Interval Cholecystectomy Is Associated With a High Risk of Complications in Patients With Mild Acute Biliary Pancreatitis

Mukaddes Tozlu (✉ mukaddestozlu@sakarya.edu.tr)

Sakarya University Faculty of Medicine: Sakarya Universitesi Tıp Fakültesi <https://orcid.org/0000-0002-8534-8027>

Busra Karaca

Sakarya University Faculty of Medicine: Sakarya Universitesi Tıp Fakültesi

Sencan Acar

Sakarya University Faculty of Medicine: Sakarya Universitesi Tıp Fakültesi

Bilal Toka

Ozel Silivri Anadolu Hastahanesi

Cengiz Karacaer

Sakarya University Faculty of Medicine: Sakarya Universitesi Tıp Fakültesi

Ahmet Tarik Eminler

Sakarya University Faculty of Medicine: Sakarya Universitesi Tıp Fakültesi

Aydin Seref Koksall

Sakarya University Faculty of Medicine: Sakarya Universitesi Tıp Fakültesi

Research Article

Keywords: Acute biliary pancreatitis, gallstone, complications, cholecystectomy

Posted Date: February 21st, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1163448/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background

Although current guidelines recommend cholecystectomy during the same admission in patients with mild acute biliary pancreatitis (ABP), it involves a waiting list most of the time.

Aim

We aimed to assess the risk of gallstone-related biliary events (GRBEs) such as cholecystitis, cholangitis, and pancreatitis during the waiting period for cholecystectomy and determine predictors of complications after the first episode of ABP.

Methods

A prospective observational study was conducted at a tertiary hospital for six months in patients with mild ABP. Follow-ups were done by phone calls or using electronic health records for a maximum of 6 months after discharge or until cholecystectomy.

Results

A total of 194 patients were included in the study. Although all patients were referred to surgeons, only 81 (41.8%) underwent cholecystectomy within 6 months after discharge. During the observation period, GRBEs developed in 68 (35.1%) patients which included biliary colic, recurrent ABP, acute cholecystitis, choledocholithiasis, gallbladder perforation, cholangitis, and liver abscess. The overall readmission rate was 25.2%, and 44.8% occurred within 4 weeks after discharge. The odds ratio of any complication was 1.58 (95% CI; 1.42-1.76, $p=0.028$) and 1.59 (95% CI; 1.42-1.78, $p=0.009$) in the patients who did not have surgery within 2-7 days and 8-15 days, respectively. There was a 4-fold increased risk of readmission (95% CI; 1.16-13.70, $p=0.019$) if cholecystectomy was not performed within 31-90 days. The patients who developed complications had significantly higher C-reactive protein levels at admission, longer waiting time for cholecystectomy, and had three or more gallstones on imaging than those who did not develop complications.

Conclusion

Interval cholecystectomy was associated with a high risk of complications during the waiting period in patients with mild ABP.

Background

Acute biliary pancreatitis (ABP) is a common disease with varying severity. Most cases are mild, and treatment consists of supportive care with subsequent cholecystectomy to prevent gallstone-related biliary events (GRBEs) such as recurrent pancreatitis, acute cholecystitis, cholangitis, and choledocholithiasis.

Although there is a clear consensus that patients with gallstone pancreatitis should undergo cholecystectomy, the actual timing of surgery remains controversial. Some guidelines recommend cholecystectomy during the index admission, while others have the option up to 2-4 weeks (1, 2). However, the exact time for cholecystectomy to minimize the GRBEs risk in mild ABP patients is still not precise.

In current clinical practice, cholecystectomy is delayed due to many factors, such as surgeons' opinion that inflammation and edema will cause more difficult dissection in the early days following pancreatitis and limited resources in the hospital and health care system. Most specialists choose interval cholecystectomy and postpone surgery until complete resolution of the inflammatory process(3). When cholecystectomy is delayed, the recurrence rate for biliary pancreatitis ranges between 4-50% and even up to 61% in some series(4). Recurrent pancreatitis may be more severe than the initial presentation, with 10% and 40% mortality and morbidity rates, respectively(5–7).

