SMJ- Sohag Medical Journal, Vol. 28 No(3) 2024

Print ISSN1687-8353 Online ISSN2682-4159

Original Article

Prediction of Difficult Biliary Cannulation During ERCP for Common Bile Duct Stones

Mohamed Mostafa Ahmed Malak [1], Amr Mohammed Zaghloul[2], Ali Hussein Mohammed[1.]

1- Internal Medicine Department, Faculty of Medicine, Sohag University, Sohag, Egypt
2- Tropical Medicine and Gastroenterology Department, Faculty of Medicine, Sohag University, Sohag, Egypt

Abstract:

Background: Common bile duct stones (CBDS) represent a widespread problem, and the commonly used approach for this issue is endoscopic retrograde cholangiopancreatography (ERCP). Nevertheless, the difficult biliary cannulation (DBC) throughout ERCP for biliary duct stones continues to pose a considerable obstacle, hence elevating the likelihood of post-ERCP pancreatitis (PEP) and other unfavorable occurrences. This study aimed to recognize pre-procedural aspects that can expect DBC during ERCP for CBDS, thereby facilitating appropriate preventive measures and optimizing patient outcomes.

Methods: This prospective cohort study involved 100 participants aged ≥ 18 years with CBDS undergoing ERCP. DBC is failing to access the papilla after five attempts, spending over five minutes attempting cannulation after initially contacting the papilla, and encountering unwanted cannulation or opacification of the pancreatic duct on more than one occasion.

Results: DBC was present in 43% of the patients. Distal biliary stricture (odds ratio (OR) 4.33, p=0.012), interdiverticular papilla (OR 6.27, p=0.027), attempted stone removal (OR 6.13, p=0.018), precut sphincterotomy (OR 11.121, p=0.036), prophylactic pancreatic stent placement (OR 10.645, p=0.005), AST (OR 0.903, p=0.003), direct bilirubin (OR 288.94, p=0.006), uric acid (OR 1.557, p=0.031), C-reactive protein (OR 2.268, p<0.001), triglycerides (OR 1.034, p<0.001), and glucose (OR 1.120, p<0.001) were independent predictors for DBC.

Conclusion: The incidence of DBC in patients was 43%. Several factors that could predict DBC during ERCP for CBDS patients, including anatomical, procedural, and biochemical parameters.

Keywords: Common bile duct stones, difficult biliary cannulation, ERCP, predictors.

DOI : 10.21608/smj.2024.323729.1500 **Received:** October 13, 2024 **Accepted:** Novamber 02, 2024

Published: January 01, 2025

Corresponding Author: Mohamed Mostafa Ahmed Malak **E.mail**: m.malak500@yahoo.com

Citation: Mohamed Mostafa Ahmed Malak. et al Prediction of Difficult Biliary Cannulation During ERCP for Common Bile Duct Stones SMJ,2025 Vol. 29 No(1) 2025: 37-43

Introduction:

Common bile duct stones (CBDS) represent a prevalent affliction within the biliary tract, arising from a spectrum of etiological factors encompassing biliary tract infection, cholestasis, mechanical alterations within the biliary system, as well as viral infections such as hepatitis B virus. Their incidence is noteworthy, manifesting in approximately 10-15% of individuals afflicted with cholelithiasis.(1)

The annual escalation in cholelithiasis incidence is a notable curve, with prevalence rates of 10% observed among American adults, and varying ranges of 5.9%-21.9% documented in Western Europe and 3.2%-15.6% recorded in Asia .(2)

Endoscopic retrograde cholangiopancreatography (ERCP) is the standard treatment for CBDS, and it is a technique that requires advanced technical skills.(3, 4)

Furthermore, post-ERCP pancreatitis (PEP), a condition closely associated with difficult biliary cannulation (DBC), was recently recognized as the prevailing and severe consequence following ERCP, with an occurrence rate ranging from 3% to 10%. (5-7)

The main risk factor for PEP is widely recognized to be DBC. (8)

It is important to find pre-procedural characteristics that might predict problematic biliary cannulation during ERCP so minimize the prevalence of PEP, considering low intrinsic morbidity associated with CBDS. (9)

