Rationale of on admission surgical intervention on outcomes after cholecystectomy for mild gallstone pancreatitis

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Objectives
To evaluate the association of timing for cholecystectomy with clinical outcomes in patients with gallstone pancreatitis (GSP).
Background
Patients with mild GSP who undergo cholecystectomy sooner rather than later tend to have shorter hospital stays.
Patients and methods
From October 2019 to January 2023, the number of adult hospitalizations at Menoufia University Hospitals due to GSP was recorded. We classified patients into early (operated on within 2 days of admission) as well as late (operated on over 2 days after admission) groups based on when they had laparoscopic cholecystectomy. The date of cholecystectomy was then correlated with nonhome discharge, postoperative hospital length of stay, and readmission rate within a month of discharge using multivariable logistic and linear regression.
Results
An estimated 129 patients were admitted with acute GSP, and 25.6% of those admissions were classified as belonging to the early cohort. The remaining admissions were classified as belonging to the late cohort. After taking into account potential confounding factors, a late cholecystectomy was found to be linked with a greater risk of significant adverse outcomes [adjusted odds ratio 1.40, 95% confidence interval (CI): 1.24–1.51]. Also, participants in the late cohort had a greater chance of being readmitted within 30 days (adjusted odds ratio 1.12, 95% CI: 1.03–1.23) and nonhome discharge (adjusted odds ratio 1.41, 95% CI: 1.29–1.53).
Conclusion
Cholecystectomy that was performed after 2 days of admission for mild GSP was associated with increased major adverse events and 30-day readmissions, in addition to nonhome discharge.

Keywords:
cholecystectomy, gallstone pancreatitis, nonhome discharge, outcomes, readmission

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Introduction

Thirty-five to 40% of all cases of acute pancreatitis are caused by gallstones [1]. Laparoscopic cholecystectomy is still the gold standard for treating gallstone pancreatitis (GSP) because it eliminates the risk of recurrence in people without end-organ damage [2,3]. It has been proven that same-admission cholecystectomy for mild GSP reduces recurrent problems and readmission rates from gallstones when compared to delayed intervention [4,5]. In addition, it has been demonstrated that early intervention within 2 days of admission is both safe and cost-effective [6–8]. For patients with mild GSP, preoperative endoscopic retrograde cholangiopancreatography (ERCP) has been proven by Chang *et al.* [9] to prolong treatment. It has been reported that only 40–51% of individuals with mild GSP undergo operational intervention during the index admission, despite the availability of data recommending early cholecystectomy [10]. There needs to be more research into the gap among recommendations as well as clinical practice.

The aim of this work was to evaluate the association of timing for cholecystectomy with clinical outcomes in patients with GSP.

Patients and methods

This was a prospective cohort trial of all adults (above 18 years) undergoing nonelective cholecystectomy for mild GSP in the period from October 2019 to January

2023. The participants in this study were selected from general surgery and tropical medicine departments, at Menoufia University Hospitals. Patient's clinical data, including age, sex, and other relevant covariates and complications were determined. Patients with end-organ dysfunction were considered to have moderate to severe GSP according to the Atlanta classification of acute pancreatitis. Therefore they were not included in this study [11]. The remainder became part of the mild GSP group. Patient records were removed from the analysis if they lacked age or mortality information or if laparoscopic cholecystectomy was performed more than 2 weeks after the index admission.

The 30-day in-hospital mortality rate, as well as perioperative complications defined as major adverse event (MAE) were the primary outcomes of interest. Lung problems (failure, pneumonia), heart problems (tamponade, arrest), and digestive issues (biliary leak), along with infection at the operating site were all examples of complications that could arise during operation. Timing of ERCP, length of hospital stay (LOS) following surgery, and rates of nonhome discharge, in addition to 30-day readmission, were the secondary outcomes.

To estimate MAE along with 30-day nonelective readmission, multivariable regressions were established [12]. The inflection point of these models, as identified by the exploratory analysis, occurs 2 days after admission, when laparoscopic cholecystectomy is performed (Fig. 1). Time to operational intervention was used to categorize participants into 'early' (operated on within 2 days of admission) and 'late' (operated on over 2 days after admission) groups [13].