This study aimed to assess the risk of GRBEs during the waiting period for cholecystectomy. In addition, we aimed to identify the factors that determine the occurrence and severity of the disease complications after the first episode of ABP to predict which patient group may benefit more from closer evaluation and referral for cholecystectomy during the index admission.

Methods

Study design and participants

A prospective observational study was conducted in the gastroenterology department of a tertiary hospital. All adult patients (aged ≥ 18 years) who were admitted to our gastroenterology clinic with acute pancreatitis (AP) were assessed for eligibility, and those with the first episode of mild ABP were included in the study. Patients were excluded if they had choledocholithiasis or cholangitis necessitating endoscopic retrograde cholangiopancreatography (ERCP), moderate or severe pancreatitis, chronic pancreatitis, pregnancy, and history of cholecystectomy. Revised Atlanta criteria were used to diagnose AP. ABP was defined when at least two of the following three features were present: upper abdominal pain consistent with the disease, elevated amylase and/or lipase level to at least three times the upper limit of normal, and characteristic findings of AP on abdominal imaging with the presence of stone or sludge in the gallbladder or biliary ducts. Mild AP was defined by the absence of organ failure and local complications such as pancreatic necrosis or peripancreatic collections according to the Atlanta criteria(8). Cholecystitis and cholangitis were defined according to the Tokyo Guidelines 2018 diagnostic criteria(9, 10).

Data

Patients' demographics, medical history, clinical characteristics, comorbidity (Charlson index), and laboratory data were recorded. All patients were evaluated with abdominal ultrasonography (US) at admission. The gallbladder stones' number and size, the gallbladder wall's thickness, presence of pericholecystic fluid, biliary dilation, and bile duct stones were evaluated. Computerized tomography (CT) was performed if there was no clinical improvement three days after admission to exclude moderate or severe AP. In case of increased serum bilirubin levels or signs of cholestasis such as biliary dilatation, magnetic resonance cholangiopancreatography (MRCP) was performed to exclude choledocholithiasis.

Outcomes

The primary endpoint was to determine the development of biliary colic and gallstone-related complications within the six months following the first ABP episode. Gallstone-related complications were acute cholecystitis, recurrent biliary pancreatitis, choledocholithiasis, and cholangitis. Secondary outcomes included the timing of cholecystectomy after index admission, the need for hospital readmission during the waiting period for cholecystectomy, and factors affecting the development of GRBEs.

Data collection and follow-up

Patients were followed by phone calls and electronic health records for a maximum of 6 months after discharge from the hospital or until cholecystectomy. Follow-up was terminated if the primary outcome was reached. Phone follow-up contacts were done at the 1st, third and sixth months after discharge from the hospital. Patients were asked if they experienced GRBEs or underwent cholecystectomy. Those who had symptoms or were admitted to the hospital were seen in the outpatient clinic and evaluated in detail.

Ethics

All participants provided written informed consent for participation in the study. Approval for the study was obtained from the Ethics Committee of Sakarya University, Faculty of Medicine (16214662/050.01.04/34496/116). All procedures were in accordance with the ethical standards of the committee and the Declaration of Helsinki.

Statistical analysis

Descriptive analyses were presented using medians and interquartile range (IQR) for the non-normally distributed variables. Mann-Whitney U test was used for nonparametric tests to compare these parameters. Wilcoxon test was used for nonparametric variables. Odd's ratio and Chi-square tests were used to compare the categorical variables and risk analyses between two groups. Categorical variables were presented as frequency (% percentage). $p < 0.05$ was considered significant. SPSS statistical software version 21 was used for the analyses.

Results

Study group:

Two hundred and thirty-six patients with mild ABP were hospitalized during the study period. Twenty-one patients with concomitant choledocholithiasis, 5 with the previous cholecystectomy, 7 with the previous episode of pancreatitis, and 1 with pregnancy were excluded from the study. The remaining 202 eligible patients constituted the study group. Eight patients were lost to follow-up after discharge.