Although there have been many studies on the parameters related to DBC in pancreaticobiliary disorders, there is a lack of publications particularly examining DBC in the management of CBDS. (10-14)

Multiple pre-procedural characteristics have been identified as potential predictors of DBC .(15)

The potential contribution of identifying risk variables related to PEP to its prevention in clinical practice is substantial. ERCP may be postponed for individuals classified as high-risk, in favor of alternate endoscopic treatments that provide protection. Additionally, the identification of risk variables associated with PEP has the potential to lead to a decrease in healthcare expenses, while concurrently improving clinical outcomes. (16)

This study aimed to explore pre-procedural issues that are predictive of DBC during ERCP for CBDS, thereby facilitating appropriate preventive measures and optimizing patient outcomes.

Patients and Methods:

A cohort prospective study was undertaken on a sample of 100 patients aged ≥ 18 years, both sexes, with CBDS who underwent ERCP. The study was performed at Sohag University Hospitals, Egypt, between January 2024 and April 2024. An approval from the institutional ethical committee as well as an informed consent were obtained. The participants were categorized into two distinct groups; Group I incorporate patients with DBC, while Group II consisted of those without DBC.

DBC is designated by the European Society of Gastrointestinal Endoscopy according to the following criteria: surpassing five attempts to access the papilla through cannulation, exceeding five minutes of cannulation effort after initial contact with the papillary orifice, and experiencing more than one occurrence of unintentional cannulation or opacification of the pancreatic duct. (14)

Exclusion criteria included presence of a hidden major duodenal papilla, particular pancreatic duct cannulation, pregnancy, uncontrolled coagulopathy (international normalized ratio more than 1.5 or a count of platelet below 50,000/mm^3), medically unstable cardiopulmonary disability requireing conscious sedation, past history of Billroth-II gastrectomy or Roux-en-Y bypass, and cases where CBDS was not recognized throughout ERCP.

Comprehensive patient-related data were collected, including age, sex, end-stage renal failure requiring dialysis, interdiverticular papilla, presentation of the major duodenal papilla, history of cholecystectomy, gastrectomy, hilar bile duct stricture, distal biliary stricture, smoking, hypertension, diabetes, and coronary heart disease.

Laboratory investigations including alanine aminotransferase enzyme (ALT), aspartate aminotransferase enzyme (AST), gamma-glutamyl transferase enzyme (GGT), alkaline phosphatase enzyme (ALP), direct bilirubin, creatinine, uric acid, C-reactive protein (CRP), glucose, international

normalized ratio (INR), total cholesterol, and triglycerides.

Procedure-related data were also collected, such as contrast-assisted cannulation, pancreatic guidewire (PGW)-assisted cannulation, precut sphincterotomy, endoscopic sphincterotomy, pancreatic guidewire approaches, placement of a biliary stent, papillary dilatation using balloon, attempted stone removal, balloon usage, basket usage, complete stone removal, nasobiliary drainage, DBC, injection of contrast media to the pancreatic duct, epinephrine injection surrounding the papilla, extrahepatic bile duct dilatation and pancreatic duct stenting.

The principal outcome of this research was the incidence of DBC during ERCP for CBDS. The consequent outcomes were to identify the factors predicting DBC during ERCP for CBDS.

Calculation of sample size

Epi-Info 2002, a statistical software package designed by the World Health Organization and the Centers for Disease Control and Prevention, was employed to determine the appropriate sample size. The sample size calculation based on a 95% confidence level and an anticipated prevalence of DBC of 57.3% based on a previous study. [17] with a confidence interval of ± 10%. To account for potential participant dropout, the sample size was inflated by six cases. Consequently, 100 participants were recruited for this investigation.

Statistical analysis

Statistical analysis using SPSS v27 (IBM©, Armonk, NY, USA). Quantitative parametric data were represented as mean and standard deviation (SD) and were analyzed by unpaired student t-test. Qualitative variables were represented as frequency and percentage (%) and analyzed using the Chi-square test or Fisher's exact test when appropriate. Multivariate regression was also used to assess the correlation between a dependent variable and other independent variables. A two-tailed P value < 0.05 was recognized as statistically significant.

