with predictive mean matching. A p value of < 0.05 was considered statistically significant. All statistical analyses were performed using R software (version 2023.12.1 + 402). A sensitivity analysis was conducted by excluding extreme values, specifically observations above the 95th percentile and below the 5th percentile

Results

A total of 123 patients were included in the study. The median age was 75.0 years (IQR 69.0–81.0), and the majority were male (56.1%). The rate of major complications was 22.2% (95% CI 11.9–32.4%) in the ≤ 8 weeks group and 10.0% (95% CI 2.4–17.6%) in the > 8 weeks group (Table 1). The distribution of the timing of cholecystectomy after per cutaneous cholecystostomy is shown in Fig. 1. A binary logistic regression analysis was conducted to identify factors associated with major complications following cholecystectomy after cholecystostomy. An open surgical approach was consistently associated with a significantly higher risk of major complications across all evaluated models. In contrast, the time interval between cholecystostomy and cholecystectomy was not significantly associated with the risk of major complications in any model. Similarly, variables such as ASA classification and the Charlson Comorbidity Index were not significantly associated with major complications. Older age was statistically significant only in the model that included a multiplicative interaction between ASA and time to surgery, treated as a continuous variable (OR 1.08, 95% CI 1.01–1.18). In all other models, age did not emerge as a significant predictor (Table 2). In the sensitivity analysis, after excluding outliers above the 95th percentile and below the 5th percentile, the incidence of major complications was 21.1% (95% CI 10.5–31.7%) in the ≤ 8 weeks group compared to 11.3% (95% CI: 2.8-19.8%) in the > 8 weeks group. This differ ence was not statistically significant in either the bivariate analysis ($p = 0.262$) or the multivariate analysis ($p = 0.216$), which is consistent with the results obtained when analyzing the full dataset (Supplement 1).

Fig. 1 Histogram time to surgery

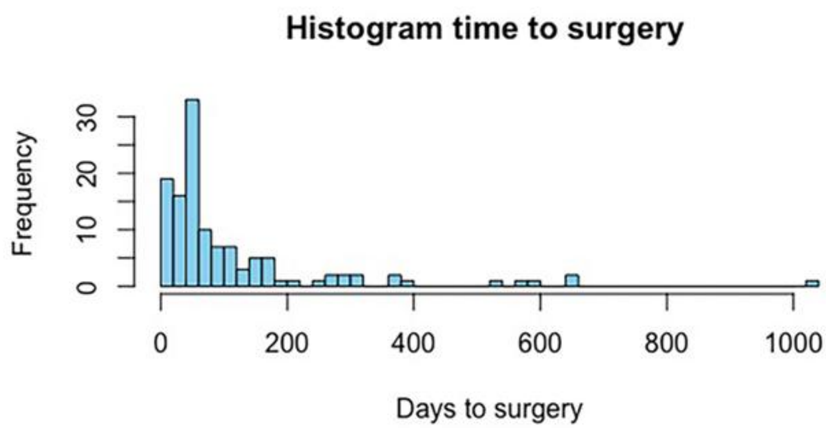

Table 1 Demographic, clinical, and surgical characteristics according to the timing of cholecystectomy