Clinical characteristics and laboratory findings:

A total of 194 patients (123 female, 63.4%) were analyzed. The median age was 63 (range 20-93) years. Abdominal US was performed in all patients to identify gallstones and/or sludge in the gallbladder and/or common bile duct (CBD). MRCP was performed in 165 (85%) patients, CT scan in 145 (74.7%), upper abdominal magnetic resonance imaging (MRI) in 5 (2.4%), and endoscopic ultrasonography in 8 (3.9%). The baseline characteristics of the patients are summarized in Table 1.

Timing of surgery:

Seven patients (3.6%) were operated on before discharge. The remaining 187 patients could not be operated on during the index admission and were discharged with the recommendation of cholecystectomy. Patients were followed up for six months or until cholecystectomy or complications developed.

Although all of the patients were referred to surgeons, only 81 (41.8%) underwent cholecystectomy within the six months after discharge (19.6% in the first month, 17% between 1-3 months, and 5.2% between 3-6 months]. The median time from discharge to cholecystectomy was 36 (IQR 15-70) days. One hundred and thirteen (58.2%) patients did not have cholecystectomy during the follow-up period. 29.2% of the patients refused, 27.4% were not eligible for surgery, and 34.5% were still on the waiting list at the end of the follow-up period. Follow-up was terminated early in 5 (4.4%) patients because of mortality due to cardiac reasons in 4 and burn injury in one. Five (4.4%) patients did not undergo surgery because of other reasons such as lack of health insurance.

Biliary events during follow-up:

Biliary events developed in 68 (35.1%) patients during the observation period. (17.5% in the first month, 11.8% between 1-3 months, and 5.6% between 3-6 months). Fifty-three (27.6%) patients reported one or more biliary colic before cholecystectomy, irrespective of the need for readmission. Biliary colic requiring hospital readmission was reported in 18 patients (9.2%). The interval between discharge and GRBEs is shown in Table 2. Thirty-one patients (16%) developed gallstone-related complications (6.1% in the first month, 6.1% between 1-3 months, and 3.6% between 3-6 months). The most common complications were recurrent AP in 11 (5.7%) patients, followed by acute cholecystitis in 6 (3.1%), and choledocholithiasis in 4 (2.1%). Two of the recurrent AP cases were moderate, and none were severe. All GRBEs are shown in Table 3. The median time from discharge to the development of complications was 31 (IQR 12.5-60)

days. The overall hospital readmission rate was 25.2%, and 44.8% occurred within the 4 weeks after discharge.

ERCP was performed in 6 (6.1%) patients due to choledocholithiasis or cholangitis. One patient with acute cholecystitis had gallbladder perforation and necessitated emergent surgery. There was no mortality due to the complications.

Factors related to complications:

The patients who developed GRBEs had significantly higher C-reactive protein (CRP) levels at admission [18.8 (8.6-48.7) vs. 11.4 (5-31.3), $p=0.003$] and a longer median waiting time for cholecystectomy [65 days (39-115) vs. 30 days (12-52), $p=0.006$]. Clinical and laboratory characteristics of the patients with respect to the development of biliary events are presented in Table 4. Approximately 1/3 of the patients (53 patients, 27%) experienced biliary colic after discharge. The patients who experienced biliary colic during the waiting time for cholecystectomy had also significantly higher BMI [30.5 (27.3-35.2) vs. 28.1 (25.7-32.3) ($p=0.034$)] at admission, compared to those who did not.

GRBEs developed in 58 (46.7%) of 124 patients with three or more gallstones. GRBEs were seen in 86% of the patients with three or more gallstones and 14% of those with one or less than three gallstones ($p<0.001$). There was no relationship between other parameters (stone size, presence of sludge or cholecystitis, biochemical parameters) and complications.

During the waiting time; GRBEs developed in 4.1% (1/24, all biliary colic), 14.2% (2/14), 24.2% (8/33), 50% (5/10), and 46% (52/113) of the patients who underwent cholecystectomy in the first 15 days, 16-30 days, 1-3 months, 3-6 months and without cholecystectomy, respectively (Table 5) (Figure 1). Hospital readmission rates were 4.1% (1/24), 7.1% (1/14), 9% (3/33), 30% (3/10), and 36.2% (41/113) in the patients who underwent cholecystectomy in the first 15 days, 16-30 days, 1-3 months, 3-6 months and without cholecystectomy, respectively (Table 6).