Results:

One hundred patients with CBDS were divided into two groups: Group I with DBC and Group II without DBC, the incidence of DBC was 43%.

The presence of an interdiverticular papilla was more prevalent in Group I (18.6%) than in Group II (3.51%), with a p-value of 0.017. Moreover, distal biliary stricture was significantly higher in Group I than in Group II with p-value 0.026. Table 1

Table 1: Patient-related data of the studied groups

		Group I (n=43)	Group II (n=57)	P value
Age (years)		66.95 ± 11.69	64.05 ± 12.18	0.233
Sex	**Male**	24 (55.81%)	35 (61.4%)	0.574
	Female	19 (44.19%)	22 (38.6%)	
End-stage renal failure requiring dialysis		2 (4.65%)	1 (1.75%)	0.575
Interdiverticular papilla		8 (18.6%)	2 (3.51%)	**0.017***
Appearance of the major duodenal papilla	**Type 1**	20 (46.51%)	29 (50.88%)	0.933
	Type 2	18 (41.86%)	21 (36.84%)	
	Type 3	2 (4.65%)	2 (3.51%)	
	Type 4	3 (6.98%)	5 (8.77%)	
History of cholecystectomy		4 (9.3%)	7 (12.28%)	0.753
Gastrectomy history		2 (4.65%)	1 (1.75%)	0.575
Smoking history		9 (20.93%)	8 (14.04%)	0.363
Hypertension		14 (32.56%)	16 (28.07%)	0.628
Diabetes		8 (18.6%)	7 (12.28%)	0.381
Coronary heart disease		2 (4.65%)	1 (1.75%)	0.575
Hilar bile duct stricture		1 (2.33%)	0 (0%)	0.430
Distal biliary stricture		13 (30.23%)	7 (12.28%)	**0.026***

Presentation of data as mean ± SD or frequency (%).

Contrast-assisted cannulation was significantly lower in Group I (46.51%) than in Group II (84.21%), with a p-value < 0.001. Conversely, PGW-assisted cannulation, precut sphincterotomy, prophylactic pancreatic stent placement, were significantly elevated in Group I than in Group II, with respective p-values of 0.007, 0.040, and 0.003. while attempted stone removal and complete stone removal were significantly higher in Group II than in Group I, with p-values of 0.029 and 0.027, respectively. Table 2

Table 2: Procedure-related data of the studied groupsp:

	Group I (n=43)	Group II (n=57)	P value
Contrast-assisted cannulation	20 (46.51%)	48 (84.21%)	**<0.001***
PGW-assisted cannulation	11 (25.58%)	3 (5.26%)	**0.007***
Wire-guided cannulation	6 (13.95%)	5 (8.77%)	0.412
Precut sphincterotomy	5 (11.63%)	1 (1.75%)	**0.040***
Attempted stone removal	40 (93.02%)	43 (75.44%)	**0.029***
Balloon	33 (76.74%)	45 (78.95%)	0.792
Basket	18 (41.86%)	25 (43.86%)	0.842
Biliary stent placement	36 (83.72%)	47 (82.46%)	0.868
Prophylactic pancreatic stent placement	10 (23.26%)	2 (3.51%)	**0.003***
Complete stone removal	34 (79.07%)	54 (94.74%)	**0.027***

Presentation of data as mean ± SD or frequency (%).

Group I exhibited lower levels of ALT, AST, direct bilirubin and total cholesterol, with p-values < 0.001. In contrast, creatinine, uric acid, C-reactive protein, triglycerides, and glucose levels were significantly elevated in Group I in comparison to Group II, with respective p-values of 0.008, 0.008, < 0.001, < 0.001, and < 0.001. However, GGT, ALP, and INR did not differ significantly between the two groups. Table 3

