ORIGINAL ARTICLE

Might be over-evaluated: Predicting choledocholithiasis in patients with acute biliary pancreatitis

Aykut Çelik, Cemalettin Ertekin, Leman Damla Ercan, İrem Gider, Feza Ekiz, Mehmet İlhan, Hakan Yanar, Mustafa Kayıhan Günay, Ali Fuat Kaan Gök

Department of General Surgery, Istanbul University Faculty of Medicine, Istanbul-*Türkiye*

ABSTRACT

BACKGROUND: The increase in liver cholestasis enzyme and bilirubin levels, especially due to pancreatitis, mimics choledocholithiasis. This study aimed to examine the relationship between demographic and laboratory cut-off values and the presence of choledocholithiasis in patients with acute biliary pancreatitis (ABP).

METHODS: Patients diagnosed with ABP in the Department of General Surgery at Istanbul Faculty of Medicine between January 2010 and December 2022 were retrospectively analyzed. The presence of stones in the common bile duct was determined based on the results of magnetic resonance cholangiopancreatography (MRCP), endoscopic ultrasound (EUS), and endoscopic retrograde cholangiopancreatography (ERCP). Demographic and laboratory values of patients with and without bile duct stones were compared. Cut-off values were determined using receiver operating characteristic (ROC) curve analysis, and logistic regression analysis and modeling was performed for each variable.

RESULTS: A total of 1,026 ABP patients were evaluated. Patients whose enzyme levels were not elevated and those who did not undergo MRCP were excluded. A total of 584 patients were included in the study, and choledocholithiasis was detected in 188 (32.2%) patients. In multivariate analysis, age, gamma-glutamyl transferase (GGT), alkaline phosphatase (ALP), and direct bilirubin (DB) were found to be statistically associated with choledocholithiasis. The cut-off values were determined as 65 years for age, 394 U/L for GGT, 173 U/L for ALP, and 1.42 mg/dL for direct bilirubin. In the group where all four parameters were below these cut-off values, suggesting a clean common bile duct, it was observed that the negative predictive value was 97%.

CONCLUSION: Based on the demographic and laboratory data of patients with ABP, we were able to predict with more than 97% accuracy that the common bile duct was clean. Considering that our study only included patients who underwent MRCP due to elevated enzyme levels and suspicion of choledocholithiasis, the negative predictive value would be even higher if patients with acute biliary pancreatitis with normal enzyme levels were included. Additionally, no complications were observed in any of the patients during follow-up. This finding suggests that patients whose common bile duct is predicted to be clean can initially be monitored and supported with additional imaging methods if necessary. As a result, unnecessary imaging can be avoided, reducing costs and preventing the mortality and morbidity associated with unnecessary procedures.

Keywords: Choledocholithiasis; pancreatitis; magnetic resonance cholangiopancreatography (MRCP); cost-effective.

INTRODUCTION

Gallbladder stones are very common, affecting 15-20% of the population.[1] Although they are mostly asymptomatic, complications such as cholecystitis, choledocholithiasis, cholangitis, or pancreatitis may occur in 20% of cases.[2] Additionally, gallstones are the most common cause of acute pancreatitis, accounting for up to 60% of cases in Western countries.[3]

Although the exact mechanism of acute pancreatitis is not

Cite this article as: Çelik A, Ertekin C, Ercan LD, Gider İ, Ekiz F, İlhan M, et al. Might be over-evaluated: Predicting choledocholithiasis in patients with acute biliary pancreatitis. Ulus Travma Acil Cerrahi Derg 2025;31:249-258.

Address for correspondence: Aykut Çelik
Department of General Surgery, Istanbul University Faculty of Medicine, Istanbul, Türkiye
E-mail: celikaykut91@gmail.com

Ulus Travma Acil Cerrahi Derg 2025;31(3):249-258 DOI: 10.14744/tjtes.2024.36114
Submitted: 29.10.2024 Revised: 12.12.2024 Accepted: 26.12.2024 Published: 03.03.2025

fully understood, it is believed that reflux into the pancreatic duct due to temporary obstruction of the ampulla Vater by stones passing through the common bile duct triggers trypsin activation and autodigestion.[4] While most stones pass into the duodenum spontaneously, persistent stones in the common bile duct are observed in up to 15% of patients with acute biliary pancreatitis (ABP).[5]

Choledocholithiasis is a condition that should be treated regardless of the presence of underlying acute pancreatitis. If there is an obstruction in the bile ducts, it can lead to complications such as cholangitis, sepsis, and even death. For this reason, it is crucial to diagnose choledocholithiasis accurately and perform stone extraction with endoscopic retrograde cholangiopancreatography (ERCP) without delay.[2]

When investigating choledocholithiasis, liver function tests, including alanine transaminase (ALT) and aspartate aminotransferase (AST), as well as cholestasis enzymes such as alkaline phosphatase (ALP) and gamma-glutamyl transferase (GGT), along with direct bilirubin (DB) and total bilirubin (TB) levels, are used. Among these markers, GGT is considered the most sensitive. Additionally, the prevalence of common bile duct stones increases with age.[6] GGT and ALP are enzymes that elevate in the bloodstream following cholestasis-related biliary tract injury, whereas ALT and AST increase after liver hepatocyte injury.[7]

Diagnosing choledocholithiasis is not always straightforward, particularly in patients with biliary pancreatitis. It is well known that liver function tests, cholestasis enzymes, and bilirubin levels are elevated in both choledocholithiasis and ABP. When these two conditions coexist, diagnosing choledocholithiasis becomes more difficult, as the laboratory value elevations may overlap.[8] In such cases, further evaluation with additional imaging methods is necessary. Although ultrasound (US) is inexpensive and widely accessible, its sensitivity in evaluating the bile duct can be as low as 50%.[9] While endosonographic ultrasound (EUS) is considered a better method for bile duct assessment, its use is limited due to accessibility challenges, operator dependency, and the need for experienced personnel. Magnetic resonance cholangiopancreatography (MRCP), on the other hand, is a more accessible diagnostic method, with sensitivity and specificity values comparable to EUS.[10] ERCP for purely diagnostic purposes has largely been abandoned due to its complication rates, which include bleeding, perforation, pancreatitis, and cholangitis, occurring in up to 15% of cases, except in a limited number of situations.[2] Additionally, the harmful effects against of contrast agents and radiation exposure are further disadvantages of ERCP.[11] As a result, diagnostic evaluations have been replaced by MRCP and EUS, which achieve success rates similar to ERCP while posing significantly lower risks.[12] Another advantage of EUS is that, if necessary, stone extraction can be performed in the same session by transitioning directly to ERPC .