The study was approved by Menoufia University's Faculty of Medicine's ethical review board (Approval number. 10/2023SURG2-1) and followed all guidelines outlined in the Helsinki Declaration.

Sample size estimation

Based on a review of past literature, Isbell *et al.* [14] found that the mean (SD) of index hospital LOS in both early cholecystectomy and control cholecystectomy was 2.8 (2.2) and 3.9 (2.2). The last sample size calculated using statistics and sample size pro is 126 participants. The power of the study is 80% and the confidence interval (CI) is 95%.

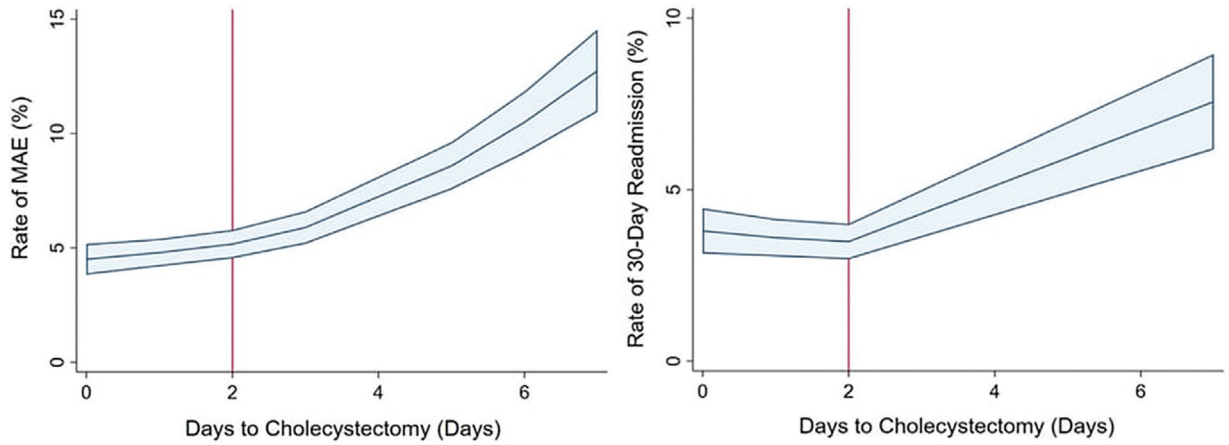
Statistical analysis

Continuous variables were reported as the median and interquartile range, whereas categorical variables were expressed as group proportions. For categorical variables, we used the χ^2 test, as well as for continuous variables, we used the Student's t test to establish statistical significance among groups. The timing of cholecystectomy was analyzed about the medical results of interest using multivariate logistic and linear regression. Optimizing models with the receiver operator characteristic raised the estimation probability [15]. Adjusted odds ratios (AORs) or beta coefficients (b) are provided, together with 95% CIs, as the results of regression analyses. The level of significance chosen was under 0.05.

Results

Thirty-three (25.6%) patients were stratified into the early cohort out of an expected 129 hospitalizations for mild GSP, with the other participants making up the late cohort. Late patients were mostly males (36.6 vs.

Figure 1



Analysis of risk-adjusted major adverse event (MAE) and 30-day readmission by timing of cholecystectomy (Reference: late cholecystectomy threshold).

Table 1 Demographic of patients and unadjusted outcomes in patients with mild gallstone pancreatitis stratified by timing of cholecystectomy (early, <2 days of admission; late, >2 days of admission groups)

Variables	Early (*N*=33)	Late (*N*=96)	*P* value
Female sex [*n* (%)]	66.2	63.4	<0.001
Male sex [*n* (%)]	33.8	36.6	
Age (years)	53 (37–66)	56 (40–69)	<0.001
Major adverse event (%)	4.9	8.1	<0.001
Cardiovascular complication (%)	0.2	0.4	<0.001
Infectious complication (%)	2.5	4.3	<0.001
Respiratory complication (%)	1.0	1.6	<0.001
Neurological complication (%)	2.1	2.8	<0.001
Thromboembolic complication (%)	0.1	0.2	<0.001
ERCP (%)			
Precholecystectomy	10.9	22.2	<0.001
Postcholecystectomy	7.5	4.4	<0.001
Days until ERCP	1 (0–2)	2 (1–3)	<0.001
Days until cholecystectomy	1 (0–1)	3 (2–4)	<0.001
Postoperative LOS	2 (1–2)	1 (1–2)	<0.001
Nonhome discharge (%)	4.4	7.6	<0.001
Readmission <30 days (%)	4.3	5.6	<0.001

ERCP, endoscopic retrograde cholangiopancreatography; LOS, hospital duration of stay.