The odds ratios and 95% confidence intervals (CI) were calculated for the risk of all complications associated with each time delay to cholecystectomy. The odds ratio of any complication was 1.58 (95% CI; 1.42-1.76, $p=0.028$) and 1.59 (95% CI; 1.42-1.78, $p=0.009$) for patients who did not have surgery within 2-7 days and 8-15 days, respectively. There was a significant increase in the odds of complication in patients who did not have surgery within six months (OR=3.46, $p<0.001$) (Table 7). The risk of readmission increased four times if surgery was not performed within 31-90 days (95% CI; 1.16-13.70, $p=0.019$). If surgery was delayed to 6 months, the risk of readmission increased to 5.2-fold (95% CI; 2.28-11.85, $p<0.001$) (Table 8).

Discussion

Our study shows that cholecystectomy time plays an essential role in the early management of ABP. Despite wide acceptance of early cholecystectomy in clinical practice guidelines, there is a scarcity of clinical trial data on long-term consequences with every time delay to definite treatment after

hospitalization in ABP. Several studies showed that early cholecystectomy was safe, had a shortened hospital stay, and had no impact on surgery complications compared to late cholecystectomy (5, 11–13). Randomized controlled trials revealed that delayed cholecystectomy had a higher rate of complications than early one (11, 14, 15). However, early cholecystectomy is not well defined in recent literature. The British Society of Gastroenterology recommends cholecystectomy during the same hospital admission or within the next two weeks in patients with biliary pancreatitis(2). The American Gastroenterological Association suggests that cholecystectomy should be performed as soon as possible and in no case beyond 2-4 weeks after discharge from index admission(1). The International Association of Pancreatology(16) and American College of Gastroenterology(17) recommends cholecystectomy during the index admission. Our study suggests that even planned elective cholecystectomies within 2 to 4 weeks of discharge may not protect adequately because of the high biliary event risk in the first 15 days.

A multicenter study was designed to compare same-admission and interval cholecystectomy, which was defined as 25-30 days after randomization, and revealed a higher rate of readmission due to gallstone-related complications or mortality in the interval cholecystectomy group(15). However, it is not usually possible to undergo cholecystectomy immediately or within 30 days after discharge in clinical practice. This period is often prolonged for various reasons, such as the common belief of more difficult dissection and increased occurrence of surgical complications in early surgery group, busy operating rooms, and scarcity of hospital resources(5). Available resources are usually allocated to emergent cases. Patients are usually put on a waiting list, and the waiting time for surgery can range between 3 and 12 months (3, 18, 19). In a German study, although all gastroenterologists were aware that the same admission cholecystectomy should be performed, only 23% of them could comply with this policy (20). A Swedish survey with 8419 mild ABP patients showed that 9.9% and 9.8% of the patients had index and interval cholecystectomy, respectively, within 30 days of index admission. 44% of the patients did not undergo surgery within one year of admission(21). In our study, only 3.6% of the patients had index cholecystectomy, and 19.6% underwent surgery in the first month. One hundred and thirteen (58.2%) patients did not have cholecystectomy within 6 months.

There is an important risk of recurrent biliary events in the interval between hospital discharge and cholecystectomy. The overall hospital readmission rate was reported between 7-32% in previous studies(22). In a retrospective study from the UK, 23.7% of the patients required emergency admission due to gallstone-related complications while awaiting surgery(18). The patients who developed complications had a 30% increase in the operating time, a four-fold increase in conversion to open cholecystectomy, and a ten-fold increase in hospital stay(18). Ito et al. compared patients in the index and interval cholecystectomy group and showed that 31% of pancreatitis recurrences occurred within the 2 weeks after discharge from index admission(23). These studies were mainly retrospective and designed to compare index and interval cholecystectomy. Although the findings showed an increase in the recurrence rates with interval cholecystectomy and supported early cholecystectomy, they were insufficient to provide data on the increasing gallstone-related biliary event rates with every delay to cholecystectomy and the risk factors related to the development of biliary events in patients waiting for cholecystectomy.