Management of Choledocholithiasis in Patients with ABP in Istanbul University, Department of General Surgery, Trauma, and Emergency Surgery

In patients presenting to our clinic, the diagnosis of pancreatitis is established based on three criteria: 1) the presence of abdominal pain, 2) blood levels of amylase (25-110 U/L) or lipase (0-60 U/L) exceeding three times the upper limit, and 3) imaging findings consistent with pancreatitis. If at least two of these three criteria are met, the patient is diagnosed with pancreatitis according to the revised Atlanta Criteria and is hospitalized.[13] Ultrasonography is routinely performed to assess the presence of gallbladder stones, as gallstones are a primary component of biliary pancreatitis. Patients without gallstones or those with a non-biliary etiology of pancreatitis are not considered to have biliary pancreatitis. Further investigation is warranted in cases of elevated liver enzymes, cholestasis enzymes, or bilirubin levels. MRCP is performed to evaluate the extrahepatic bile ducts. If choledocholithiasis is detected, ERCP is performed. In cases where enzyme levels remain elevated or if there is any suspicion of choledocholithiasis, further evaluation is conducted using EUS or repeat MRCP. Intraoperative cholangiogram and bile duct exploration are not routinely performed in our clinic. Additionally, due to its complications, diagnostic ERCP is not performed. Patients with ABP without choledocholithiasis undergo cholecystectomy once the acute inflammation subsides. In contrast, patients with choledocholithiasis first undergo stone extraction via ERCP, followed by cholecystectomy at a later stage.

In our study, we aimed to evaluate choledocholithiasis in patients with ABP using demographic and laboratory values at the time of admission, with the goal of reducing unnecessary imaging costs and preventing the mortality and morbidity associated with invasive procedures.

MATERIALS AND METHODS

Patients admitted to Istanbul University, Department of General Surgery, Trauma, and Emergency Surgery between January 2010 and December 2022 with a diagnosis of biliary pancreatitis were retrospectively evaluated. After excluding non-biliary etiologies, only patients with pancreatitis confirmed to be associated with gallstones via ultrasonography were included in the study. To exclude cases of spontaneous stone passage, only patients who had blood samples taken at the time of admission and underwent common bile duct imaging within the first 24 hours were included in the study. Demographic data and laboratory values, including GGT (5-85 U/L), ALP (35-104 U/L), AST (5-42 U/L), TB (0.2-1 mg/dL), DB (0-0.3 mg/dL), lactate dehydrogenase (LDH) (135-250 U/L), and glucose (70-100 mg/dL), were collected at the time of hospital admission. Patients under the age of 18, those without elevated enzyme levels (ALT, AST, ALP, GGT, TB, or DB), and those who did not undergo MRCP were excluded from the study. There were no missing values for any of the patients included in the study. Based on MRCP reports, as well as EUS and ERCP results where applicable, patients were divided into two groups: those with and those without stones in the common bile duct. Demographic and biochemical values were compared between these two groups. Since pancreatitis is a progressive condition and we only analyzed patients' values at the time of admission, we determined that it would not be appropriate to consider the severity of pancreatitis in this study.

All procedures performed in the study were conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Istanbul Medical Faculty Clinical Research Ethics Committee (Approval No: 2023/1753, Date: 13.09.2023)."

Statistical Analysis

For statistical analysis, Statistical Package for the Social Sciences (SPSS) version 26 (IBM Corp., Armonk, NY, USA) was used. The normality of the scores obtained from each continuous variable was assessed using descriptive, graphical, and statistical methods. The Kolmogorov-Smirnov test was applied to determine whether the scores followed a normal distribution. Descriptive statistical methods, including number, percentage, median, and interquartile range (IQR) (P25, P75), were used to evaluate the study data. Comparisons between the two groups for quantitative data were performed using the Mann-Whitney U test, while categorical data comparisons were conducted using the Pearson Chi-Square test. In this study, the presence of stones in the common bile duct was considered the dependent variable, while demographic and laboratory markers were treated as independent variables. Univariate and multivariate logistic regression models were used to assess the effect of independent variables on the dependent variable, employing the forward stepwise method. Additionally, receiver operating characteristic (ROC) analysis was performed to determine the most appropriate age and biochemical values for predicting choledocholithiasis. The results were evaluated within a 95% confidence interval, and statistical significance was set at $p<0.05$.

RESULTS

Demographic and Laboratory Findings of the Patients

A total of 1,026 patients with ABP were evaluated between January 2010 and December 2022. A total of 419 patients whose enzyme levels (ALT, AST, ALP, GGT, TB, and DB) were not elevated and who did not undergo MRCP were excluded from the study. Of the remaining 607 patients, three were excluded due to post-ERCP pancreatitis, three were excluded due to hepatitis, one was excluded due to a history of hepaticojejunostomy, two were excluded due to a history of Whipple surgery, 11 were excluded due to hepatopancreatobiliary malignancy, two were excluded due to a history of biliary injury, and one was excluded due to having undergone percutaneous cholecystostomy.

Ultimately, 584 patients with ABP were included in the study.

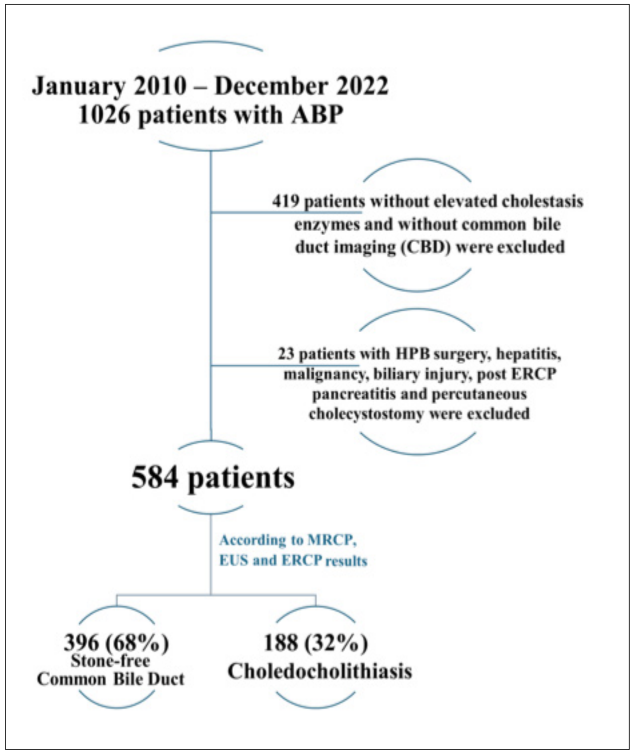

Figure 1. Flowchart of the patients.