	N (%)	≤ ~ 8 weeks (n=63)	> ~ 8 weeks (n=60)	p value	Standardized difference
Age (median) (IQR) (years)	75.00 (69.00–81.00)	75.00 (70.00–80.50)	74.50 (69.00–82.00)	0.781*	0.13
Sex				1	0.125
Female	54 (43.9)	28 (44.4)	26 (43.3)		
Male	69 (56.1)	35 (55.6)	34 (56.7)		
ASA				**0.001**	0.775
I	4 (3.3)	0 (0.0)	4 (6.7)		
II	10 (8.1)	4 (6.3)	6 (10.0)		
III	88 (71.5)	41 (65.1)	47 (78.3)		
IV	21 (17.1)	18 (28.6)	3 (5.0)		
Charlson comorbidity index (median) (IQR) (points)	6.00 (5.00–7.00)	6.00 (5.00–7.00)	5.00 (4.00–7.00)	**0.017**	0.561
Tokyo classification				**0.023**	0.482
I	6 (4.9)	0 (0.0)	6 (10.0)		
II	51 (41.5)	30 (47.6)	21 (35.0)		
III	66 (53.7)	33 (52.4)	33 (55.0)		
Leukocytes ($\times 10^3$)		15.0 (10.6–18.7)	13.6 (9.6–18.1)	0.706	0.023
Approach				0.455	0.283
Laparoscopic	92 (74.8)	46 (73.0)	46 (76.7)		
Conversion to open	10 (8.1)	7 (11.1)	3 (5.0)		
Open	21 (17.1)	10 (15.9)	11 (18.3)		
Subtotal cholecystectomy				0.713	0.237
No	105 (85.4)	55 (87.3)	50 (83.3)		
Yes	18 (14.6)	8 (12.7)	10 (16.7)		
Length of stay (median) (IQR) (days)	4.00 (3.00–10.00)	4.00 (3.00–10–50)	3.50 (1.00–9.00)	0.055	0.144
Major complication (Clavien–Dindo ≥ III)				0.111	0.267
No	103 (83.7)	49 (77.8)	54 (90.0)		
Yes	20 (16.3)	14 (22.2)	6 (10.0)		

Patients who underwent surgery within ≤ 8 weeks demonstrated a higher proportion of ASA class 3–4 status, greater severity of cholecystitis (Tokyo II and III), and higher Charlson Comorbidity Index scores. Regarding surgical outcomes, these patients also exhibited longer hospital stays and a higher incidence of complications compared to those who underwent surgery after > 8 weeks. p values were obtained using the Chi-squared test. Bold values indicate statistically significant p values ($p < 0.05$)

*p values were obtained using the Mann–Whitney U test

Table 2 Binary logistic regression model to identify factors related to major complications

	Model 1[a] OR (CI 95%)	Model 2[b]	Model 3[c]	Model 4[d]
Age	1.07 (1.00–1.16)	**1.08 (1.01–1.18)**	1.08 (1.00–1.17)	1.08 (1.00–1.17)
ASA				
I–II	Reference	Reference	Reference	Reference
III–IV	0.84 (0.12–17.0)	10.0 (0.25–1704)	1.09 (0.16–21.9)	1.10 (0.16–22.0)
Charlson comorbidity index	1.20 (0.84–1.74)	1.24 (0.84–1.85)	1.15 (0.73–1.86)	1.21 (0.84–1.77)
Approach				
Laparoscopic	Reference	Reference	Reference	Reference
Conversion to open	1.23 (0.06–9.64)	1.48 (0.07–12.7)	1.37 (0.06–10.9)	1.35 (0.06–10.8)
Open	**5.93 (1.77–20.9)**	**5.38 (1.61–18.5)**	**5.49 (1.66–18.7)**	**5.38 (1.63–18.2)**
Time to surgery		1.02 (0.98–1.04)	0.99 (0.96–1.01)	1.00 (0.99–1.00)
≤ ~ 8 weeks	Reference			
> ~ 8 weeks	0.37 (0.11–1.17)			
Time to surgery*ASA III-IV		0.98 (0.95–1.01)		
Time to surgery*Charlson comorbidity index			1.15 (0.73–1.86)	

Bold values indicate statistically significant

[a]Model without interactions

[b]Model with a multiplicative interaction between ASA and time to surgery as a continuous variable

[c]Model with a multiplicative interaction between Charlson comorbidity index and time to surgery as a continuous variable

