Thieme

Optimal timing for discontinuation of ERCP in cases of difficult selective biliary cannulation

Authors
Han Taek Jeong[1], Jimin Han[1]

Institutions
1 Internal Medicine, Daegu Catholic University School of Medicine, Daegu, Korea (the Republic of)

Key words
Pancreatobiliary (ERCP/PTCD), ERC topics, Stones, Strictures

received 5.12.2024
accepted after revision 30.1.2025
accepted manuscript online 10.2.2025

Bibliography
Endosc Int Open 2025; 13: a25368241
DOI 10.1055/a-2536-8241
ISSN 2364-3722

Georg Thieme Verlag KG, Oswald-Hesse-Straße 50, 70469 Stuttgart, Germany

Corresponding author
Prof. Jimin Han, Daegu Catholic University School of Medicine, Internal Medicine, Daegu, Korea (the Republic of)
jmhan@cu.ac.kr

Supplementary Material is available at https://doi.org/10.1055/a-2536-8241

ABSTRACT

Background and study aims Prolonged cannulation during endoscopic retrograde cholangiopancreatography (ERCP) increases risk of complications, particularly post-ERCP pancreatitis (PEP). This study aimed to determine optimal timing to discontinue ERCP when selective biliary cannulation (SBC) cannot be easily achieved.

Patients and methods Patients with naïve papilla who underwent ERCP between January 2021 and December 2021 were analyzed. The primary outcome was to determine optimal timing for discontinuing ERCP based on cannulation success rate and complication rate.

Results A total of 272 patients with naïve papilla underwent ERCP. Trainees did not participate in any of the procedures. Median age was 71 years, and 152 patients (55.9%) were male. The most common indication for ERCP was choledocholithiasis (60.7%), followed by malignant obstruction (24.3%) and benign stricture (4.8%). SBC was achieved in 249 patients (91.5%). After excluding patients with pre-procedure amylase elevation or preexisting pancreatitis, 232 patients were analyzed for complications. Eighteen patients (6.7%) experienced complications, with PEP occurring in 15 patients (5.5%). SBC success was achieved in 50% of cases at 3.3 minutes and in 90% at 12.1 minutes. In contrast, the PEP rate reached 10% after 7.9 minutes and 14.5% after 12.1 minutes. Multivariate analysis identified distal biliary stricture and age over 70 as significant predictors of difficult SBC.

Conclusions In cases of difficult SBC, discontinuing attempts at around 8 minutes may minimize risk of PEP. However, extending attempts up to 12 minutes can be justified to achieve higher success rates. Beyond 12 minutes, likelihood of successful SBC diminishes significantly.

Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is a crucial procedure for diagnosing and treating pancreaticobiliary disorders [1]. However, achieving selective biliary cannulation (SBC) during ERCP is challenging, particularly in cases with complex anatomy [2, 3, 4]. The European Society of Gastrointestinal Endoscopy (ESGE) has established criteria to define difficult biliary cannulation, which include more than five minutes of cannulation attempts, more than five contacts with the papilla, or more than one unintended pancreatic duct (PD) cannulation or opacification. These factors are associated with an increased risk of complications, particularly post-ERCP pancreatitis (PEP) [1].

The importance of optimizing cannulation time during ERCP has been emphasized by recent studies showing that prolonged cannulation times are independent risk factors for PEP. Lou et al. reported that cannulation times exceeding 15 minutes significantly increased risk of moderate-to-severe PEP, with prolonged attempts linked to increased need for intensive care and poor patient outcomes [5]. Similarly, Mandai et al. highlighted that shorter cannulation times were generally associated with reduced complications, suggesting that an experienced endoscopist plays a critical role in minimizing risk of prolonged cannulation [6].

However, determining the appropriate time to discontinue ERCP remains challenging, because the success of SBC is influenced by multiple factors, including operator expertise, patient anatomy, and disease characteristics [1, 3, 4]. Therefore, this study aimed to determine optimal timing for discontinuing ERCP when SBC is difficult to achieve, considering various factors such as papillary morphology, patient characteristics, and indications for ERCP.

Materials and methods

Study design

This was a retrospective, single-center study. The data used in this study were derived from our study published in 2024. For this analysis, the entire original dataset was utilized, including cases that were excluded in the previous study. The following data were obtained from the dataset: demographics, laboratory findings, comorbidities, and endoscopic findings. For this study, morphology of papilla was assessed by reviewing the endoscopic pictures. We evaluated SBC and complication rates over time to determine optimal discontinuation timing. In addition, the SBC rate was evaluated according to various factors including papillary morphology, patient characteristics, and indications for ERCP. The study protocol was reviewed and approved by the Institutional Review Board of Daegu Catholic University Medical Center (Institutional Review Board number: 2024–10–039). Need for informed consent was waived because this study was performed retrospectively.

Study population

A total of 657 patients who underwent ERCP at the Daegu Catholic University Medical Center between January 2021 and December 2021 were eligible. All patients were at least 18 years old with a naïve papilla. Exclusion criteria were as follows: history of previous ERCP, failure of duodenoscope insertion, ERCP performed for pancreatic intervention, cannulation through choledochoduodenal fistula, or Billroth II anastomosis. However, patients with Billroth I anastomosis or a history of liver transplantation were not excluded because the direction of the ampulla was not altered. After applying these criteria, 272 patients were included in the analysis. For evaluation of complication rates, patients who had acute pancreatitis or amylase levels exceeding three times the normal limit prior to ERCP were excluded. Following this additional exclusion, 238 patients were eligible for complication analysis.