Choledocholithiasis was diagnosed in 188 patients (32.2%) based on the results of initial MRCP, ERCP, and EUS evaluations (Fig. 1). Since non-biliary etiologies were excluded, the remaining 67.8% of patients were considered to have experienced pancreatitis due to the passage of a stone from the common bile duct into the duodenum. The median age of patients diagnosed with choledocholithiasis was 58 years (P25-P75, 46-70; min-max: 18-88), and 56% were female. The median age of patients without choledocholithiasis was 55 years (P25-P75, 40-65; min-max: 18-98), with 63% being female. The median age was significantly higher in patients diagnosed with choledocholithiasis ($p=0.048$). Additionally, age, GGT, ALP, AST, TB, and DB levels were significantly higher in the patient group with choledocholithiasis ($p<0.001$ and $p<0.05$) (Table 1).

ROC Curve Analysis Results

The ROC analysis results for determining the presence of choledocholithiasis are presented in Table 2 and Figure 2. According to the analysis, the most appropriate cut-off values for identifying choledocholithiasis were: age ≥65 years (sensitivity: 38%, specificity: 73%), GGT ≥394 U/L (sensitivity: 59%, specificity: 78%), ALP ≥173 U/L (sensitivity: 80%, specificity: 60%), TB ≥2.30 mg/dL (sensitivity: 70%, specificity: 62%), DB ≥1.42 mg/dL (sensitivity: 69%, specificity: 65%), and AST ≥84 U/L (sensitivity: 89%, specificity: 26%).

Logistic Regression Analysis Results and Independent Variables Associated with Choledocholithiasis

In univariate logistic regression analysis, a multivariate logis-

Table 1. Presence of choledocholithiasis according to demographic and biochemical values of the patients

Variables	Choledocholithiasis			P-value
	All Patients (n=584)	With Choledocholithiasis (n=188; 32.2%)	Without Choledocholithiasis (n=396; 67.8%)	
Age#	56 (42-68)	58 (46-70)	55 (40-65)	0.048[a*]
†	18-98	18-88	18-98	
Sex, n (%)				0.092[b]
Male	229 (39.2)	83 (44.1)	146 (36.9)	
Female	355 (60.8)	105 (55.9)	250 (63.1)	
GGT (5-85 U/L)#	292 (166-489)	460 (280-633)	238 (134-381)	<0.001[a*]
†	9-2105	24-2105	9-1610	
ALP (35-104 U/L)#	180 (121-266)	245 (184-365)	155 (106-220)	<0.001[a*]
†	42-1509	58-1509	42-964	
TB (0.2-1 mg/dL)#	2.2 (1.2-4.1)	3.4 (1.9-5.8)	1.8 (0.97-3.3)	<0.001[a*]
†	0.14-31.93	0.38-31.93	0.14-11.36	
DB (0-0.3 mg/dL)#	1.3 (0.5-2.9)	2.4 (1.1-4.1)	0.97 (0.36-2.1)	<0.001[a*]
†	0.01-23.98	0.01-23.98	0.01-10.1	
AST (5-42 U/L)#	187 (100-335)	193 (135-350)	183 (81-329)	0.036[a*]
†	11.2-1177	25-1073	11.2-1177	
LDH (135-250 U/L)#	355 (263-520)	370 (273-521)	349 (258-520)	0.276[a]
†	24-2723	123-2124	24-2723	
Glucose (70-100 mg/dL)#	126 (105-155)	131 (105-157)	124 (106-154)	0.352[a]
†	61-594	61-594	61.8-481	

[a]: Mann-Whitney U test, [b]: Pearson Chi-Square test, *p<0.05, #Median (Interquartile Range), †Minimum-maximum values, **Adjusted for age.

Table 2. Receiver operating characteristic (ROC) analysis for determining age and biochemical values (gamma-glutamyl transferase [GGT], alkaline phosphatase [ALP], aspartate aminotransferase [AST], total bilirubin [TB], and direct bilirubin [DB]) in the presence of choledocholithiasis

Diagnostic Value	Age	GGT	ALP	TB	DB	AST
AUC (95% CI)	0.55 (0.50-0.60)	0.74 (0.70-0.78)	0.75 (0.71-0.79)	0.71 (0.66-0.75)	0.72 (0.68-0.76)	0.55 (0.51-0.60)
p-value	0.048*	<0.001*	<0.001*	<0.001*	<0.001*	0.036*
Cut-off value	≥65	≥394	≥173	≥2.30	≥1.42	≥84
Sensitivity	0.38	0.59	0.80	0.70	0.69	0.89
Specificity	0.73	0.78	0.60	0.62	0.65	0.26
PPV	0.40	0.56	0.49	0.47	0.48	0.36
NPV	0.71	0.80	0.87	0.81	0.82	0.84
Accuracy	0.62	0.72	0.67	0.65	0.66	0.46

*p<0.05, ROC curve analysis. AUC: Area Under the Curve; PPV: Positive Predictive Value; NPV: Negative Predictive Value; CI: Confidence Interval; DB: Direct Bilirubin; TB: Total Bilirubin.

tic regression model was established using the forward stepwise method, including variables that were statistically significantly associated with the presence of choledocholithiasis (p<0.05). These variables included age, GGT, ALP, AST, TB, and DB. The most appropriate model was obtained in the fourth step of the forward stepwise method. In the final step,