To our knowledge, our prospective study is the first in the literature that analyzes the risk increase with every time delay to cholecystectomy up to 6 months. We showed that the complication risk was related to waiting time. Delaying cholecystectomy for each week for the first 15 days was associated with a 1.58 and 1.59 fold increase in the risk of gallstone related biliary events. Patients who did not undergo index cholecystectomy should be carefully followed, especially first 15 days. A significantly increased risk was also seen in patients who did not have surgery within six months (OR=3.46, $p<0,001$). The relative risk of readmission increased 4-fold and 5.2-fold if cholecystectomy was not performed within 31-90 days and six months, respectively.

Because of the long waiting list for cholecystectomy, we tried to determine which patients would benefit more from early intervention. We investigated the factors associated with complication risk. In contrast to previous studies(24), the size of gallstones was not associated with an increased risk of complications in this study. However, patients with three or more gallstones and high CRP levels at admission were more prone to develop complications. We might think that some patients can be prioritized by utilizing available resources, especially those with multiple gallstones since we have shown significantly increased complication risk compared to patients with less than three gallstones.

Our study has some limitations. It is a single-center study and has a relatively small sample size. However, this study is one of the studies with a considerable number of patients assessed the readmission and complication risk in patients with mild ABP if they do not undergo index cholecystectomy. Other studies on this issue are either retrospective(25) or limited to a small number of cases(18, 23). Another limitation of our study is the lack of a control group to assess recurrence risk after cholecystectomy. However, this study was designed as an observational study.

Conclusions

In conclusion, hospital readmissions due to GRBEs can occur after the first episode of ABP if cholecystectomy is delayed. These readmissions pose a significant risk of comorbidity. Management of ABP should also focus on preventing recurrent pancreatobiliary complications, especially in patients with multiple gallstones. Cholecystectomy should be performed as early as possible after the first ABP episode. The later the cholecystectomy is performed, the higher gallstone-related complications occur. The high incidence of GRBEs suggests that these patients should be followed more closely if the same admission cholecystectomy is not performed.

Abbreviations

Acute pancreatitis (AP)

Acute biliary pancreatitis (ABP)

Charlson comorbidity index (CCI)

Common bile duct (CBD)

Confidence intervals [CI]

C-reactive protein (CRP)

Endoscopic retrograde cholangiopancreatography (ERCP)

Gallstone-related biliary events (GRBEs)

Magnetic resonance cholangiopancreatography (MRCP)

Magnetic resonance imaging (MRI)

Ultrasonography (US)

Declarations

Ethics approval and consent to participate: Ethics Committee of Sakarya University, Faculty of Medicine (16214662/050.01.04/34496/116). All participants provided written informed consent for participation in the study.

Consent for publication: Not applicable

Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests

Funding: No funding is accepted.

Authors' contributions: MT, BT, and SA, carried out the experiment. ASK conceived and planned the experiments. BK collected the data. ATE analyzed and interpreted the data. MT wrote the manuscript with support from ASK. CK contributed to sample preparation. All authors read and approved the final manuscript.

Acknowledgements: Not applicable

References

1. Forsmark CE, Baillie J, Practice AGAIC, Economics C, Board AGAIG. AGA Institute technical review on acute pancreatitis. *Gastroenterology*. 2007;132(5):2022–44.
2. Working Party of the British Society of G, Association of Surgeons of Great B, Ireland, Pancreatic Society of Great B, Ireland, Association of Upper GI SoGB, et al. UK guidelines for the management of acute pancreatitis. *Gut*. 2005;54 Suppl 3:iii1-9.