[d]Model without interactions using time to surgery as a continuous variable

Discussion

This study investigated the optimal timing for laparoscopic cholecystectomy following percutaneous cholecystostomy by categorizing patients based on whether surgery was performed within or beyond approximately 8 weeks. Across all models, no association was observed between early and delayed surgery regarding complications rates, and this finding remained consistent after excluding outliers in the sensitivity analysis ($p = 0.262$). These findings suggest that, within the observed range of intervals, no clearly superior timing strategy can be identified in terms of major perioperative outcomes. A significant proportion of patients in our cohort underwent cholecystectomy more than 6 months after percutaneous cholecystostomy. This delay highlights the multifactorial nature of surgical scheduling in real-world clinical practice. In some cases, late intervention was driven by clinical fac tors such as patient frailty, active comorbidities requiring stabilization, or poor functional status. In others, organizational issues—such as limited operating room availability, prioritization of urgent or oncologic cases, or delays in outpatient follow-up—were the main contributors. Collectively, these scenarios illustrate how surgical timing often reflects a dynamic interplay between patient-specific and system level factors. This real-world variability enhances the interpretability of study findings by emphasizing that surgical timing is not determined solely by predefined intervals, but rather by a complex interaction of clinical trajectories, institutional resources, and care continuity. Accordingly, the modest differences observed between early and delayed groups should be interpreted within this broader healthcare context. To assess postoperative complications, we used the Clavien–Dindo classification, an internationally validated and reproducible framework, for grading surgical adverse events [7]. This approach enabled consistent comparisons across institutions with varying documentation systems. Our analysis focused on major complications, defined as Clavien–Dindo grade ≥ III. Logistic regression identified the open surgical approach as the only variable consistently associated with an increased risk of major complications. In addition, older age reached statistical significance in certain models. Although specific complications—such as bile duct injury or intra-abdominal abscess—were not analyzed individually, the use of a severity-based classification ensured analytical consistency and reproducibility. Nevertheless, we acknowledge that future prospective studies should incorporate standardized coding of individual complications to improve clinical interpretability and benchmarking accuracy. Age emerged as an independent risk factor for major com plications. Older patients typically have reduced physiological reserves and a higher burden of comorbidities, which can increase the likelihood of challenging cholecystectomies, the need for bailout procedures, and, consequently, postoperative complications [8, 9]. In addition, an open surgical approach was identified as an independent predictor of major complications. Since the introduction of laparoscopic cholecystectomy, open surgery has become less favored due to its association with poorer postoperative outcomes [10]. Our study reported a relatively high rate (17.1%) of upfront open procedures. This finding should be interpreted within the context of real-world clinical practice across a multicenter cohort comprising tertiary referral hospitals that routinely manage patients with complex anatomical and clinical profiles. In many of these cases, the surgical teams deliberately chose an open approach preoperatively, based on individualized assessments. Contributing factors included giant incisional hernias, extensive prior abdominal surgery with anticipated dense adhesions, and radiological evidence of severe local inflammation or other high-risk features. These scenarios underscore the inherent heterogeneity of surgical decision-making in high-risk populations, where the primary objective is to minimize intraoperative complications and ensure procedural safety. The choice to forego a laparoscopic attempt was not arbitrary but rather a risk-adjusted strategy intended to reduce the likelihood of intraoperative conversion or increased morbidity. This highlights the potential divergence between protocol-driven recommendations and the nuanced clinical judgments required in complex, real-world settings. We believe that recognizing this variability provides valuable insight into contemporary surgical practice. It underscores the importance of flexible, context-sensitive guidelines that account for patient-specific complexity, sur geon expertise, and institutional capabilities—rather than rigid adherence to standardized algorithms. Currently, the available evidence offers limited consensus on the optimal timing for laparoscopic cholecystectomy following percutaneous cholecystostomy. One of the most influential studies on this topic, conducted by Woodward et al. [11] using a national registry, found that performing interval cholecystectomy within the first month after cholecystostomy was associated with higher complication rates. Beyond this period, no significant differences in complication risk were observed. Interestingly, in their institutional cohort, higher complication rates were noted when surgery was delayed beyond 8 weeks. Based on findings from both the national and institutional cohorts, the authors proposed an optimal surgical window between 4 and 8 weeks. However, the institutional cohort was limited by a small sample size (n = 68) and lacked adjustment for potential confounders [10]. Another notable registry-based study by Altieri et al. [12], involving 2998 patients, reported that early cholecystectomy (< 8 weeks) was associated with higher overall complication rates and longer hospital stays [12]. In contrast, Noubani et al. [13], analyzing data from the same registry over a different time period, stratified patients into quartiles based on the interval between cholecystostomy and surgery. They found that cholecystectomy performed between 5 and 12 weeks (second and third quartiles) was associated with shorter hospital stays (3 vs. 5 days). However, hospital stay is a relatively soft endpoint, and no adjustments for multiple comparisons were made [13]. Giannopoulos et al. [14], in a study involving 132 patients, found that a longer interval between cholecystostomy and cholecystectomy was associated with increased intensity care unit (ICU) stay. However, no statistically significant differences in complication rates were observed when comparing patients undergoing surgery at ≤ 8 weeks versus > 8 weeks [14]. Spaniolas et al. [15] also investigated this issue; however, their study had several methodological limitations, as pointed out in a recently published commentary [16].