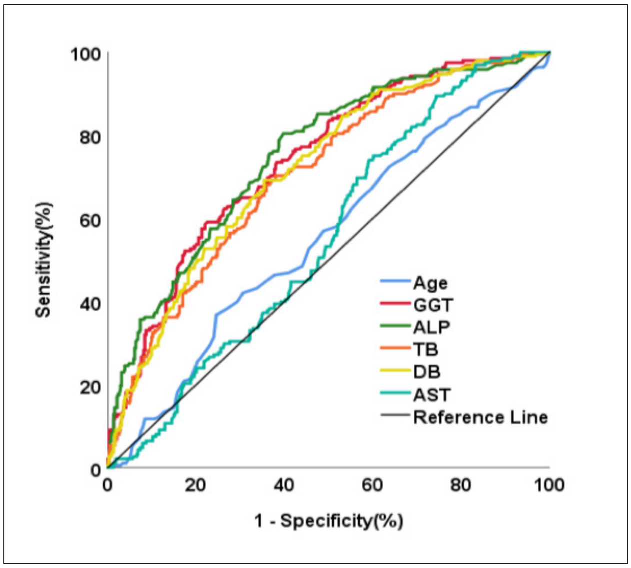

Figure 2. Receiver operating characteristic (ROC) curve analysis results.

four independent factors were identified as being associated with the presence of choledocholithiasis. According to the regression analysis, the model determination coefficient was R2 (Nagelkerke) = 0.33, indicating that 33% of the variance in the dependent variable was explained by the independent variables. The model's probability of correct classification was determined to be 74%. According to the multivariate logistic regression model, the following factors were found to increase the odds of choledocholithiasis: age ≥65 increased the odds 2.1 times (95% confidence interval [CI]: 1.4-3.2), GGT ≥394 U/L increased the odds 3.1 times (95% CI: 2-4.7), ALP ≥173 U/L increased the odds 3.9 times (95% CI: 2.5-6.1), and DB ≥1.42 mg/dL increased the odds 2.5 times (95% CI: 1.7-3.8) (Table 3).

Diagnostic Values of the Clinical "Cut-Off" Values

We developed two different models using the identified cut-off values. The first model was designed for predicting choledocholithiasis, while the second model was designed for excluding choledocholithiasis. The diagnostic values of the model combinations, including sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), are detailed in Tables 4 and 5.

Predicting Stones in the Common Bile Duct

In Table 4, we created our first model by analyzing parameters that exceed the cut-off values together. According to this model, choledocholithiasis was considered present if all specified variables exceeded their respective cut-off values. Each variable was also assessed separately by grouping them in various combinations. Although high specificity was achieved in the group where age, GGT, ALP, and DB values all above their cut-off values, sensitivity was low. The PPV for choledocholithiasis was found to be 0.85, meaning that choledocholithiasis was incorrectly diagnosed in 15% of patients. This is a significant proportion, as additional procedures performed on these patients could lead to increased complications and higher healthcare costs.

Predicting a Stone-Free Common Bile Duct

In Table 5, we developed our second model by evaluating parameters that were lower than the cut-off values together. According to this model, choledocholithiasis was considered absent if all specified variables remained below their respective cut-off values. Each variable was also analyzed separately and grouped in various combinations. As a result, when age, GGT, ALP, and DB were all below the cut-off values, high sensitivity but low specificity was achieved. With an NPV of 97% in this group, we observed that patients without choledocholithiasis could be accurately identified with high success.

Table 3. Univariate and multivariate logistic regression analysis results

			Univariate Analysisa			Multivariate Analysisb(step-4)		
No.	**Variable**	**Cutoff**	**OR**	**95% CI**	**P-value**	**OR**	**95% CI**	**P-value**
1	Age (years)	≥65	1.68	[1.16-2.42]	0.006*	2.08	[1.35-3.21]	0.001*
2	GGT (U/L)	≥394	4.97	[3.42-7.23]	<0.001*	3.08	[2.02-4.69]	<0.001*
3	ALP (U/L)	≥173	6.21	[4.11-9.38]	<0.001*	3.90	[2.49-6.11]	<0.001*
4	DB (mg/dL)	≥1.42	4.10	[2.83-5.94]	<0.001*	2.49	[1.65-3.76]	<0.001*
5	TB (mg/dL)	≥2.30	3.87	[2.66-5.61]	<0.001*	N/A	N/A	NS
6	AST (U/L)	≥84	2.91	[1.74-4.88]	<0.001*	N/A	N/A	NS

*p<0.01, a: Univariate logistic regression analysis, b: Multivariate logistic regression analysis (Forward Stepwise Model), R2 (Nagelkerke)=0.326, Model χ^2=155.113, p<0.001. CI: Confidence Interval; OR: Odds Ratio; DB: Direct Bilirubin; TB: Total Bilirubin; N/A: Not Available; NS: Not Significant. Dependent variable: Choledocholithiasis (1=yes, 0=no). Variables not included in the equation: TB (p=0.398) and AST (p=0.082). Correct classification probability of the model: 74%.

Table 4. Model for predicting common bile duct stones

Cut-off Group Model	Sensitivity	Specificity	PPV	NPV
Age≥65, GGT≥394	0.23 (44/188)	0.97 (386/396)	0.81 (44/54)	0.73 (386/530)
Age≥65, ALP≥173	0.30 (56/188)	0.91 (359/396)	0.60 (56/93)	0.73 (359/491)
Age≥65, DB≥1.42	0.25 (47/188)	0.89 (352/396)	0.52 (47/91)	0.71 (352/493)
GGT≥394, ALP≥173	0.50 (94/188)	0.84 (334/396)	0.60 (94/156)	0.78 (334/428)
GGT≥394, DB≥1.42	0.43 (81/188)	0.87 (346/396)	0.62 (81/131)	0.76 (346/453)
ALP≥173, DB≥1.42	0.57 (108/188)	0.80 (318/396)	0.58 (108/186)	0.80 (318/398)
Age≥65, GGT ≥394, ALP≥173	0.20 (38/188)	0.98 (390/396)	0.86 (38/44)	0.72 (390/540)
Age≥65, GGT≥394, DB≥1.42	0.18 (33/188)	0.98 (390/396)	0.85 (33/39)	0.72 (390/545)
Age≥65, ALP≥173, DB≥1.42	0.20 (37/188)	0.95 (375/396)	0.64 (37/58)	0.71 (375/526)
GGT≥394, ALP≥173, DB≥1.42	0.38 (71/188)	0.90 (358/396)	0.65 (71/109)	0.75 (358/475)
Age≥65, GGT≥394, ALP≥173, DB≥1.42	0.15 (29/188)	0.99 (391/396)	0.85 (29/34)	0.71 (391/550)

