

Cholecystectomy in Mild and Moderate Acute Pancreatitis: A Retrospective Study

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Rezumat

Colecistectomie în pancreatita acută ușoară și moderată: un studiu retrospectiv

Introducere: Colecistectomia a fost un subiect de dezbatere cu privire la momentul și utilitatea acesteia în cazurile de pancreatită acută (PA) ușoară și moderat severă. Scopul acestui studiu a fost să evalueze critic rolul colecistectomiei precoce în gestionarea PA ușoară și moderată, luând în considerare caracteristicile pacienților, procedurile asociate și impactul general asupra rezultatelor pacientului.

Metode: Studiul a comparat rezultatele legate de pacienții internați într-un centru chirurgical de îngrijire terțiară supuși unei colecistectomii laparoscopice (LC) precoce (< 96 ore) față de una tardivă (> 96 ore) pentru pancreatita acută biliară ușoară și moderat severă, între ianuarie 2019 și decembrie 2022.

Rezultate: Studiul a inclus 54 de cazuri [vârsta medie [abatere standard], 59,4 (16,5) ani; 31 (57,4%) ani femei]. Toți pacienții au fost supuși LC, cu 29 de cazuri supuse unui regim terapeutic în două faze pentru tratamentul litiazei căii biliare comune (CBD), constând în colangiopancreatografie retrogradă endoscopică și LC consecutivă. Grupul de colecistectomie precoce (EC) a cuprins 17 pacienți (31,5%), în timp ce grupul colecistectomiei tardive (DC) a inclus 37 de pacienți (68,5%). EC a fost corelată în mod semnificativ cu o durată mai mică a spitalizării (valoarea $p < 0,0001$) și o rată semnificativ mai mică de utilizare a ERCP în perioada perioperatorie.

Received: 13.05.2024

Accepted: 16.06.2024

Concluzii: EC în primele 4 zile după internare oferă beneficii semnificative, cum ar fi prevenirea pancreatitei recurente, reducerea complicațiilor și scăderea duratei spitalizării la pacienții cu PA ușoară și moderat severă.

Cuvinte cheie: pancreatită acută, litiază veziculară, chirurgie, colecistectomie

Abstract

Background: Cholecystectomy has been a subject of debate regarding its timing and utility in cases of mild and moderately severe acute pancreatitis (AP). We aimed to critically evaluate the role of early cholecystectomy in the management of mild and moderate AP, considering patients' characteristics, associated procedures, and overall impact on patient outcomes.

Methods: The study compared the outcomes between patients admitted in a tertiary care surgical center undergoing early (<96h) versus delayed (>96h) laparoscopic cholecystectomy (LC) for mild and moderately severe acute gallstone pancreatitis between January 2019 and December 2022.

Results: The study included 54 cases [mean (standard deviation) age, 59.4 (16.5) years; 31 (57.4%) years females]. All patients underwent LC, with 29 cases undergoing a two-phase therapeutic regimen for common bile duct (CBD) lithiasis, consisting of endoscopic retrograde cholangio-pancreatography followed by sequential LC. The early cholecystectomy group (EC) comprised 17 patients (31.5%), while the delayed cholecystectomy group (DC) included 37 patients (68.5%). EC was significantly correlated with lower length of stay (p-value < 0.0001) and significantly lower rate of ERCP usage during perioperative period.

Conclusions: EC in the first 4 days after admission provides significant benefits such as prevention of recurrent pancreatitis, reduction in complications, and decreased length of stay for patients with mild and moderately severe AP.

Key words: acute pancreatitis, gallstones, surgery, cholecystectomy

Background

Acute pancreatitis (AP) is a challenging medical condition characterized by inflammation of the pancreas, often resulting in severe abdominal pain, nausea, vomiting, and potentially life-threatening complications. Among the various etiological factors contributing to AP, gallstones are one of the leading causes, accounting for a significant proportion of cases (1). Cholecystectomy plays a crucial role in the management of AP, particularly when gallstones are identified as the underlying cause. However, the management of AP in these particular cases poses a dilemma regarding the optimal timing and necessity of cholecystectomy (2,3).

Traditionally, early cholecystectomy (EC) performed within the index admission for AP was considered risky due to concerns regarding increased surgical complications and mortality rates. However, recent evidence suggests that index laparoscopic cholecystectomy (LC), within the same hospital admission or shortly thereafter, may offer several benefits. Early removal of the gallbladder reduces the risk of recurrent pancreatitis episodes, decreases the length of hospital stay, and lowers healthcare costs compared to delayed or interval cholecystectomy (4-7).

The aim of this study was to analyze the optimal timing of cholecystectomy in the context of acute biliary pancreatitis.