3. Rutledge D, Jones D, Rege R. Consequences of delay in surgical treatment of biliary disease. *Am J Surg.* 2000;180(6):466–9.
4. Hernandez V, Pascual I, Almela P, Anon R, Herreros B, Sanchiz V, et al. Recurrence of acute gallstone pancreatitis and relationship with cholecystectomy or endoscopic sphincterotomy. *Am J Gastroenterol.* 2004;99(12):2417–23.
5. Cucher D, Kulvatunyou N, Green DJ, Jie T, Ong ES. Gallstone pancreatitis: a review. *Surg Clin North Am.* 2014;94(2):257–80.
6. Moreau JA, Zinsmeister AR, Melton LJ 3rd, DiMagno EP. Gallstone pancreatitis and the effect of cholecystectomy: a population-based cohort study. *Mayo Clin Proc.* 1988;63(5):466-73.
7. Lankisch PG, Bruns A, Doobe C, Weber-Dany B, Maisonneuve P, Lowenfels AB. The second attack of acute pancreatitis is not harmless. *Pancreas.* 2008;36(2):207–8.
8. 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(1):102–11.
9. Kiriya S, Kozaka K, Takada T, Strasberg SM, Pitt HA, Gabata T, et al. Tokyo Guidelines 2018: diagnostic criteria and severity grading of acute cholangitis (with videos). *J Hepatobiliary Pancreat Sci.* 2018;25(1):17–30.
10. Okamoto K, Suzuki K, Takada T, Strasberg SM, Asbun HJ, Endo I, et al. Tokyo Guidelines 2018: flowchart for the management of acute cholecystitis. *J Hepatobiliary Pancreat Sci.* 2018;25(1):55–72.
11. 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(4):615–9.
12. Gurusamy KS, Koti R, Fusai G, Davidson BR. Early versus delayed laparoscopic cholecystectomy for uncomplicated biliary colic. *Cochrane Database Syst Rev.* 2013(6):CD007196.
13. Taylor E, Wong C. The optimal timing of laparoscopic cholecystectomy in mild gallstone pancreatitis. *Am Surg.* 2004;70(11):971–5.
14. Jee SL, Jarmin R, Lim KF, Raman K. Outcomes of early versus delayed cholecystectomy in patients with mild to moderate acute biliary pancreatitis: A randomized prospective study. *Asian J Surg.* 2018;41(1):47–54.
15. 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 randomised controlled trial. *Lancet.* 2015;386(10000):1261–8.
16. Working Group IAPAAPAG. IAP/APA evidence-based guidelines for the management of acute pancreatitis. *Pancreatol.* 2013;13(4 Suppl 2):e1–15.
17. Tenner S, Baillie J, DeWitt J, Vege SS, American College of G. American College of Gastroenterology guideline: management of acute pancreatitis. *Am J Gastroenterol.* 2013;108(9):1400-15; 16.

18. Somasekar K, Shankar PJ, Foster ME, Lewis MH. Costs of waiting for gall bladder surgery. *Postgrad Med J.* 2002;78(925):668–9.
19. Salman B, Yuksel O, Irkorucu O, Akyurek N, Tezcaner T, Dogan I, et al. Urgent laparoscopic cholecystectomy is the best management for biliary colic. A prospective randomized study of 75 cases. *Dig Surg.* 2005;22(1-2):95–9.
20. Lankisch PG, Weber-Dany B, Lerch MM. Clinical perspectives in pancreatology: compliance with acute pancreatitis guidelines in Germany. *Pancreatology.* 2005;5(6):591–3.
21. Sandzen B, Haapamaki MM, Nilsson E, Stenlund HC, Oman M. Cholecystectomy and sphincterotomy in patients with mild acute biliary pancreatitis in Sweden 1988 - 2003: a nationwide register study. *BMC Gastroenterol.* 2009;9:80.
22. 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 A.* 2018;28(4):379–88.
23. Ito K, Ito H, Whang EE. Timing of cholecystectomy for biliary pancreatitis: do the data support current guidelines? *J Gastrointest Surg.* 2008;12(12):2164–70.
24. Kim SB, Kim TN, Chung HH, Kim KH. Small Gallstone Size and Delayed Cholecystectomy Increase the Risk of Recurrent Pancreatobiliary Complications After Resolved Acute Biliary Pancreatitis. *Dig Dis Sci.* 2017;62(3):777–83.
25. Nguyen GC, Rosenberg M, Chong RY, Chong CA. Early cholecystectomy and ERCP are associated with reduced readmissions for acute biliary pancreatitis: a nationwide, population-based study. *Gastrointest Endosc.* 2012;75(1):47–55.