Table 5. Model for predicting a stone-free common bile duct

Cut-off Group Model	Sensitivity	Specificity	PPV	NPV
Age<65, GGT<394	0.74 (139/188)	0.53 (210/396)	0.43 (139/325)	0.81 (210/259)
Age<65, ALP<173	0.89 (167/188)	0.43 (169/396)	0.42 (167/394)	0.89 (169/190)
Age<65, DB<1.42	0.82 (155/188)	0.49 (193/396)	0.43 (155/358)	0.85 (193/226)
GGT<394, ALP<173	0.89 (168/188)	0.54 (212/396)	0.48 (168/352)	0.91 (212/232)
GGT<394, DB<1.42	0.85 (160/188)	0.55 (217/396)	0.47 (160/339)	0.89 (217/245)
ALP<173, DB<1.42	0.92 (173/188)	0.45 (177/396)	0.44 (173/392)	0.92 (177/192)
Age<65, GGT<394, ALP<173	0.95 (178/188)	0.37 (146/396)	0.42 (178/428)	0.94 (146/156)
Age<65, GGT<394, DB<1.42	0.93 (174/188)	0.40 (158/396)	0.42 (174/412)	0.92 (158/172)
Age<65, ALP<173, DB<1.42	0.95 (179/188)	0.33 (130/396)	0.40 (179/445)	0.94 (130/139)
GGT<394, ALP<173, DB<1.42	0.96 (180/188)	0.41 (162/396)	0.43 (180/414)	0.95 (162/170)
Age<65, GGT<394, ALP<173, DB<1.42	0.98 (184/188)	0.30 (118/396)	0.40 (184/462)	0.97 (118/122)

DISCUSSION

Diagnosing choledocholithiasis in patients with ABP is difficult and complex, yet it is crucial in determining the need for ERCP. There are few studies in the literature investigating the relationship between ABP and choledocholithiasis, and the evidence is limited. To our knowledge, this study is the largest in the literature on this subject.

In patients with ABP, peripancreatic inflammation complicates the evaluation of the distal common bile duct, which can reduce the diagnostic accuracy of MRCP. Additionally, although some studies suggest that MRCP has reduced sensitivity in detecting small stones,[14] it has been reported in literature that MRCP can successfully detect stones as small as 2 mm.[15] Despite these limitations, studies have shown that MRCP maintains a sensitivity between 80.9% and 100%, a specificity between 83.3% and 98%, and a negative predictive value of up to 100% in patients with ABP. For this reason, MRCP remains the most effective non-invasive method for evaluating the biliary tract in patients with ABP.[16]

Abdominal ultrasound is insufficient for detecting common bile duct stones, although studies have found a correlation between common bile duct width and choledocholithiasis. However, ultrasound is not always reliable, as it is an operator-dependent procedure.[2] For EUS, reported sensitivity ranges from 77% to 100%, while specificity ranges from 85% to 100%. While some studies suggest that EUS is superior to MRCP, others argue that there is no significant difference between the two methods.[17] Despite its high diagnostic accuracy, EUS is not always accessible, as it is only available in advanced centers and requires an experienced team.[18] Some centers recommend EUS evaluation before ERCP in cases of diagnostic uncertainty, followed by ERCP in the same session if necessary. This approach is beneficial both in terms of cost-effectiveness and patient safety, as it eliminates the need for repeat sedation. This approach eliminates the need for a second procedure and prevents complications related to choledocholithiasis during the waiting period.[19]

Another challenge in planning the treatment of choledocholithiasis is the phenomenon of spontaneous stone passage. Although the exact etiology is not fully understood, it is believed that stones obstructing the papilla cause increased pressure due to bile stasis in the common bile duct and the Wirsung duct, which ultimately facilitates stone passage. Small stones, in particular, are known to migrate through the papilla into the duodenum. Studies have reported spontaneous stone passage rates of up to 50% in patients with ABP.[20] This phenomenon explains why stones detected on MRCP may no longer be visible on ERCP. Additionally, the passage of stones over time before ERCP can lead to an incorrect calculation of MRCP accuracy. Therefore, performing EUS before ERCP in patients with suspected stones on MRCP can help prevent unnecessary ERCP and its associated complications.[20] Even if laboratory values are negative, conservative treatment is not recommended when stones are detected in the common bile duct by any imaging method. This is because complication rates can rise to 20%, making stone extraction via ERCP the preferred approach.[21] In our clinic, patients with common bile duct stones undergo ERCP for stone extraction, followed by early cholecystectomy. As a result, long-term follow-up data is not available.

It is of vital importance that the common bile duct is free of stones before cholecystectomy. In cases where stones are present in the common bile duct, early cholecystectomy is recommended after ERCP and stone extraction.[2] We believe that the laboratory values in our study may help guide early cholecystectomy by ruling out common bile duct stones.

The low accuracy of MRCP in detecting small stones, particularly in patients with ABP, complicates clinical diagnosis. However, it can still be used safely, as small stones are more likely to migrate to the duodenum and less likely to cause complications. In patients with ABP, if choledocholithiasis is uncertain on MRCP and persistent choledocholithiasis is suspected, laboratory follow-up and additional imaging are recommended.[20]

Unnecessary use of MRCP and EUS in the investigation of choledocholithiasis results in wasted costs and labor. Scheiman et al.[22] found that the cost per patient for MRCP and EUS was extremely high, with a minimum of over 1,100 USD. They also highlighted the additional costs that may arise during diagnosis and treatment. In our study, we found that approximately two-thirds of ABP patients suspected of having choledocholithiasis underwent unnecessary MRCP. Only 32.2% of patients had common bile duct stones. This suggests that, without our model, the cost of investigating choledocholithiasis with MRCP would have been three times higher. While costs vary by country, this translates to savings of approximately 700 USD per patient solely for MRCP evaluation. MRCP is not suitable for patients with claustrophobia or implants incompatible with magnetic resonance imaging (MRI). Additionally, many hospitals still lack sufficient MRI devices and qualified personnel for evaluation. EUS, on the other hand, is an invasive procedure that requires experienced personnel and is often difficult to access. When used unnecessarily, it leads to extra costs, increased morbidity and mortality, and delayed treatment for patients who genuinely need it.[23] Therefore, while these two methods are highly effective in diagnosing choledocholithiasis, they have limitations and are unfortunately expensive.