33.8%, $P<0.001$) and significantly older [56 (40–69) against 53 (37–66) years, $P<0.001$]. Comparing the late group to the early cohort, we found that the late cohort experienced significantly higher rates of MAE (8.1 vs. 4.9%, $P<0.001$) as well as significantly lower postoperative LOS [1 (1–2) vs. 2 (1–2) days, $P<0.001$). The late group who underwent cholecystectomy had a greater rate of preoperative ERCP (22.2 vs. 10.9%, $P<0.001$). Moreover, nonhome discharge rates for the late cohort were 7.6 versus 4.4% for the early cohort ($P<0.001$), in addition to 30-day readmission rates were 5.6 versus 4.3% for the late cohort ($P<0.001$) (Table 1).

An elevated risk of MAE was observed following risk adjustment for late cholecystectomy (AOR 1.40, 95% CI: 1.29–1.51). The postoperative LOS for the late cohort was reduced by 0.3 days (95% CI: 0.3–0.4) compared to that of the early cohort. Patients with mild GSP who undergo late cholecystectomy had an increased risk of developing infectious, cardiovascular, as well as pulmonary complications. Nonhome discharge was more likely to occur in the late cohort (AOR 1.42, 95% CI: 1.33–1.52), and 30-day nonelective readmission was more likely in the late group (AOR 1.18, 95% CI: 1.09–1.27), relative to the early cohort (Table 2).

Table 2 Adjusted outcomes and resource utilization of late cholecystectomy in patients with mild gallstone pancreatitis

	Estimate	95% CI
Major adverse events	1.40	1.24–1.51
Mortality	2.77	0.64–1.11
Cardiovascular	1.70	1.16–2.48
Infectious	1.44	1.18–1.26
Respiratory	1.33	1.13–1.57
Neurologic	1.01	0.89–1.14
Thromboembolic	1.43	0.88–2.34
Postcholecystectomy ERCP	0.61	0.58–0.64
Postoperative LOS (d)	−0.33	−0.37–0.30
Nonhome discharge	1.41	1.29–1.53
Readmission <30 days	1.12	1.03–1.23

Estimates are reported as adjusted odds ratio for dichotomous outcomes and *b* coefficients for continuous outcomes with corresponding 95% confidence interval for both (Reference: Early cholecystectomy). CI, confidence interval; d, days; ERCP, endoscopic retrograde cholangiopancreatography; LOS, hospital duration of stay.

Discussion

GSP is a common emergency diagnosis for general surgeons. Given the correlation between postponing surgery and worse clinical outcomes, determining the best time to perform a laparoscopic cholecystectomy is crucial [16]. We observed in this study that cholecystectomy performed earlier is linked to a lower risk of MAE. Subgroup analysis showed that regardless of when the surgery was performed, outcomes were better at facilities that performed several cholecystectomies each year. A meta-analysis of early versus late cholecystectomies demonstrated that the former had lower risks of perioperative complications and readmission [17]. Early intervention was defined differently in different trials; some included cholecystectomy performed within 48 h, others within 72 h, and still others within 2 weeks after admission. There is a shortage of literature analyzing the costs across the country after early intervention is implemented. In this current work, we discovered that participants receiving laparoscopic

cholecystectomy who had their procedure more than 2 days after admission had a significantly higher MAE as well as 30-day readmission rate. However, cholecystectomy was performed on 74.4% of our research group on or after day 2 of hospitalization.