Tables

Table 1. Baseline clinical characteristics and laboratory findings of the patients

	n, (%)	Median (range), %
Age (years)	194	63 (20-93)
Sex: Female	123 (63.4)	
Male	71 (36.6)	
Body mass index (kg/m ²)	194	28.4 (25.8-33.2)
Diabetes mellitus	31	16
Smoking	55	29.6
Alcohol	11	5.9
CCI: 0-2	70 (36)	
3-4	78 (40.2)	
5-8	54 (26.7)	
Laboratory values at admission,	194	
ALT (U/L)		179.5 (74-347)
AST (U/L)		177 (83-337)
GGT (U/L)		224 (118-421)
ALP (U/L)		129 (99-189)
Total bilirubin (mg/dl)		6.0 (0.8-3.2)
CRP (mg/l)		13.6 (5.6-41)
WBC ($\times 10^3$ cells/ μ L)		10.0 (7.8-13.1)
Imaging:		
Abdominal US	194 (100)	
MRCP	165 (85)	
CT	145 (74.7)	
Upper Abdominal MRI	5 (2.4)	
EUS	8 (3.9)	
USG findings of the gallbladder	194	
No stone	23 (11.9)	
< 3	47 (24.2)	
Three or more stones	124 (63.9)	

Sludge	76 (39.6)	
Wall thickening/pericholecystic fluid	79 (40.9)	
Length of hospital stay (days)	194	4 (3-5)

ALT; Alanine aminotransferase, AST; Aspartate aminotransferase, ALP; Alkaline Phosphatase, CRP; C-reactive protein, CCI; Charlson comorbidity index, CT; Computerized tomography, EUS; Endoscopic ultrasonography, GGT; Gamma-glutamyl transferase, WBC; White blood cell, MRCP; Magnetic resonance cholangiopancreatography, MRI; Magnetic resonance imaging.

Table 2. Interval Between Discharge and Gallstone-Related Events		
	All gallstone-related events (n=68)	Other than biliary colic (n=31)
	N, %	N, %
Within 1 week	13 (6.7)	0 (0)
Within 15 days	25 (12.8)	4 (2)
Within 1 month	34 (17.5)	12 (6.2)
Within 3 months	57 (29.3)	24 (12.4)
Within 6 months	68 (35.1)	31 (16)

Table 3: Recurrent Biliary Events in Patients with Delayed Cholecystectomy

n	%	Days (med, IQR)
---	---	-----------------

ary colic	53	27.3	30 (10-60)
Biliary colic only	37	19	
Biliary colic accompanied by other ary complications	16	8.2	
mplications requiring hospital mission	49	25.2	39 (21-64)
iliary colic	18	9.2	
cute pancreatitis	11	5.7	
cute cholecystitis	6	3.1	60 (40-90)
cute pancreatitis + Acute lecystitis	5	2.6	
4	2.1	35	
holedocholithiasis	1	0.5	30
holangitis+Acute pancreatitis	1	0.5	24 (20-28)
cute cholecystitis+Gallbladder oration	1	0.5	
1	0.5	180	
cute pancreatitis+ ledocholithiasis	1	0.5	40
cute lecystitis+Choledocholithiasis			9
			33
cute pancreatitis+ lecystitis+Choledocholithiasis+Liver cess			43
al	68	35.1	

Table 4. Clinical and laboratory characteristics of patients with/without biliary events