Material and Methods

Study Design

We retrospectively gathered the AP patient sample data from January 2019 to December 2022 from the Ist Surgical Department of the Emergency County Hospital of Craiova.

The 10th Edition of the International Classification of Diseases, Clinical Modification (ICD-10-AM) coding system was employed to analyze adult patients who were hospitalized with a principal diagnosis of acute gallstone pancreatitis (coded as 587). Using ICD-10-AM codes, we searched for independent covariates, including potentially pertinent comorbidities such as cardiovascular disease, diabetes mellitus, obesity, end-stage or chronic kidney disease, and liver disease. Furthermore, we analyzed a list of diagnostic and therapeutic procedures relevant to the main diagnosis, including magnetic resonance cholangiopancreatography (MRCP), endoscopic retrograde cholangiopancreatography (ERCP), abdominal ultrasound, computed tomography (CT) scan of the abdomen, cholecystectomy, and the medication administered during the entire duration of the initial hospital admission.

The study analyzed all patients admitted with mild and moderately severe acute gallstone pancreatitis who underwent early (<96h) versus delayed (>96h) LC, along with the incidence of associated complications. The patients were allocated to either EC or DC, based on surgeon's preference and operative schedule. A secondary objective was to scrutinize outcomes such as morbidity, mortality, length of hospital stay (LoS), and postoperative hospitalization associated with immediate laparoscopic cholecystectomy during the above-mentioned time interval.

Inclusion and Exclusion Criteria:

Admission criteria included all adult cases with mild and moderately severe biliary AP who underwent LC. The diagnosis of mild and moderate AP was based on the adherence to

the 2012 revised Atlanta classification (8). Mild AP was defined by the absence of both local and systemic complications and organ failure, whereas moderately severe AP was characterized by local complications with or without organic failure persisting for less than 48 hours.

Exclusion criteria comprised individuals below 18 years of age, those diagnosed with severe AP, patients with mild and moderate AP that failed to undergo LC, cases with incomplete demographic, clinical or therapeutic data, and instances where patients were lost from follow-up.

Statistical Analysis

All statistical analysis were performed using GraphPad Prism 10.2.2 (GraphPad Software, LLC). The p values less than 0.05 were considered significant. Descriptive statistics were calculated, including percentages for categorical variables, and means±standard deviation (SD), median (interquartile range, IQR), and range for continuous variables. Independent Samples Mann-Whitney U Test was used for continuous variables and Chi-squared test for categorical variables.

Results

This study included 54 participants (mean (SD) age, 59.4 (16.5) years; 31 (57.4%) females). All subjects underwent LC, with 29 cases receiving a two-stage treatment approach for common bile duct (CBD) lithiasis, involving ERCP followed by sequential LC. The EC group comprised 17 patients (31.5%), while the DC group included 37 patients (68.5%). The mean hospital stay was 10.6 days. No statistical difference was recorded between groups in terms of comorbidities, such as diabetes mellitus, obesity, end-stage or chronic kidney disease, cirrhosis, and cardiovascular disease. The main characteristics of patients undergoing early or delayed cholecystectomy are synthesized in *Table 1*. The incidence of CBD lithiasis was 57.4%, with MRCP as the main method of diagnosis in 32 cases (59.2%).

Table 1. Patient characteristics of early (less than 4 days) versus delayed (more than 4 days) cholecystectomy