It is concerning that most participants still wait to have their cholecystectomy performed despite the many studies showing the safety besides effectiveness of early cholecystectomy in mild GSP. These lags might be attributed to a wide variety of causes. Even though randomized trials have shown that it is not required to wait for pancreatitis symptoms to resolve before an operation, some doctors still adhere to this practice [18]. Whether an individual is admitted to the operation or medicine unit may also affect how quickly the operation can be scheduled. Patients with mild GSP who are admitted to a surgical facility are more often to have an early cholecystectomy, according to a study by Kulvatunyou *et al.* [19]. Another proposed reason to postpone cholecystectomy is the need to remove stones from the common bile duct beforehand. However, previous research has shown that preoperative ERCP is typically unneeded and is linked to higher expenses and longer hospital stays in mild GSP. Standard treatment for mild GSP has been advocated as primary definitive care via cholecystectomy with selective postoperative ERCP. The percentage of patients who had preoperative ERCP ranged from 10.9% in the early cohort to 22.2% in the late cohort in the current research. However, the early cohort showed significantly superior perioperative results as well as resource consumption, even after accounting for the number of comorbidities as well as preoperative ERCP. We hypothesize that in patients with mild GSP, minimizing time to operational intervention should be emphasized, but we lack the means to evaluate the decision-making of individual patients and doctors. Across a variety of surgical procedures, higher hospital throughput has been linked to lower rates of death and perioperative problems [20–22]. Patients with mild GSP may benefit from the deployment of resources to ensure prompt access to early intervention as more centers embrace acute care surgery models of care [23]. Concurrently, to deliver consistent care, it is essential to assess which processes and care routes are most effective at improving results.

There are some limitations in this research. For assessing the severity of pancreatitis, we could not calculate it by using the existing scoring methods. Preoperative ERCP indications could not be defined either. The paucity of longitudinal data also prevented us from properly defining the reasons for delayed cholecystectomy, despite our success in determining the correlation among individual variables and operation scheduling. We could tell when a cholecystectomy took place in terms of hospital days, but not in terms of specific hours or minutes. The study also does not account for the potential importance of physicians' levels of experience or other patient-specific details in clinical judgment. However, we employed statistically sound methods to control for bias along with illustrating how the scheduling of surgery affects results following cholecystectomy for mild GSP.

Conclusion

We noticed in this trial that cholecystectomy after 2 days of admission is connected with a higher risk of significant adverse events as well as readmission per each additional day. Our results further show that the risk of MAEs, nonhome discharge, along 30-day nonelective readmissions is lower when cholecystectomy is done within 48 h of admission for mild GSP. Our results imply early cholecystectomy must be emphasized in patients with mild GSP, while the standard of care may vary according to the resources and characteristics of the patient. Additional randomized controlled trials assessing the optimal time for performing cholecystectomy are needed.

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Conflicts of interest

There are no conflicts of interest.

References

1 Negi N, Mokta J, Sharma B, Sharma R, Jhobta A, Bodh V, *et al.* Clinical profile and outcome of acute pancreatitis: a hospital-based prospective observational study in Subhimalayan State. J Assoc Physicians India 2018; 66:22–24

2 Moody N, Adiamah A, Yanni F, Gomez D. Meta-analysis of randomized clinical trials of early versus delayed cholecystectomy for mild gallstone pancreatitis. Br J Surg 2019; 106:1442–e1451.

3 Hazem Z. Acute biliary pancreatitis: diagnosis and treatment. Saudi J Gastroenterol 2009; 15:147.

4 Da Costa DW, Bouwense SA, Schepers NJ, Besselink MG, van Santvoort HC, Van Brunschot S, *et al.* Same-admission versus interval cholecystectomy for mild gallstone pancreatitis (PONCHO): a multicentre randomized controlled trial. Lancet 2015; 386:1261–1268.

5 Van Baal MC, Besselink MG, Bakker OJ, van Santvoort HC, Schaapherder AF, Nieuwenhuijs VB, *et al.* Dutch Pancreatitis Study Group. Timing of cholecystectomy after mild biliary pancreatitis: a systematic review. Ann Surg 2012; 255:860–866.

6 Dubina ED, de Virgilio C, Simms ER, Kim DY, Moazzez A. Association of early vs delayed cholecystectomy for mild gallstone pancreatitis with perioperative outcomes. JAMA Surg 2018; 153:1057.