Table 3: Laboratory findings of the studied groups

	Group I (n=43)	Group II (n=57)	P value
ALT (U/L)	236.4 ± 51.78	332.05 ± 68.36	**<0.001***
AST (U/L)	169.88 ± 38.9	241.49 ± 30.13	**<0.001***
GGT (U/L)	513.7 ± 57	502.12 ± 42.88	0.249
ALP (U/L)	457.6 ± 22.85	449.02 ± 24.65	0.078
Direct bilirubin (mg/dL)	3.46±0.44	4.43 ± 0.53	**<0.001***
Creatinine (mg/dL)	1.72 ± 0.36	1.51 ± 0.41	**0.008***
Uric acid (mg/dL)	6.73 ± 1.7	5.9 ± 1.35	**0.008***
C-reactive protein (mg/L)	6.14 ± 1.97	3.77 ± 1.38	**<0.001***
INR	1.18 ± 0.15	1.23 ± 0.14	0.100
Total cholesterol (mg/dL)	150.23 ± 17.15	162.11 ± 13.95	**<0.001***
Triglycerides (mg/dL)	431.63 ± 56.87	344.82 ± 39.11	**<0.001***
Glucose (mg/dL)	101.14 ± 9.77	92.86 ± 8.96	**<0.001***

Presentation of data as mean ± SD or frequency (%). ALT: Alanine aminotransferase enzyme, AST: Aspartate aminotransferase enzyme, GGT: Gamma-glutamyl transpeptidase enzyme, ALP: Alkaline phosphatase enzyme. INR: International normalized ratio.

The multivariate regression analysis identified several independent predictors of DBC during ERCP in patients with CBDS. Distal biliary stricture (OR 4.33, p = 0.012), interdiverticular papilla (OR 6.27, p = 0.027), attempted stone removal (OR 6.13, p = 0.018), contrast-assisted cannulation (OR 0.117, p<0.001), precut sphincterotomy (OR 11.121, p = 0.036), prophylactic pancreatic stent placement (OR 10.645, p = 0.005), AST (OR 0.903, p = 0.003), direct bilirubin (OR 288.94, p = 0.006), uric acid (OR 1.557, p = 0.031), C-reactive protein (OR 2.268, p < 0.001), triglycerides (OR 1.034, p < 0.001), and glucose (OR 1.120, p < 0.001) were identified as significant independent predictors of DBC. Table 4

Table 4: Multivariate regression of risk factor for prediction of DBC during ERCP in patients with CBDS.

	Odds ratio	95% CI	P
Distal biliary stricture	4.33	1.374-13.689	**0.012***
Interdiverticular papilla	6.27	1.231-31.947	**0.027***
Attempted stone removal	6.13	1.352-27.856	**0.018***
Contrast-assisted cannulation	0.117	0.041-0.332	**<0.001***
PGW-assisted cannulation	4.557	0.99-20.873	0.051
Precut sphincterotomy	11.121	1.161-106.49	**0.036***
Prophylactic pancreatic stent placement	10.645	1.989-56.962	**0.005***
Alanine aminotransferase (U/L)	0.974	0.945 – 1.004	0.091
Aspartate aminotransferase (U/L)	0.903	0.843 – 0.966	**0.003***
Direct bilirubin (mg/dL)	288.94	5.036 – 16577.9	**0.006***
Creatinine (mg/dL)	4.36	0.971-19.57	0.054
Uric acid (mg/dL)	1.557	1.039-2.333	**0.031***
C-reactive protein (mg/L)	2.268	1.558-3.300	**<0.001***
Total cholesterol level (mg/dL)	0.965	0.930-1.001	0.061
Triglycerides (mg/dL)	1.034	1.020-1.048	**<0.001***
Glucose (mg/dL)	1.120	1.047-1.197	**<0.001***

* P value≤0.05 is considered significant, Confidence interval: I

The rates of PEP in either patients with or without difficult biliary cannulation are enumerated in Table 5, difficult biliary cannulation contributed significantly to the development of PEP.

Table 5: Rate of post-ERCP pancreatitis (PEP).

	Group I (n=43)	Group II (n=57)	P value
PEP (%)	13 (30.23%)	7 (12.28%)	**0.026***

Endoscopic retrograde cholangiopancreatography; ERCP. post-endoscopic retrograde cholangiopancreatography pancreatitis; PEP.