Definitions

Successful SBC was defined as achieving deep cannulation, confirmed by fluoroscopic imaging and endoscopic reports. Cannulation time was measured from the point of achieving en face position to successful completion of SBC, as documented in fluoroscopic and endoscopic reports, where time was automatically recorded. For cases in which SBC failed, cannulation time was defined as duration of the attempt, measured from achieving en face position to procedure termination, as recorded in endoscopic reports. Total procedure time was defined as the interval from achieving en face position to conclusion of the procedure.

Complications included cholangitis, bleeding, perforation, and PEP. PEP was defined according to the international consensus criteria, which require amylase levels elevated at least threefold above the normal limit more than 24 hours after the procedure, along with admission or an extended planned admission of 2 to 3 days [7]. ERCP-related cholangitis was defined with reference to the Tokyo Guidelines 2018 criteria for acute cholangitis as a newly developed fever ≥ 38°C and worsening cholestasis occurring within 48 hours after the procedure [8]. Bleeding included both immediate and delayed bleeding [9]. Immediate bleeding referred to intra-procedure bleeding that caused the procedure to be aborted or altered procedure management. Delayed bleeding was defined by occurrence of hematemesis, melena, and/or hematochezia, along with a drop in hemoglobin ≥ 2 g/dL. Perforation was defined as presence of free air, detected either during the procedure by fluoroscopy or through imaging studies.

Morphology of the major papilla was classified into four types: classic, protruding, small, and creased [10], with evaluation performed by an independent endoscopist who was not involved in the procedure. Major papillae with atypical morphology due to malignancy were categorized as unclassified.

Procedure

All endoscopic procedures were performed by two experts with 17 years and more than 20 years of ERCP experience, respectively. Trainee were not involved in any of the procedures. The procedures were done using a side-viewing duodenoscope (JF-260V or TJF-260V, Olympus Medical System, Tokyo, Japan) under conscious sedation with midazolam and pethidine. SBC was initially attempted using a sphincterotome (AutotomeRX, Boston Scientific, Natick, Massachusetts, United States) preloaded with a straight 0.035-inch hydrophilic-tipped guidewire (Jagwire, Boston Scientific, Natick, Massachusetts, United States). If SBC could not be achieved easily, guidewire or catheter changes were performed at endoscopist discretion. Advanced techniques, such as the double-guidewire technique, pancreatic septotomy, and needle-knife infundibulotomy, were utilized as needed, typically in a sequential manner. Specifically, the double-guidewire technique was employed when unintended PD cannulation occurred two to three times.

To prevent PEP, all patients received hydration with crystalloid solutions, administered at a rate of 1.0–2.0 mL/kg/hr before, during, and after the procedure. Volume and type of intra-

▶ **Table 1** Baseline characteristics of patients who underwent ERCP.

Variables	Total (N = 272)	Success (N = 249, 91.5%)	Failure (N = 23, 8.5%)	*P* value
Age, yrs	71 (60–80)	70 (59–79)	80 (72–82)	< 0.001
Male	152 (55.9)	144 (57.8)	8 (34.8)	0.047
BMI, kg/m^2	23.7 (21.4–25.5)	23.9 (21.6–25.6)	22.5 (19.6–23.8)	0.010
Indication for ERCP				0.009
▪ Choledocholithiasis	165 (60.7)	158 (63.5)	7 (30.4)	
▪ Malignant obstruction	72 (26.5)	61 (24.5)	11 (47.8)	
▪ Benign stricture	15 (5.5)	13 (5.2)	2 (8.7)	
▪ Others*	20 (7.4)	17 (6.8)	3 (13.0)	
Laboratory tests before ERCP				
▪ AST, U/L	109 (48–268)	108 (44–267)	123 (66–395)	0.301
▪ ALT, U/L	141 (49–307)	142 (48–308)	113 (53–272)	0.800
▪ Total bilirubin, mg/dL	2.1 (0.8–5.2)	2.1 (0.8–5.2)	1.9 (1.0–8.1)	0.773
▪ Amylase, U/L	60 (40–97)	59 (40–95)	78 (46–126)	0.106
▪ Lipase, U/L	44 (26–91)	44 (26–86)	50 (32–233)	0.406

Data are presented as number (%) or median (interquartile range).
ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; ERCP, endoscopic retrograde cholangiopancreatography.
*Others included 13 cases of clinical cholangitis, four cases of choledochal cysts, two cases of jaundice, and one case of post-cholecystectomy bile leakage.

venous infusion were adjusted at the discretion of the treating physician on the morning after the procedure. In addition, prophylactic PD stent (Geenen, 5F 3 cm, Cook Medical, Bloomington, Indiana, United States) was placed when deemed necessary by the endoscopist. However, rectal nonsteroidal anti-inflammatory drugs (NSAIDs) were not used because they were not available in South Korea. Endoscopic and fluoroscopic images were taken at key time points, including en face position, achievement of SBC, and conclusion of the procedure. After ERCP, all patients remained fasting until the following morning.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, New York, United States). Categorical variables were compared using the chi-square test or Fisher's exact test. Continuous variables were expressed as medians with interquartile ranges (IQRs) and compared using the Mann-Whitney U test. Kaplan-Meier survival curves were used to assess cumulative SBC rates and complication rates. Statistical comparisons between groups were performed using the log-rank test. For multiple pairwise comparisons, Bonferroni correction was applied to adjust for risk of Type I error. Cox proportional hazards regression analysis was conducted to evaluate predictors of successful cannulation. Results were reported as hazard ratios (HRs) with 95% confidence interval (CI). Variables with $P < 0.2$ in the univariate analysis were included in the multivariate model, which employed backward elimination. A two-tailed $P < 0.05$ was considered statistically significant for all analyses.