Characteristic	Patients with biliary events	Patients with no biliary events	P-value
No. of patients	68	126	
Age (years)	64 (54.5-78)	62 (50-76)	0.242
Sex:Female / Male	46/22	77/49	
Body mass index (kg/m ²)	29.4(26.2-33.8)	28.2(25.7-32.3)	0.161
Diabetes mellitus, n (%)	13.0 (35.1)	18.0 (64.9)	
Smoking, n (%)	21.0 (34.9)	34.0 (65.1)	
Alcohol, n (%)	4.0 (34.9)	7.0 (65.1)	
Charlson Comorbidity Index	4.0 (2-5)	3.0 (2-5)	0.165
Laboratory values at admission, med (range)			
ALT (U/L)	144 (79-325.5)	184.5 (68-373)	0.449
AST (U/L)	160 (84.5-292) 249 (132-396) 120 (103-199)	181 (79-357)	0.457
GGT (U/L)	1.6 (0.7-3.5)	224 (113-427)	0.596
ALP (U/L)	18.8 (8.6-48.7)	135 (97-183) 1.6 (0.9-3)	0.944
Total bilirubin (mg/dl)	9.7 (7.8-13.2)	11.4 (5-31.3)	0.929
CRP (mg/l)		10.2 (7.8-13.1)	0.033
WBC (×10 ³ cells/μL)			0.817
Laboratory values at discharge, med (range)			
ALT (U/L)	54 (31-107)	61 (38-117)	0.575
AST (U/L)	35.5(22.5-49.5)	31 (24-49)	0.974
GGT (U/L)	146.5 (87-215)	135 (71-261)	0.727
ALP (U/L)	122 (92-152)	121 (86-166)	0.879
Total bilirubin (mg/dl)	0.7 (0.5-1)	0.7 (0.5-1.1)	0.787
CRP (mg/l)	33.5(14.6-86.2)	43.1(15.5-89.5)	0.879
	6.7 (5.7-8.7)	7.3 (5.7-8.8)	0.719

WBC ($\times 10^3$ cells/ μ L)			
Med length of hospital stay (days)	4 (3-5)	4 (3-6)	0.496
Med days for cholecystectomy after discharge	65 (39-115)	30 (12-52)	0.006

Table 5. Biliary event rates according to the cholecystectomy time

	Biliary events		
	Yes	No	<i>Total</i>
Operation time			
1st day	1 (1.5%)	3 (2.4%)	4 (2.1%)
2-7 days	0 (0%)	9 (7.1%)	9 (4.6%)
8-15 days	0 (0%)	11 (8.7%)	11 (5.7%)
16-30 days	2 (2.9%)	12 (9.5%)	14 (7.2%)
31-90 days	8 (11.8%)	25 (19.8%)	33 (17%)
91-180 days	5 (4%)	5 (7.4%)	10 (5.2%)
No operation in 6 months	52 (76.5%)	61 (48.4%)	113 (58.2%)
Total	68 (100%)	126 (100%)	194 (100%)

Table 6. Readmission rates according to the cholecystectomy time

	Readmission		<i>Total</i>
	Yes	No	
Operation time			
1st day	1 (2%)	3 (2.1%)	4 (2.1%)
2-7 days	0 (0%)	9 (6.2%)	9 (4.6%)
8-15 days	0 (0%)	11 (7.6%)	11 (5.7%)
16-30 days	1 (2%)	13 (9%)	14 (7.2%)
31-90 days	3 (6.1%)	30 (20.7%)	33 (17%)
91-180 days	3 (6.1%)	7 (4.8%)	10 (5.2%)
No operation in 6 months	41 (83.7%)	72 (49.7%)	113 (58.2%)
Total	49 (100%)	145 (100%)	194 (100%)

Table 7. Effect of Interval to Surgery on Odds Ratio of Complications

	Odds ratio	95% CI	<i>p</i>
Delay to Surgery			
1st day	1.63	0.17-16.13	1.000
2-7 days	1.58	1.42-1.76	0.028
8-15 days	1.59	1.42-1.78	0.009
16-30 days	3.47	0.75-15.87	0.114
31-90 days	1.85	0.79-4.39	0.153
91-180 days	0.52	0.15-1.87	0.325
No operation in 6 months	3.46	1.79-6.70	0.000

Table 8. Effect of Delay to Surgery on Odds Ratio of Readmission			
	Odds ratio	95% CI	<i>p</i>
Delay to Surgery			
1st day	1.01	0.10-10.00	1
2-7 days	1.36	1.25-1.48	0.115
8-15 days	1.37	1.25-1.49	0.069
16-30 days	4.72	0.60-37.04	0.197
31-90 days	4	1.16-13.70	0.019
91-180 days	0.78	0.19-3.13	0.715
No operation in 6 months	5.2	2.28-11.85	0.000

Figures

Figure 1

Biliary event rates according to the cholecystectomy time.