In the literature, older age and elevated ALP, GGT, and bilirubin levels are commonly observed in patients with choledocholithiasis.[2] Although AST and ALT were found to be significantly higher in choledocholithiasis in some studies, there are also articles stating that they lose their significance in multivariate analysis.[24] Additionally, it is known that these enzymes increase in patients with biliary pancreatitis. For this reason, high enzyme levels in patients with biliary pancreatitis should not always mean choledocholithiasis.[8,25] We evaluated choledocholithiasis in patients with biliary pancreatitis, so it may not be accurate to compare our findings with other choledocholithiasis studies that exclude pancreatitis in the literature. In our study, older age and high ALP, GGT, and bilirubin levels were found to be statistically significant. Although AST elevation was significant in the univariate analysis, it lost its significance in the multivariate analysis.

GGT and ALP rise due to the early effects of cholestasis on the biliary tract, followed by an increase in bilirubin as stasis continues.[26] GGT, ALP, AST, ALT, and bilirubin levels fluctuate at different times, depending on whether stasis persists in the common bile duct and the degree of hepatocyte damage.[27] In patients with ABP, enzyme elevation due to pancreatitis further complicates the situation.

In the 2019 American Society for Gastrointestinal Endoscopy (ASGE) guidelines, certain parameters were used to predict the presence of stones in the common bile duct. Risk classification was created based on dilated common bile duct, abnormal liver enzymes, age over 55, bilirubin over 4, and the presence of cholangitis.[2] Although these parameters have higher specificity compared to the 2010 ASGE guidelines, some studies argue that they are still insufficient for clinical use, and this classification does not include patients with pancreatitis.[8,25]

In the literature, some studies have investigated the presence of stones in the common bile duct using imaging methods and biochemical values together with demographic data, but the results are far from perfect, and some are difficult to apply.[28,29]

Dana A. Telem et al. investigated common bile duct stones in patients with biliary pancreatitis and found that increased ALP, GGT, and bilirubin levels, as well as common bile duct dilation, were statistically significant. A scoring system was developed based on cut-off values and logistic regression analysis. The incidence of choledocholithiasis was found to be significantly higher in patients with ALP >250, GGT >350, total bilirubin >3, and direct bilirubin >2, with a common bile duct diameter greater than 9 mm. However, in the developed scoring system, all variables were assigned 1 point without considering the odds ratio coefficients. They found a 100% positive predictive value for the presence of stones in the common bile duct in patients who scored 5 points, the highest score. However, this study is a database study, the level of evidence is low, and the number of patients is not suitable for generalization to the population. In addition, while evaluating choledocholithiasis, MRCP was not performed in every patient, diagnostic imaging methods were not standardized, and different imaging techniques were used.

From the same center, Jingjing L. Sherman et al. evaluated choledocholithiasis in patients with biliary pancreatitis and developed a risk assessment and treatment algorithm. They used the cut-off values and scoring systems from the study published by Dana A. Telem et al. According to their scoring system, the positive predictive value for those who scored 0 was found to be 100%, and the accuracy of the study was 100% for those who scored 0 or 5. Since it is a retrospective study with a small sample size, its findings may not be applicable to a larger population. Therefore, we believe that such precise results may not accurately reflect reality.[30]

We did not use a scoring system in our study because the statistical effect of each parameter was different. We also focused on biochemical and demographic values that are easily accessible everywhere. However, we did not achieve results as definitive as those reported in the previously mentioned studies. We believe that our study is more accurate than others in the literature, as it better reflects the general population due to the high number of patients and the evaluation of choledocholithiasis using MRCP, ERCP, and EUS together in some cases.

In addition, only patients with ABP who had MRCP and elevated enzyme levels were evaluated in our study. We do not perform MRCP in patients with ABP without suspected choledocholithiasis. This situation corresponds to pancreatitis patients whose biochemical values are close to normal, and in the vast majority of them, no stones are seen in the common bile duct. Considering that our study did not include this group, we might infer that the actual NPV would be even higher in all ABP patients.

As a limitation, although our study produced precise results, the accuracy of this model should be validated in different cohorts and other medical institutions with larger patient groups to ensure generalizability. In addition, cost-effectiveness should be further investigated.

We believe that detecting choledocholithiasis based solely on age and biochemical values is insufficient. Although it has high specificity, its low sensitivity and 85% PPV make it unsuitable for treatment planning. We think that if any interventional procedure is to be planned, it should be based not only on age and biochemical values but also supported by imaging methods.

Considering the general clinical approach, we found an NPV of 97% based on age and laboratory values in ABP patients who were not suspected of having choledocholithiasis (Age<65, GGT<394, ALP<173, DB<1.42). According to our model, the absence of stones in the common bile duct can be predicted with 97% accuracy. Among the remaining patients, no complications developed, cholangitis was not observed, and no cases progressed to an irreversible medical condition. Therefore, patients who are not suspected of having choledocholithiasis based on age and laboratory values can be safely monitored. If there is no regression in laboratory values or any suspicion of choledocholithiasis during follow-up, further investigation should be conducted with additional imaging.

CONCLUSION

Prediction of common bile duct stones based solely on age and laboratory values is limited in patients with ABP. Advanced imaging modalities such as MRCP and EUS are required to investigate the presence of stones in the common bile duct. However, by using the values in our model, the absence of choledocholithiasis can be predicted with high accuracy.

It is known that in choledocholithiasis and ABP, liver function tests, cholestasis enzymes, and bilirubin levels increase independently. In patients with ABP, enzyme elevation alone should not always indicate choledocholithiasis. For this reason, performing advanced tests such as MRCP, EUS, or ERCP for every elevated enzyme level in patients with ABP will not only increase costs but also lead to unnecessary use of skilled labor and higher complication rates due to avoidable procedures.

With the modeling in our study, common bile duct stones can be excluded with a success rate of more than 97%, allowing for safe follow-up in patients with ABP. As a result, both the cost of excessive evaluation will be reduced, and the mortality and morbidity associated with unnecessary procedures will be prevented.