Results

Baseline patient characteristics

A total of 272 patients received ERCP during the study period. ▶ **Table 1** presents baseline characteristics of these patients, comparing the success group (N = 249, 91.5%) with the failure group (N = 23, 8.5%). Median age of the patients was 71 years, and 152 (55.9%) were male. Patients with failed cannulation were significantly older than those in the success group (median age 80 vs. 70 years, $P < 0.001$). In addition, the failure group had a lower proportion of males (34.8% vs. 57.8%, $P = 0.047$) and a higher body mass index (BMI) (23.9 vs. 22.5 kg/m^2, $P = 0.010$) The most common indication for ERCP was choledocholithiasis (60.7%), followed by malignant obstruction (26.5%), benign stricture (5.5%), and other causes (7.4%). Distribution of these etiologies differed significantly between the two groups. In the success group, choledocholithiasis was the most frequent indication (N = 158, 63.5%), whereas in the failure group, malignant obstruction was the most common (N = 11, 47.8%; $P = 0.009$). Laboratory tests performed before ERCP, including levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin, amylase, and lipase, showed no significant differences between the two groups.

Clinical outcomes of ERCP

▶ **Table 2** outlines clinical outcomes of ERCP for all patients. Among the 272 procedures, SBC was achieved in 249 patients (91.5%). Morphology of the major papilla differed between the

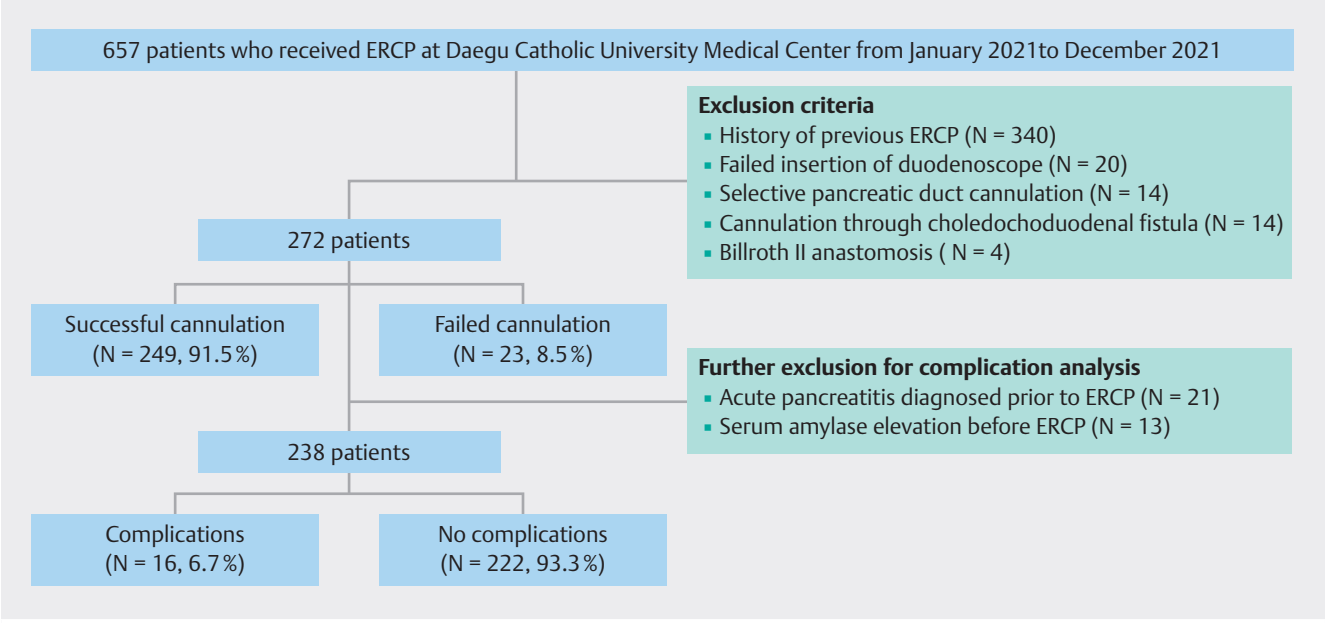
▶ **Table 2** Clinical outcomes of ERCP for naïve papilla.