Discussion

The successful handling of CBDS through ERCP is highly depending upon the achieving of biliary cannulation. However, DBC remains a significant challenge, elevating the likelihood of PEP and other unfavorable occurrences. [3, 8, 9]

Our findings revealed several elements related patient linked with DBC, including the presence of an interdiverticular papilla, and distal biliary stricture were pointedly linked with DBC, respective p value 0.017, 0.026, consistent with previous studies highlighting the technical challenges posed by this anatomical variant. [12-14]

Additionally, the study identified several procedural factors significantly associated with DBC. PGW-assisted cannulation, precut sphincterotomy, and prophylactic pancreatic stent placement were more frequent in group I than group II (p=0.007, 0.040, and 0.003, respectively). These findings align with current guidelines and recommendations for managing difficult cannulation scenarios. [3, 6-9, 14, 19]

In contrast, contrast-assisted cannulation, as a common practice of using contrast injection to facilitate cannulation as well as complete stone removal, was lower in the DBC group (p<0.001, p=0.027, respectively). These findings are consistent with previous studies that identified technical aspects of the procedure also important predictors for DBC. [11, 16]

Our study also revealed significant differences in laboratory parameters between the DBC and non-DBC groups, with uric acid, C-reactive protein, triglycerides, and glucose levels significantly higher in the DBC group (p<0.001 for all). These metabolic and inflammatory markers have not been extensively studied in the context of DBC, and their predictive value warrants further investigation. Interestingly, liver enzyme (ALT,

AST), direct bilirubin and total cholesterol levels were lower in the DBC group ($p<0.001$), potentially reflecting underlying cholestatic conditions that may impact cannulation difficulty. However, Cáceres-Escobar et al. indicated a lack of correlation between DBC and bilirubin values. [15] These parameters may play a role in predicting DBC during ERCP for CBDS.

The multivariate regression analysis identified several independent predictors of DBC, including distal biliary stricture, interdiverticular papilla, attempted stone removal, contrast-assisted cannulation, precut sphincterotomy, and prophylactic pancreatic stent placement. These results come in contact with mentioned several studies. [3, 6-10, 12-14, 18, 19]

Additionally, our study highlights the importance of multivariate regression analysis of various laboratory parameters and metabolic factors in predicting DBC (AST, direct bilirubin, uric acid, C-reactive protein, triglycerides, and glucose), which has been less extensively explored in prior research. Our data offers valuable awareness of the complex interplay of patient-related, procedural, and biochemical factors influencing the risk of DBC during ERCP for CBDS.

Compared to previous studies that examined DBC in various pancreatobiliary disorders, this study focused specifically on CBDS patients undergoing ERCP. While some predictors, such as papillary anatomy and operator experience, are consistent with the literature, the identification of metabolic and inflammatory markers as independent predictors is a novel finding that warrants further investigation.

Several limitations to the study warrant mention. First, the research was conducted at a single site center, that potentially restrict the general applicability of the results to other patients. Second, considering sample size, although adequate for the primary outcome, may have been underpowered to detect weaker effect sizes for certain predictors.

Conclusion:

This prospective study cohort revealed a considerable incidence of 43% for DBC. Multiple risk factors emerged as significant independent predictors of DBC through multivariate regression analysis. Anatomical factors, such as the presence of an interdiverticular papilla and distal biliary stricture, were associated with increased DBC risk. Procedural elements like attempted stone removal, pre-cut sphincterotomy, and prophylactic pancreatic stent placement also emerged as significant predictors of DBC. Notably, several laboratory and metabolic parameters as independent predictors, including AST, direct bilirubin, uric acid, CRP, triglycerides, and glucose.

Difficulty in biliary cannulation is a major risk factor for PEP. Those patients that exhibit factors anticipating to difficult biliary cannulation should have a strong prophylaxis, using strong nonsteroidal anti-inflammatory drugs. While doing ERCP in patients who have the previously mentioned predictive elements; early cannulation trials should be done by a qualified endoscopist, also providing immediate application of rescue procedures. (e.g., pancreatic guidewire-assisted cannulation and pre-cut sphincterotomy).

Financial support and sponsorship: Nil
Conflict of Interest: Nil

References:

1. Huang-Fu L, Qian Y-H, Qian M-J. The correlation between postoperative complications of ERCP and quality of life after discharge in patients with choledocholithiasis. Ann Palliat Med. 2021;10:7794-801.