Notably, the authors failed to adjust for multiple comparisons despite dividing patients into four groups. They suggested an optimal window within 7 weeks based on lower complication rates, although this conclusion should be interpreted with caution [16]. More recently, Kujirai et al. [17] analyzed 259 patients and found that earlier surgery was associated with a reduced risk of surgical complications. Among patients who experienced complications, the median timing of surgery was 12 days (IQR 7–14), compared to 8 days (IQR 6–10) in those without complications [17].

Other studies examining very early cholecystectomy— within 48 h or within 3, 7, 9, 10, or 13 days of cholecystostomy—have produced mixed results. These investigations were typically single-center studies with small sample sizes [17–23]. Performing surgery shortly after cholecystostomy can also be clinically challenging, as essential therapeutic goals—such as infection control, optimization of comorbidities, and patient rehabilitation—may not yet have been achieved. Supporting this concern, a registry-based study found better outcomes when cholecystectomy was per formed between days 7 and 26 after cholecystostomy [24]. In the most recently published study, Wael et al. [25] analyzed 58 patients initially managed with percutaneous transhepatic gallbladder drainage followed by laparoscopic cholecystectomy. Patients were divided into two groups: one undergoing early surgery (within 7 days) and the other delayed surgery (6–8 weeks later). The study did not report significant differences in operative time, complications related to percutaneous cholecystostomy, or major perioperative complications between the two groups [25]. However, the total length of hospital stay was significantly shorter in the early intervention group. The authors concluded that percutaneous cholecystostomy is a safe option for high-risk patients and that early laparoscopic cholecystectomy can be safely performed in well-selected individuals. The current literature exhibits considerable heterogeneity in study design, patient populations, and proposed optimal timing for laparoscopic cholecystectomy following percutaneous cholecystostomy. This variability, coupled with methodological limitations, hinders the establishment of a universally accepted “safe” timing window. In light of these challenges, our findings support the perspective that surgical timing should not be governed by rigid, calendar-based thresholds. Rather, we advocate for a more nuanced, goal-directed approach in which cholecystectomy is undertaken once key therapeutic milestones—such as infection control, clinical stabilization, and optimization of comorbid conditions—have been met. This strategy is better aligned with the complexities of high-risk surgical care, where patient trajectories and institutional capacities frequently diverge.

Limitations and strength

The current study has several limitations. First, its retrospective design introduces the risk of selection bias and unmeasured confounding. Second, the timing of cholecystectomy was determined by clinical judgment rather than randomization, potentially leading to indication bias. Specifically, sicker patients may have been triaged to later surgery, which could confound the relationship between timing and outcomes. Third, although the study was multicentric, the overall sample size was modest, potentially limiting statistical power. Lastly, variations in perioperative protocols across centers could not be fully controlled. We also acknowledge that individual surgical complications—such as hemorrhage, bile duct injury, or abscess formation—were not analyzed separately. The decision to use the Clavien–Dindo classification as the primary outcome measure was aimed at ensuring analytical consistency across centers and was aligned with our primary objective of evaluating complication severity in relation to surgical timing. Nonetheless, more granular profiling of adverse events would likely enhance the clinical interpretability of future findings. However, despite these constraints, we believe that this multicenter study reflects the complexity of real-world clinical practice, particularly the nuanced decision-making involved in determining surgical timing when percutaneous cholecystostomy is used as a bridge to definitive treatment. This flexible, goal-oriented approach may better support safe and individualized surgical care in high-risk patient populations

Conclusion

The results of this study suggest that, within the observed range of intervals, no definitive advantage can be attributed to either earlier or delayed surgery based solely on timing. Accordingly, we propose that clinical decisions regarding surgical timing should be guided by individualized therapeutic goals—such as resolution of infection, optimization of comorbidities, and overall patient readiness—rather than predetermined chronological thresholds. To establish more robust, evidence-based criteria for surgical timing, a rigorously designed multicenter randomized controlled trial or a large individual participant data metaanalysis remains essential.

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