Variables	Total (N = 272)	Success (N = 249, 91.5%)	Failure (N = 23, 8.5%)	*P* value
Morphology of major papilla				0.062
▪ Classic	120 (44.1)	113 (45.4)	7 (30.4)	
▪ Protruding	44 (16.2)	40 (16.1)	4 (17.4)	
▪ Small	83 (30.5)	76 (30.5)	7 (30.4)	
▪ Creased	21 (7.7)	18 (7.2)	3 (13.0)	
▪ Unclassified	4 (1.5)	2 (0.8)	2 (8.7)	
Periampullary diverticulum	73 (26.8)	67 (26.9)	6 (26.1)	1.000
Location of major papilla*				0.099
▪ Peridiverticular	66 (90.4)	62 (92.5)	4(66.7)	
▪ Intradiverticular	7 (9.6)	5 (7.5)	2(33.3)	
Cannulation technique				
▪ Pancreatic septotomy	34 (12.5)	29 (11.6)	5 (21.7)	0.183
▪ Double-guidewire technique	90 (33.1)	76 (30.5)	14 (60.9)	0.005
▪ Infundibulotomy	9 (3.3)	9 (3.6)	0 (0.0)	1.000
Cannulation time, minutes†	2.7 (1.3–6.4)	2.7 (1.3–6.4)	NA	NA
Procedure time, minutes	10.9 (7.1–16.0)	10.0 (6.9–15.8)	14.7 (11.6–18.1)	0.018
Procedure				
▪ Biliary stent (plastic)	111 (40.8)	111 (44.6)	NA	NA
▪ Pancreatic stent (plastic)	32 (11.8)	24 (9.6)	8 (34.8)	0.002
▪ EPBD	23 (8.5)	23 (9.2)	NA	NA
▪ Metal stent insertion	6 (2.2)	6 (2.4)	NA	NA
▪ ENBD	123 (45.2)	123 (49.4)	NA	NA
Complications (N = 238)[5]	16 (6.7)	15 (6.8)	1 (5.3)	
▪ Bleeding	2 (0.8)	2 (0.9)	0 (0.0)	1.000
▪ Perforation	0 (0.0)	0 (0.0)	0 (0.0)	NA
▪ Pancreatitis	14 (5.9)	13 (5.9)	1 (4.3)	1.000
▪ Cholangitis	0 (0.0)	0 (0.0)	0 (0.0)	NA

Data are presented as number (%) or median (interquartile range).
ENBD, endoscopic nasobiliary drainage; EPBD, endoscopic papillary balloon dilatation; ERCP, endoscopic retrograde cholangiopancreatography.
*Values are expressed based on the total number of periampullary diverticulum cases.
†Cannulation time was calculated for successful cases.
[5] Complication analysis was performed on 238 patients after excluding those with acute pancreatitis or elevated serum amylase levels prior to ERCP.

success and failure groups. The classic papilla morphology was more frequently observed in the success group (45.4% vs. 30.4%), whereas non-classic morphologies, such as creased and unclassified, were more common in the failure group (P = 0.062), although this difference was not statistically significant. ▶ **Fig. 1** summarizes the study population, showing success and failure rates for ERCP, as well as overall incidence of complications. Presence of a periampullary diverticulum was identified in 73 patients (26.8%) and did not significantly impact overall success rates (P = 1.000). Among patients with a diverticulum, the success rate was higher when the major papilla was located peridiverticularly (92.5%) compared with intradiverticularly (71.4%, P = 0.099), although this difference was also not statistically significant.

In terms of cannulation techniques, pancreatic septotomy was used in 34 patients (12.5%), the double-guidewire technique in 90 patients (33.1%), and infundibulotomy in nine patients (3.3%). Notably, the double-guidewire technique was



▶ **Fig. 1** Patient selection and analysis flow for the study. ERCP, endoscopic retrograde cholangiopancreatography.

used more frequently in the failure group (60.9% vs. 30.5%, P = 0.005). Median cannulation time for successful cases was 2.7 minutes (IQR1.3–6.4). Overall procedure time was significantly longer in the failure group compared with the success group (median 14.7 minutes vs. 10.0 minutes, P = 0.018).

Various procedures were performed during ERCP: biliary stent placement in 111 patients (40.8%), pancreatic stent placement in 32 patients (11.8%), endoscopic papillary balloon dilation in 23 patients (8.5%), metal stent insertion in six patients (2.2%), and endoscopic nasobiliary drainage (ENBD) in 123 patients (45.2%). The overall complication rate was 6.7%, with pancreatitis being the most common complication (5.9%). There was no significant difference in incidence of pancreatitis between the success group (5.9%) and the failure group (4.3%, P = 1.000). Bleeding was rare, occurring only in the success group (0.8%), with no cases reported in the failure group. No instances of perforation were observed in either group.