Characteristics Mean \pm SD Median (IQR) Range	Total (n=54)	Early cholecystectomy Surgery Days \leq 4 (n=17)	Delayed cholecystectomy Surgery Days $>$ 4 (n=37)	p-value (early vs Delayed)
Age	59.41 \pm 16.52 61 (49.5-70.5) 17-86	59.88 \pm 12.74 65 (49.5-69.50) 35-78	59.19 \pm 18.15 60 (48-74) 17-86	0.955
Leukocytes (*d/L)	11799 \pm 6652.6 9880 (7600-14060) 5078-40710	10330.24 \pm 5046.7 8855 (6713.5-13025) 5400-25320	12473.8 \pm 7233.9 10240 (7767-14415) 5078-40710	0.276
Gender, male	23 (42.6%)	5 (29.4%)	18 (48.6%)	0.242
Platelets (*d/L)	263974 \pm 221802.6 221100 (189725-269075) 100600-1758000	219282.4 \pm 97264.2 199600 (158400-254250) 100600-524100	284508 \pm 258547.6 236500 (200900-274800) 111100-1758000	0.047*
Total Bilirubin (mg/dL)	2.34 \pm 2.43 1.21 (0.55-3.52) 0-12	1.63 \pm 1.9 0.94 (0.49-2.16) 0-7	2.67 \pm 2.59 1.51 (0.61-4.24) 0-12	0.084
Direct Bilirubin (mg/dL)	1.54 \pm 2.01 0.52 (0.23-2.65) 0.09-10.5	0.97 \pm 1.58 0.25 (0.17-1) 0.1-5.1	1.8 \pm 2.1 0.73 (0.25-2.99) 0.13-10.5	0.054
ALT (mg/dL)	191.1 \pm 223.5 127.5 (43-222.5) 9-1231	91.47 \pm 90.1 43 (14.5-180.5) 9-263	236.9 \pm 253.8 168 (72-317) 10-1231	0.007*
AST (mg/dL)	142.22 \pm 217.14 87.5 (34.5-87.5) 13-1264	58.9 \pm 48.3 35 (19.5-94.5) 13-163	180.5 \pm 252.2 106 (42-174.5) 14-1264	0.005*
Amylase (U/L)	445.7 \pm 556.7 166.5 (102.3-572.8) 23-2266	417.24 \pm 580.1 125 (101.5-669.5) 23-2128	180.5 \pm 252.2 238 (103-614.5) 14-1264	0.451
Procalcitonin (ng/mL)	0.53 \pm 0.68 0.41 (0.34-0.52) 0.22-5	0.41 \pm 0.13 0.38 (0.32-0.48) 0.22-0.67	0.58 \pm 0.83 0.41 (0.34-0.52) 0.28-5	0.265
Hemoglobin (g/dL)	12.8 \pm 1.71 12.99 (11.77-13.9) 7.8-17.2	12.9 \pm 1.06 12.7 (12.2-13.95) 10.9-14.41	12.76 \pm 1.95 13.04 (11.47-13.92) 7.8-17.2	0.992
Hospital length of stay (days)	10.63 \pm 6.36 10.5 (6.75-13) 2-46	6.8 \pm 3.3 6 (5-9) 2-15	12.38 \pm 6.69 12 (9-14) 3-46	<0.0001*
Postoperative hospital stay (days)	4.48 \pm 4.1 4 (3-5) 1-30	4.3 \pm 2.8 4 (2.5-5.5) 1-12	4.57 \pm 4.58 4 (3-5) 1-30	0.992
Mortality	0	0	0	1
Morbidity	1 (1.9%)	0	1 (2.7%)	1
Choledocholithiasis, yes	11 (20.4%)	6 (35.3%)	5 (13.5%)	0.081
Cholangitis, yes	2 (3.7%)	2 (11.8%)	0	0.095
ERCP usage, yes	29 (53.7%)	13 (76.5%)	16 (43.2%)	0.039*
CRP > 6 mm, yes	36 (66.7%)	10 (58.8%)	26 (70.3%)	0.536
Pseudocyst Drainage, yes	4 (7.4%)	0	4 (10.8%)	0.296
Biliary Drainage (T-tube), yes	2 (3.7%)	1 (5.9%)	1 (2.7%)	0.535

In comparison with the DC group, the EC group was significantly correlated with lower length of stay (p-value < 0.0001).

The ERCP usage rate was compared between the 2 groups. In comparison with DC, the rate of ERCP usage during perioperative period was significantly lower in the EC group

(p-value = 0.039). In each group the endoscopic stone extraction was unsuccessful in one case, requiring open surgery and choledochotomy with T-tube placement. Choledocoduodenostomy was used in one case in the DC group. The postoperative outcome was uneventful in all cases.

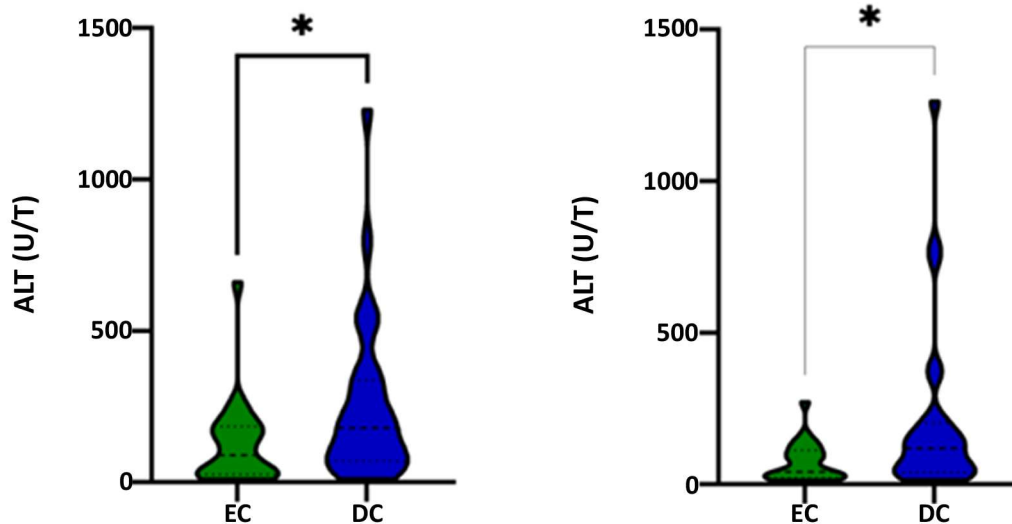


Figure 1. Clinical characteristics of early cholecystectomy (EC) versus delay cholecystectomy (DC)

EC showed better platelet count (p -value = 0.047), ALT (p -value = 0.007), and AST levels (p -value = 0.005) compared to DC (*Fig. 1*).