Ethics Committee Approval: This study was approved by the Istanbul Medical Faculty Clinical Research Ethics Committee (Date: 13.09.2023, Decision No: 2023/1753).

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: A.F.K.G.; Design: A.F.K.G., C.E.; Supervision: A.F.K.G., C.E.; Resource: A.F.K.G., C.E.; Materials: A.F.K.G., İ.G.; Data Collection and/or Processing: A.Ç., L.D.E., İ.G., M.İ., A.F.K.G.; Analysis and/or Inter-

pretation: L.D.E., İ.G., M.İ., A.F.K.G.; Literature Review: A.Ç., L.D.E., İ.G., M.İ., A.F.K.G.; Writing: A.Ç., A.F.K.G.; Critical Review: A.Ç., C.E., F.E., H.Y., M.K.G.

Conflict of Interest: None declared.

Financial Disclosure: The author declared that this study has received no financial support.

REFERENCES

1. Kratzer W, Mason RA, Kächele V. Prevalence of gallstones in sonographic surveys worldwide. J Clin Ultrasound 1999;27:1-7. [CrossRef]
2. ASGE Standards of Practice Committee; Buxbaum JL, Abbas Fehmi SM, Sultan S, Fishman DS, Qumseya BJ, Cortessis VK, et al. ASGE guideline on the role of endoscopy in the evaluation and management of choledocholithiasis. Gastrointest Endosc 2019;89:1075-105.e15. [CrossRef]
3. Frey CF, Zhou H, Harvey DJ, White RH. The incidence and case-fatality rates of acute biliary, alcoholic, and idiopathic pancreatitis in California, 1994-2001. Pancreas 2006;33:336-44. [CrossRef]
4. Frossard JL, Steer ML, Pastor CM. Acute pancreatitis. Lancet 2008;371:143-52. [CrossRef]
5. Singhvi G, Ampara R, Baum J, Gumaste V. ASGE guidelines result in cost-saving in the management of choledocholithiasis. Ann Gastroenterol 2016;29:85-90. [CrossRef]
6. Prat F, Meduri B, Ducot B, Chiche R, Salimbeni-Bartolini R, Pelletier G. Prediction of common bile duct stones by noninvasive tests. Ann Surg 1999;229:362-8. [CrossRef]
7. Tetangco EP, Shah N, Arshad HM, Raddawi H. Markedly elevated liver enzymes in choledocholithiasis in the absence of hepatocellular disease: Case series and literature review. J Investig Med High Impact Case Rep 2016;4:2324709616651092. [CrossRef]
8. Hasak S, McHenry S, Busebee B, Fatima S, Sloan I, Weaver M, et al. Validation of choledocholithiasis predictors from the "2019 ASGE Guideline for the role of endoscopy in the evaluation and management of choledocholithiasis.". Surg Endosc 2022;36:4199-206. [CrossRef]
9. Jovanović P, Salkić NN, Zerem E, Ljuca F. Biochemical and ultrasound parameters may help predict the need for therapeutic endoscopic retrograde cholangiopancreatography (ERCP) in patients with a firm clinical and biochemical suspicion for choledocholithiasis. Eur J Intern Med 2011;22:e110-4. [CrossRef]
10. Meeralam Y, Al-Shammari K, Yaghoobi M. Diagnostic accuracy of EUS compared with MRCP in detecting choledocholithiasis: A meta-analysis of diagnostic test accuracy in head-to-head studies. Gastrointest Endosc 2017;86:986-93. [CrossRef]
11. ASGE Standards of Practice Committee; Chandrasekhara V, Khashab MA, Muthusamy VR, Acosta RD, Agrawal D, Bruining DH, et al. Adverse events associated with ERCP. Gastrointest Endosc 2017;85:32-47. [CrossRef]
12. Romagnuolo J, Bardou M, Rahme E, Joseph L, Reinhold C, Barkun AN. Magnetic resonance cholangiopancreatography: A meta-analysis of test performance in suspected biliary disease. Ann Intern Med 2003;139:547-57. [CrossRef]
13. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al; Acute Pancreatitis Classification Working Group. Classification of acute pancreatitis-2012: Revision of the Atlanta classification and definitions by international consensus. Gut 2013;62:102-11. [CrossRef]
14. Diehl AK, Holleman DR Jr, Chapman JB, Schwesinger WH, Kurtin WE. Gallstone size and risk of pancreatitis. Arch Intern Med 1997;157:1674-8. [CrossRef]
15. Guibaud L, Bret PM, Reinhold C, Atri M, Barkun AN. Bile duct obstruction and choledocholithiasis: Diagnosis with MR cholangiography. Radiology 1995;197:109-15. [CrossRef]
16. Lee SL, Kim HK, Choi HH, Jeon BS, Kim TH, Choi JM, et al. Diagnostic value of magnetic resonance cholangiopancreatography to detect bile duct stones in acute biliary pancreatitis. Pancreatology 2018;18:22-8. [CrossRef]
17. Giljaca V, Gurusamy KS, Takwoingi Y, Higgie D, Poropat G, Štimac D, et al. Endoscopic ultrasound versus magnetic resonance cholangiopancreatography for common bile duct stones. Cochrane Database Syst Rev 2015;2015:CD011549. [CrossRef]
18. Garrow D, Miller S, Sinha D, Conway J, Hoffman BJ, Hawes RH, et al. Endoscopic ultrasound: A meta-analysis of test performance in suspected biliary obstruction. Clin Gastroenterol Hepatol 2007;5:616-23. [CrossRef]
19. Fusaroli P, Lisotti A. EUS and ERCP in the same session for biliary stones: From risk stratification to treatment strategy in different clinical conditions. Medicina (Kaunas) 2021;57:1019. [CrossRef]
20. Frossard JL, Hadengue A, Amouyal G, Choury A, Marty O, Giostra E, et al. Choledocholithiasis: A prospective study of spontaneous common bile duct stone migration. Gastrointest Endosc 2000;51:175-9. [CrossRef]
21. Anderloni A, Repici A. Role and timing of endoscopy in acute biliary pancreatitis. World J Gastroenterol 2015;21:11205-8. [CrossRef]
22. Scheiman JM, Carlos RC, Barnett JL, Elta GH, Nostrant TT, Chey WD, et al. Can endoscopic ultrasound or magnetic resonance cholangiopancreatography replace ERCP in patients with suspected biliary disease? A prospective trial and cost analysis. Am J Gastroenterol 2001;96:2900-4. [CrossRef]
23. Wani S, Keswani R, Hall M, Han S, Ali MA, Brauer B, et al. A Prospective multicenter study evaluating learning curves and competence in endoscopic ultrasound and endoscopic retrograde cholangiopancreatography among advanced endoscopy trainees: The rapid assessment of trainee endoscopy skills study. Clin Gastroenterol Hepatol 2017;15:1758-67.e11. [CrossRef]
24. Yang MH, Chen TH, Wang SE, Tsai YF, Su CH, Wu CW, et al. Biochemical predictors for absence of common bile duct stones in patients undergoing laparoscopic cholecystectomy. Surg Endosc 2008;22:1620-4.
25. Wang L, Mirzaie S, Dunnsiri T, Chen F, Wilhalme H, MacQueen IT, et al. Systematic review and meta-analysis of the 2010 ASGE non-invasive predictors of choledocholithiasis and comparison to the 2019 ASGE predictors. Clin J Gastroenterol 2022;15:286-300. [CrossRef]
26. Lin H, Zhou X, Zhang Z. The diagnostic value of GGT-based biochemical indicators for choledocholithiasis with negative imaging results of magnetic resonance cholangiopancreatography. Contrast Media Mol Imaging 2022;2022:7737610. [CrossRef]
27. Resnick E, Shteingart S, Melamud B, Bdolah-Abram T, Zalut T, Reuben A, et al. Enzyme pattern of biliary colic: A counterintuitive picture. World J Hepatol 2016;8:1629-36. [CrossRef]
28. Khalfallah M, Dougaz W, Bedoui R, Bouasker I, Chaker Y, Nouira R, et al. Validation of the lacaine-huguier predictive score for choledocholithiasis: Prospective study of 380 patients. J Visc Surg 2012;149:e66-72. [CrossRef]
29. Van Santvoort HC, Bakker OJ, Besselink MG, Bollen TL, Fischer K, Nieuwenhuijs VB, et al; Dutch Pancreatitis Study Group. Prediction of common bile duct stones in the earliest stages of acute biliary pancreatitis. Endoscopy 2011;43:8-13. [CrossRef]
30. Sherman JL, Shi EW, Ranasinghe NE, Sivasankaran MT, Prigoff JG, Divino CM. Validation and improvement of a proposed scoring system to detect retained common bile duct stones in gallstone pancreatitis. Surgery 2015;157:1073-9. Erratum in: Surgery. 2016;160:1424. [CrossRef]