Cannulation rate over time

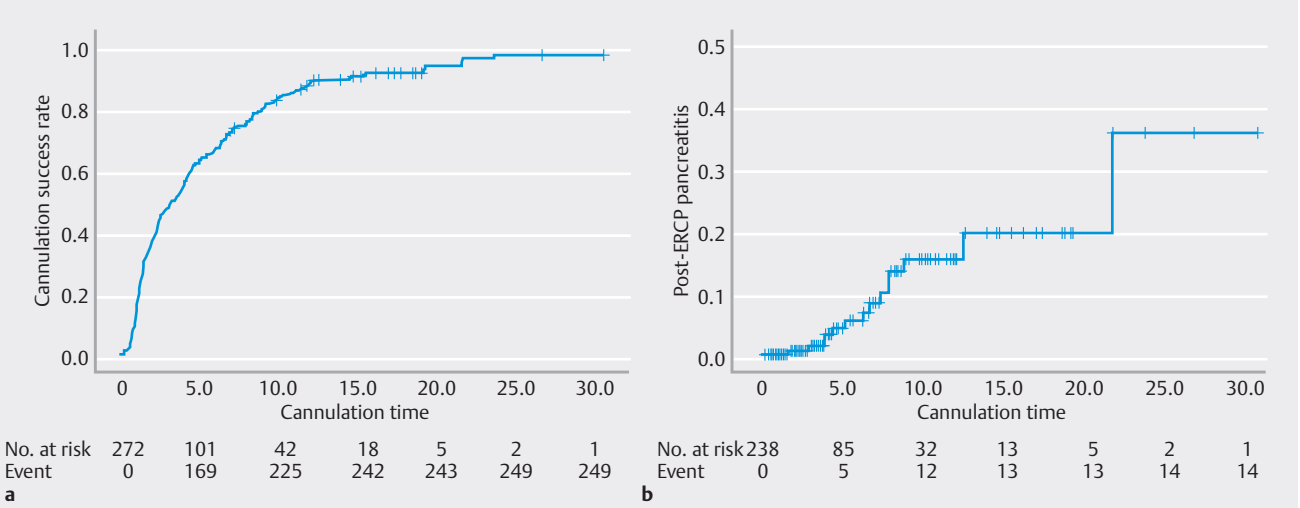
▶ **Fig. 2a** illustrates the cumulative cannulation success rate over time during ERCP. The graph shows a steep increase in success rate within the first few minutes of cannulation attempts. The success rate reaches approximately 60% to 70% within the first 5 minutes. After the initial rapid increase, the curve starts to plateau around the 10-minute mark, with the success rate approaching 80% to 85%. Beyond this point, the rate of increase slows down significantly and 90% of SBC is achieved at 12.1 minutes.

Complication rate over time

▶ **Fig. 2b** depicts cumulative incidence rates for PEP over time during ERCP. In the initial few minutes of cannulation attempts, the cumulative incidence rate for PEP remains relatively low, with minimal increases. However, between 5 and 15 minutes, the graph shows a gradual increase in incidence rates for PEP. The PEP rate was 10% at 7.4 minutes and 14.5% at 12.1 minutes. The graph displays a steeper incline around the 15- to 20-minute mark, with incidence rates reaching approximately 35% by 20 minutes.

Predicting factors associated with successful cannulation

When comparing classic and non-classic papillary morphology (▶ **Fig. 3a**), cumulative success rates reveal that cannulation success is achieved more quickly in patients with classic papilla. Median cannulation time for classic papilla was 2.4 minutes (95% CI 1.63–3.08) compared with 4.0 minutes (95% CI 3.08–4.92) for non-classic papilla (P = 0.052). Furthermore, 90% of SBC was achieved at 11.5 minutes for classic papilla, whereas non-classic papilla required 14.5 minutes to reach the same success rate. For each specific papillary morphology, median cannulation time was 4.8 minutes (95% CI 2.81–6.69) for protruding papilla, 4.0 minutes (95% CI 3.06–4.94) for small papilla, and 2.6 minutes (95% CI 1.73–3.47) for creased papilla (Supplementary Fig. 1). Similarly, presence of a periampullary diverticulum (▶ **Fig. 3b**) appears to facilitate cannulation success. Patients with a diverticulum achieved a 90% success rate earlier at 11.9 minutes than those without a diverticulum, who reached this threshold at 14.7 minutes. Median cannulation time was also shorter for patients with a diverticulum (2.5 minutes; 95% CI 1.77–3.14) compared with those without (4.0 minutes; 95% CI 3.10–4.80).



▶ **Fig. 2** Cannulation success and post-ERCP pancreatitis rate over time. **a** Cannulation success rate over time. At 12.1 minutes, 90% of selective biliary cannulation is achieved, but the rate of increase slows significantly beyond this point. **b** Post-ERCP pancreatitis rate over time. Between 5 and 15 minutes, the incidence rate gradually increases, reaching 10% at 7.4 minutes and 14.5% at 12.1 minutes. ERCP, endoscopic retrograde cholangiopancreatography.

When considering the impact of age (▶ **Fig. 3c**), cannulation success was achieved more slowly in patients older than age 70 years, reaching an 85% success rate at 12.1 minutes, compared with a 90% success rate at 10.2 minutes for younger patients. Median cannulation time was 4.0 minutes (95% CI 2.45–5.55) for elderly patients, compared with 2.9 minutes (1.85–3.89) for younger patients (P = 0.023). BMI had minimal impact on cannulation success (▶ **Fig. 3d**) Median cannulation time was 3.3 minutes (95% CI 2.22–4.38) for patients with a BMI over 23 and 3.2 minutes (95% CI 2.10–4.34) for those with a BMI under 23 (P = 0.299). Regarding sex differences (▶ **Fig. 3e**), the analysis indicated no significant effect on cannulation success. Median cannulation time was 3.3 minutes (95% CI 2.14–4.36) for males and 3.8 minutes (95% CI 2.60–5.00) for females (P = 0.372).