No statistical difference was observed between groups in terms of in-hospital mortality and morbidity (*Table 1*).

Discussions

Despite the potential benefits, the decision to perform cholecystectomy in the setting of AP is not without controversy. One of the primary concerns is the risk of exacerbating the inflammatory process and precipitating complications, such as pancreatic necrosis, infected pancreatic pseudocysts, or exacerbation of systemic inflammation. The inflammatory milieu associated with AP may pose technical challenges during surgery, increasing the likelihood of intraoperative complications, such as bleeding, bile duct injury, or inadvertent pancreatic injury (9). The risk is potentially higher in case of moderate and severe AP (10-12).

Another challenge is the feasibility of early surgical intervention in resource-limited settings or in cases where timely access to surgical expertise is limited. Interval cholecys-

tectomy may be considered in such scenarios, with appropriate measures taken to manage and prevent recurrent biliary events during the interim period. However, delaying surgery increases the risk of recurrent pancreatitis and its associated complications, necessitating close monitoring and proactive management strategies. Factors such as multiple main bile duct lithiasis and increased levels of alanine aminotransferase are known predictors for increased recurrence risk in case of interval cholecystectomy (13).

Conversely, EC in the context of biliary pancreatitis mitigates the need for repeated hospital admissions and interventions, leading to better utilization of healthcare resources and cost-effectiveness. Furthermore, early cholecystectomy facilitates the prompt resumption of oral intake and hastens the recovery process, improving the overall quality of life for patients (14,15). Our study indicated better results concerning the length of hospital stay, postoperative biological status, and ERCP usage, which is consistent with other data from literature (16). On the other hand, there were no significant differences in terms of complication rate or gallstone-related events between EC and DC.

Another potential factor that may interfere with the surgical outcomes is the Balthazar score, as certain studies indicate an increased postoperative complication rate associated with elevated scores (17).

The levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) demonstrated significant variation between the groups. A plausible explanation for this observation is the extended interval between the onset of the disease and surgical intervention in patients with delayed cholecystectomy. This delay may be linked to recurrent common bile duct (CBD) events, including stone migration in some instances, which could result in liver injury. Nevertheless, the small sample size and the heterogeneity among the groups could also account for these findings.

One particular aspect that needs to be addressed is the coexistence of common bile duct (CBD) lithiasis. This situation can be generally addressed in two ways: either by preoperative ERCP for CBD clearance, followed by interval laparoscopic cholecystectomy (two-stage approach), or by laparoscopic single-stage management with cholecystectomy and intraoperative cholangiogram succeeded by laparoscopic bile duct exploration. None of these options showed their superiority in the treatment of mild biliary pancreatitis in case of early cholecystectomy (18-20). In our study, its incidence of CBD lithiasis was 57.4%, requiring ERCP and CBD stone removal as a two-stage approach in 29 cases. In 2 cases, endoscopic stone extraction was unsuccessful, requiring open surgery and choledochotomy with T-tube placement, with good postoperative outcomes. Both cases were in the delayed-cholecystectomy group, possibly indicating the necessity of addressing any biliary event as soon as possible in order to prevent untoward complications. Nevertheless, during the analysis of the findings, it is imperative to consider two significant limitations inherent in this study: the restricted sample size and its retrospective design. An additional constraint, stemming from the aforementioned limitations, is the relative lack of homogeneity between groups, as

evidenced by the EC population displaying lower preoperative platelet, ALT, and AST levels compared to the DC cohort.

Conclusions

Early cholecystectomy performed during the first 4 days after admission is safe and effective in case of mild biliary pancreatitis, providing significant benefits such as prevention of recurrent pancreatitis, reduction in complications, and improved patient outcomes.

Conflicts of Interest

The author reports no conflicts of interest in this work.

Funding

This study was supported from the research grant “Modern therapeutic options in the management of acute biliary pancreatitis (Optiuni Terapeutice Moderne in Managementul Pancreatitei Acute Biliare - OPTIMA)”, no. 26/307/1 from 07.05.2024, University of Medicine and Pharmacy of Craiova, Romania.

Institutional Review Board Statement

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of the University of Medicine and Pharmacy of Craiova (protocol code 87/19.02.2024).

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

Data Availability Statement

Data available on request.

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