7 Falor AE, de Virgilio C, Stabile BE, Kaji AH, Caton A, Kokubun BA, *et al.* Early laparoscopic cholecystectomy for mild gallstone pancreatitis: time for a paradigm shift. Arch Surg 2012; 147:1031–1035.

8 Aboulian A, Chan T, Yaghoubian A, Kaji AH, Putnam B, Neville A, *et al.* Early cholecystectomy safely decreases hospital stay in patients with mild gallstone pancreatitis: a randomized prospective study. Ann Surg 2010; 251:615–619.

9 Chang L, Lo S, Stabile BE, Lewis RJ, Toosie K, de Virgilio C. Preoperative versus postoperative endoscopic retrograde cholangiopancreatography in mild to moderate gallstone pancreatitis: a prospective randomized trial. Ann Surg 2000; 231:82.

10 Liu JK, Braschi C, de Virgilio CM, Ozao-Choy J, Kim DY, Moazzez A. Early cholecystectomy in gallstone pancreatitis patients with and without end-organ dysfunction: a nqsip analysis. Am Surg 2022; 88:2579–e2583.

11 Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, *et al.* Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. Gut 2013; 62:102–111.

12 Verma A, Hadaya J, Richardson S, Vadlakonda A, Ramezani R, Benharash P. The presence of a cost-volume relationship in robotic-assisted thoracoscopic lung resections. Ann Surg 2023; 278:e377–e381.

13 Johnstone M, Marriott P, Royle TJ, Richardson CE, Torrance A, Hepburn E, *et al.* Gallstone Pancreatitis Study Group. The impact of timing of cholecystectomy following gallstone pancreatitis. Surgeon 2014; 12:134–140.

14 Isbell KD, Wei S, Dodwad SJ, Avritscher EB, Mueck KM, Bernardi K, *et al.* Impact of early cholecystectomy on the cost of treating mild gallstone pancreatitis: gallstone PANC trial. J Am Coll Surg 2021; 233:517–525.

15 Vrieze SI. Model selection and psychological theory: a discussion of the differences between the Akaike information criterion (AIC) and the Bayesian in-formation criterion (Bic). Psychol Methods 2012; 17:228–e243.

16 Gutt CN, Encke J, Köninger J, Harnoss JC, Weigand K, Kipfmüller K, *et al.* Acute cholecystitis: early versus delayed cholecystectomy, a multicenter randomized trial (ACDC study, NCT00447304). Ann Surg 2013; 258:385–393.

17 Yang DJ, Lu HM, Guo Q, Lu S, Zhang L, Hu WM. Timing of laparoscopic cholecystectomy after mild biliary pancreatitis: a systematic review and meta-analysis. J Laparoendosc Adv Surg Tech 2018; 28:379–e388.

18 McCarty TR, Farrelly J, Njei B, Jamidar P, Muniraj T. Role of prophylactic cholecystectomy after endoscopic sphincterotomy for biliary stone disease: a systematic review and meta-analysis. Ann Surg 2021; 273:667–e675.

19 Kulvatunyou N, Watt J, Friese RS, Gries L, Green DJ, Joseph B, *et al.* Management of acute mild gallstone pancreatitis under acute care surgery: should patients be admitted to the surgery or medicine service?. Am J Surg 2014; 208:981–987.

20 Madrigal J, Mukdad L, Han AY, Tran Z, Benharash P, St. John MA, Blackwell KE. Impact of hospital volume on outcomes following head and neck cancer surgery and flap reconstruction. Laryngoscope 2022; 132:1381–1387.

21 Dobaria V, Kwon OJ, Hadaya J, Sanaiha Y, Sareh S, Aguayo E, *et al.* Impact of center volume on outcomes of surgical repair for type A acute aortic dissections. Surgery 2020; 168:185–192.

22 Birkmeyer JD, Siewers AE, Finlayson EV, Stukel TA, Lucas FL, Batista I, *et al.* Hospital volume and surgical mortality in the United States. New Engl J Med 2002; 346:1128–1137.

23 Murphy PB, Paskar D, Parry NG, Racz J, Vogt KN, Symonette C, *et al.* Implementation of an acute care surgery service facilitates modern clinical practice guidelines for gallstone pancreatitis. J Am Coll Surg 2015; 221:975–981.