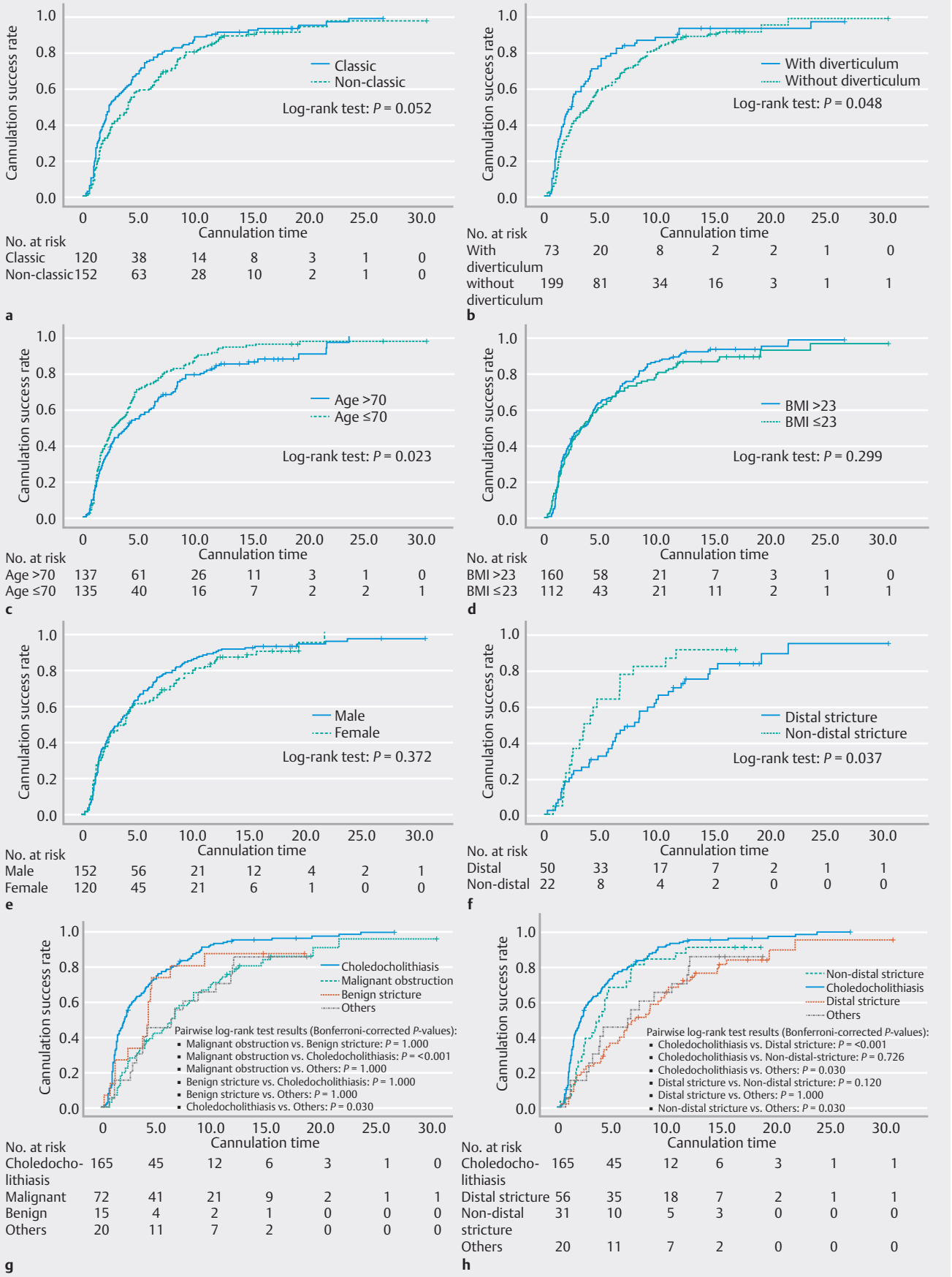
Etiology plays a significant role in determining cannulation success (▶ **Fig. 3g**). Patients with choledocholithiasis achieved faster and more consistent success, with a 90% success rate reached at 9.1 minutes. In contrast, for malignant obstruction, it took 15.4 minutes to achieve an 85% success rate for SBC (P < 0.001). Median cannulation times also varied according to etiology: 2.2 minutes (95% CI 1.73–2.61) for choledocholithiasis, 6.4 minutes (95% CI 5.30–7.44) for malignant obstruction, 4.23 minutes (95% CI 3.60–4.86) for benign strictures, and 2.8 minutes (95% CI 0.92–11.88) for others. Further analysis focused on malignant etiologies, comparing distal and non-distal strictures (▶ **Fig. 3f**). Lower rates of cannulation success were seen in patients with distal strictures, in whom it took 15.4 minutes to achieve an 83% success rate, with a median cannulation time of 7.1 minutes (95% CI 4.70–9.47). In contrast, a higher success rate was achieved earlier in patients with non-distal strictures, with 90% success reached at 11.7 minutes, and median cannulation time of 3.5 minutes (95% CI 2.16–4.88) (P = 0.037). To further refine the analysis, etiologies were reclassified into distal and non-distal strictures instead of malignant and benign obstruction (▶ **Fig. 3h**). Consistent with previous findings, success rates were lower in patients with distal strictures, in whom 15.4 minutes was required to reach an 83% success rate, with a median cannulation time of 7.1 minutes (95% CI 4.72–9.44). In comparison, a 90% success rate at 11.7 minutes was achieved in patients with non-distal strictures, with a median cannulation time of 3.8 minutes (95% CI 2.53–5.03).