ORİJİNAL ÇALIŞMA - *ÖZ*

Akut biliyer pankreatitli hastalarda koledokolitiazisin öngörülmesi: Gereğinden fazla mı değerlendiriyoruz?

AMAÇ: Pankreatite bağlı gelişen karaciğer ve kolestaz enzim yüksekliği ile bilirubin değerlerindeki artış koledokolitiazisi taklit etmektedir. Bu çalışmamızda akut biliyer pankreatitli (ABP) hastaların demografik ve laboratuvar cut-off değerleri ile koledokolitiazis varlığı arasındaki bağlantıyı açıklamayı amaçladık.

GEREÇ VE YÖNTEM: Ocak 2010 ile Aralık 2022 tarihleri arasında İstanbul Tıp Fakültesi Genel Cerrahi Anabilim Dalı'nda ABP tanısı konulmuş hastalar retrospektif olarak incelendi. Manyetik rezonans kolanjiopankreatografi (MRCP), endoskopik ultrason (EUS) ve endoskopik retrograd kolanjiopankreatografi (ERCP) sonuçlarına göre koledokta taş varlığı belirlendi. Koledokta taş bulunan ve bulunmayan grupların demografik ve laboratuvar değerleri karşılaştırıldı. ROC eğrisi ve Lojistik regresyon analizine göre cut-off değerleri belirlendi ve her değişken için ayrı ayrı modellemeler oluşturuldu.

BULGULAR: Toplam 1026 ABP hastası değerlendirildi. MRCP'si olmayan ve kolestaz enzimleri yüksek olmayan hastalar çıkartıldı. Dahil edilen 584 hastanın 188'inde (%32.2) koledokolitiazis saptandı. Multivariate analizde yaş, gama-glutamil transferaz (GGT), alkalen fosfataz (ALP), direkt bilirubin istatistiksel olarak koledokolitiazis ile ilişkili bulundu. Her bir değişkenin cut-off değerleri; yaş için 65, GGT için 394 U/L, ALP için 173 U/L, direkt bilirubin için 1.42 mg/dL saptandı. Bu 4 parametrenin cut-off değerlerinin altında kaldığı ve koledoğun temiz olduğunu tahmin ettiğimiz grupta negatif prediktif değerin %97'ye kadar çıktığı görüldü.

SONUÇ: Akut biliyer pankreatitli hastaların başvuru anındaki demografik ve laboratuvar verileriyle koledoğun taştan temiz olduğunu %97'den fazla başarıyla tahmin edebildik. Çalışmamıza sadece koledokolitiazis şüphesi nedeniyle MRCP çektiğimiz hastaları dahil ettiğimiz düşünülürse, enzimleri normal seyreden ve koledokolitiazis görülmeyen akut biliyer pankreatit hastaları da bu gruba eklendiğinde negatif prediktif değerimiz daha da yüksek çıkacaktır. Ayrıca bu hastaların takiplerinde hiçbir hastada komplikasyon izlenmedi. Bu durum bize koledokta taş düşünülmeyen hastaların öncelikle takip edilebileceğini ve gerektiğinde ek görüntüleme yöntemleri ile desteklenebileceğini düşündürmektedir. Bu sayede hem koledokolitiazis düşünülmeyen hastalara gereksiz görüntüleme yapılmayarak maliyet düşürülürken hem de gereksiz işlemlerden doğabilecek mortalite ve morbiditenin önünde geçilmiş olacaktır.

Anahtar sözcükler: Koledokolitiazis; MRCP; maliyet; pankreatit.

Ulus Travma Acil Cerrahi Derg 2025;31(3):249-258 DOI: 10.14744/tjtes.2024.36114