2. Gyedu A, Adae-Aboagye K, Badu-Peprah A. Prevalence of cholelithiasis among persons undergoing abdominal ultrasound at the Komfo Anokye Teaching Hospital, Kumasi, Ghana. Afr Health Sci. 2015;15:246-52.

3. Chen JH, Wang HP. Endoscopic retrograde cholangiopancreatography training and education. Dig Endosc. 2024;36:74-85.

4. Wu CCH, Lim SJM, Khor CJL. Endoscopic retrograde cholangiopancreatography-related complications: risk stratification, prevention, and management. Clin Endosc. 2023;56:433-339.

5. 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.

6. Mine T, Morizane T, Kawaguchi Y, Akashi R, Hanada K, Ito T, et al. Clinical practice guideline for post-ERCP pancreatitis. J Gastroenterol. 2017;52:1013-22.

7. Dumonceau J-M, Kapral C, Aabakken L, Papanikolaou IS, Tringali A, Vanbiervliet G, et al. ERCP-related adverse events: European Society of Gastrointestinal Endoscopy (ESGE) guideline. Endoscopy. 2020;52:127-49.

8. Chung MJ, Park SW, Lee KJ, Park DH, Koh DH, Lee J, et al. Clinical impact of pancreatic steatosis measured by CT on the risk of post-ERCP pancreatitis: a multicenter prospective trial. Gastrointest Endosc. 2024;99:214-23.

9. Borrelli de Andreis F, Mascagni P, Schepis T, Attili F, Tringali A, Costamagna G, et al. Prevention of post-ERCP pancreatitis: current strategies and novel perspectives. Therap Adv Gastroenterol. 2023;16:984-9.

10. Keswani RN, Qumseya BJ, O'Dwyer LC, Wani S. Association between endoscopist and center endoscopic retrograde cholangiopancreatography volume with procedure success and adverse outcomes: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2017;15:1866-75.

11. Berry R, Han JY, Tabibian JH. Difficult biliary cannulation: Historical perspective, practical updates, and guide for the endoscopist. World J Gastrointest Endosc. 2019;11:5-21.

12. Haraldsson E, Kylänpää L, Grönroos J, Saarela A, Toth E, Qvigstad G, et al. Macroscopic appearance of the major duodenal papilla influences bile duct cannulation: a prospective multicenter study by the Scandinavian Association for Digestive Endoscopy Study Group for ERCP. Gastrointest Endosc. 2019;90:957-63.

13. Yue P, Zhu K-X, Wang H-P, Meng W-B, Liu J-K, Zhang L, et al. Clinical significance of different periampullary diverticulum classifications for endoscopic retrograde cholangiopancreatography cannulation. World J Gastroenterol. 2020;26:2403-15.

14. Abdallah KB, Hamzaoui L, Mahmoudi M, Cherif I, Mohamed AB, Yakoubi M, et al. Predictive factors of difficult biliary cannulation: An experience of a tunisian tertiary center. Heliyon. 2022;8:526-31.

15. Cáceres-Escobar D, Muñoz-Velandia OM, Vargas-Rubio R. Factors associated with difficult biliary cannulation in a training center for endoscopic intervention of the biliary tract. Arq Gastroenterol. 2022;59:29-34.

16. Zhou B, Zhao L, Xing X, Wang H, Kuwantai A, Chen K. Risk factors for post-retrograde cholangiopancreatography pancreatitis in patients with common bile duct stones: A meta-analysis. Exp Ther Med. 2024;27:32-5.

17. Saito H, Kadono Y, Shono T, Kamikawa K, Urata A, Nasu J, et al. Factors predicting difficult biliary cannulation during endoscopic retrograde cholangiopancreatography for common bile duct stones. Clin Endosc. 2022;55:263-9.

18. Coté GA, Imler TD, Xu H, Teal E, French DD, Imperiale TF, et al. Lower provider volume is associated with higher failure rates for endoscopic retrograde cholangiopancreatography. Med care. 2013;51:1040-7.

19. Akaydın M, Demiray O. Evaluation of the causes for Repeated Endoscopic Retrograde Cholangiopancreatography in the early period. J Acad Res Med. 2021;11:219-26.