▶ **Table 3** consolidates findings from Cox regression analysis, identifying key predictors of successful cannulation. Multivariate analysis underscores that age > 70 (HR 0.743; 95% CI 0.578–0.955; P = 0.020) and distal strictures (HR 0.429; 95% CI 0.307–0.598; P < 0.001) are significantly associated with lower cannulation success.

Discussion

The current study aimed to determine optimal timing for discontinuing ERCP in situations where SBC is challenging. American Society for Gastrointestinal Endoscopy (ASGE) guidelines

▶ **Fig. 3** Factors influencing cannulation success rates. **a** Cannulation success rates and times according to papillary morphology. **b** Impact of presence of a periampullary diverticulum on cannulation success rates and times. **c** Comparison of cannulation success rates between patients older than 70 years and younger patients. **d** Effect of BMI (over 23 vs. 23 or below) on cannulation success rates. **e** Sex-based differences in cannulation success rates. **f** Comparison of cannulation success rates for malignant obstruction: distal vs. non-distal strictures. **g** Cannulation success rates by etiology (choledocholithiasis, malignant obstruction, benign strictures, other causes). **h** Reclassification of etiologies into distal and non-distal strictures and their impact on cannulation success rates.


Cannulation success rate
Cannulation time
Classic
Non-classic
Log-rank test: P = 0.052
No. at risk
Classic 120 38 14 8 3 1 0
Non-classic 152 63 28 10 2 1 0
a
With diverticulum
Without diverticulum
Log-rank test: P = 0.048
No. at risk
With diverticulum 73 20 8 2 2 1 0
without diverticulum 199 81 34 16 3 1 1
b
Age >70
Age ≤70
Log-rank test: P = 0.023
No. at risk
Age >70 137 61 26 11 3 1 0
Age ≤70 135 40 16 7 2 2 1
c
BMI >23
BMI ≤23
Log-rank test: P = 0.299
No. at risk
BMI >23 160 58 21 7 3 1 0
BMI ≤23 112 43 21 11 2 1 1
d
Male
Female
Log-rank test: P = 0.372
No. at risk
Male 152 56 21 12 4 2 1
Female 120 45 21 6 1 0 0
e
Distal stricture
Non-distal stricture
Log-rank test: P = 0.037
No. at risk
Distal 50 33 17 7 2 1 1
Non-distal 22 8 4 2 0 0 0
f
Choledocholithiasis
Malignant obstruction
Benign stricture
Others
Pairwise log-rank test results (Bonferroni-corrected P-values):
Malignant obstruction vs. Benign stricture: P = 1.000
Malignant obstruction vs. Choledocholithiasis: P = <0.001
Malignant obstruction vs. Others: P = 1.000
Benign stricture vs. Choledocholithiasis: P = 1.000
Benign stricture vs. Others: P = 1.000
Choledocholithiasis vs. Others: P = 0.030
No. at risk
Choledocholithiasis 165 45 12 6 3 1 0
Malignant 72 41 21 9 2 1 1
Benign 15 4 2 1 0 0 0
Others 20 11 7 2 0 0 0
g
Non-distal stricture
Choledocholithiasis
Distal stricture
Others
Pairwise log-rank test results (Bonferroni-corrected P-values):
Choledocholithiasis vs. Distal stricture: P = <0.001
Choledocholithiasis vs. Non-distal-stricture: P = 0.726
Choledocholithiasis vs. Others: P = 0.030
Distal stricture vs. Non-distal stricture: P = 0.120
Distal stricture vs. Others: P = 1.000
Non-distal stricture vs. Others: P = 0.030
No. at risk
Choledocholithiasis 165 45 12 6 3 1 1
Distal stricture 56 35 18 7 2 1 1
Non-distal stricture 31 10 5 3 0 0 0
Others 20 11 7 2 0 0 0
h

▶ **Fig. 3**

▶ **Table 3** Predictors of cannulation success using Cox regression analysis.

Variables	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Sex				
▪ Female*				
▪ Male	1.122 (0.871–1.445)	0.373		
Age > 70				
▪ ≤ 70*				
▪ > 70	0.750 (0.585–0.963)	0.024	0.743 (0.578–0.955)	0.020
Periampullary diverticulum				
▪ Absent*				
▪ Present	1.328 (1.001–1.761)	0.049		
BMI > 23.0				
▪ ≤ 23.0*				
▪ > 23.0	1.144 (0.887–1.476)	0.301		
Papillary morphology				
▪ Non-classic*				
▪ Classic	1.280 (0.997–1.645)	0.053		
Etiology		< 0.001		< 0.001
▪ Choledocholithiasis*				
▪ Distal stricture	0.435 (0.312–0.607)	< 0.001	0.429 (0.307–0.598)	< 0.001
▪ Non-distal stricture	0.717 (0.479–1.073)	0.105	0.718 (0.480–1.075)	0.108
▪ Others	0.485 (0.293–0.803)	0.005	0.501 (0.302–0.829)	0.007

*Reference category.
BMI, body mass index; CI, confidence interval; HR, hazard ratio.

recommend that endoscopists achieve SBC in at least 90% of procedures, and the ESGE guidelines also recommend a 90% SBC rate along with a PEP rate of less than 10% [11, 12]. In this study, the overall SBC success rate was 91.5%, with time to achieve 90% SBC being 12.1 minutes. Regarding PEP, the overall PEP rate was 5.9%, with the PEP rate reaching 10% at 7.4 minutes and 14.5% at 12.1 minutes. Extending attempts beyond 12 minutes did not significantly improve success rates but was associated with an increased risk of complications, particularly PEP. These findings align with prior studies, which suggest that prolonged cannulation times may not further enhance success rates but, instead, increase risks of complications [5, 13, 14].

We evaluated various factors affecting SBC rate and cannulation time. Morphology of the major papilla plays a critical role in determining the success rate and optimal timing for cannulation. Our study observed that classic papilla tended to be associated with shorter cannulation times and higher success rates compared with non-classic morphologies. Although the differences did not reach statistical significance ($P = 0.052$), these findings align with previous studies, which reported longer cannulation times and a higher proportion of difficult cannulations in non-classic papilla [2, 15]. The primary reason is that a protruding papilla indicates a longer biliary tract within the intramural distance, causing misalignment between the papillotome and the biliary tract axis [2]. In addition, a small papilla makes it challenging to insert the papillotome into the narrow biliary orifice [2].

A periampullary diverticulum can exert varying influences on SBC, as reported in several studies. When the papilla is located inside the diverticulum, SBC can be more challenging. This difficulty arises because the diverticulum wall may obstruct the papillary opening, making it difficult to achieve proper cannulation [4, 16]. Conversely, when the papilla is located at the margin of the diverticulum, SBC can become easier. In such cases, the diverticulum may weaken or disrupt the function of the papillary sphincter, facilitating cannulation as long as the misaligned axis caused by the diverticulum is properly corrected [16]. In our study, 90% of patients with a periampullary diverticulum had their papilla located at the margin. This finding may explain why SBC was achieved more easily in patients with a diverticulum in this study.

Interestingly, SBC was achieved earlier in younger patients than in elderly patients in this study, and the difference was statistically significant in multivariate analysis. Whereas previous studies have reported that age alone is not associated with difficult cannulation, they identified comorbidities and anatomical changes as contributing factors [17, 18, 19]. Moreover, comorbidities, such as cardiovascular and neurological conditions, are more common among older patients, potentially complicating sedation management and reducing procedure tolerance [20]. Further research is needed to explore these potential interactions more comprehensively.

Finally, etiology was a significant determinant of cannulation success and time required. Success was achieved faster and more consistently in patients with choledocholithiasis, compared with those with malignant obstruction. Within the malignant obstruction group, for distal malignant strictures, 83% success was achieved at 15.4 minutes, compared with 90% success at 11.7 minutes for non-distal strictures. Based on these findings, we hypothesized that the stricture site plays a more critical role in cannulation success than simple classification of etiologies as benign or malignant strictures. Consequently, etiology was reclassified into choledocholithiasis, distal strictures, non-distal strictures, and others. Distal strictures were significantly associated with slow cannulation and low success rate, and they remained a significant factor in multivariate analysis. A long, narrow distal bile duct segment is a well-known factor associated with difficult cannulation [21]. In addition, Fuzzi et al, reported that distal malignant obstruction was associated with difficult biliary cannulation [3]. They also noted that presence of tumoral infiltration can obscure ampullary anatomy and increase rigidity, further complicating the procedure.

In this study, most patients underwent ERCP due to choledocholithiasis, followed by malignant obstruction and benign stricture. In addition, 40.8% of patients received biliary stents, and 45.2% received ENBD. At our center, patients with both choledocholithiasis and cholecystolithiasis typically underwent cholecystectomy during hospitalization. After removal of choledocholithiasis through ERCP, an ENBD was placed and post-surgical confirmation was performed using ENBD-cholangiography. For patients who could not undergo surgery during their hospital stay, plastic stent insertion was performed instead. This clinical practice may explain the higher rates of ENBD and biliary stent observed in patients in this study.

PEP is one of the most feared complications of ERCP, particularly in the context of prolonged cannulation. Our study confirmed that prolonged cannulation time is a significant risk factor for PEP, with incidence rates increasing sharply when cannulation attempts reach between 5 and 10 minutes. This pattern is consistent with findings of Lou et al.[5], who demonstrated that prolonged cannulation was associated with increased rates of moderate-to-severe PEP. In addition, the ESGE guidelines identify cannulation attempt duration of more than 10 minutes as a definite risk factor for PEP [22]. Given that the overall PEP incidence rate in this study was 5.9%, caution is needed when directly interpreting sections of the Kaplan-Meier curve where the cumulative incidence exceeds this rate. However, a steep increase at certain points may indicate periods when risk of PEP rises significantly. In ▶ **Fig. 2**b, cumulative incidence increases sharply around the 8-minute mark, which we identified as a critical point for deciding when to stop the procedure to minimize risks.

Despite its significant findings, this study has several limitations. The retrospective design of this medical record-based study inherently limits completeness and accuracy of the data, particularly regarding post-discharge adverse events, which may introduce bias and restrict the ability to draw definitive conclusions. In addition, this was a single-center study, which may limit generalizability of the findings to other settings or populations. Another limitation is that many factors associated with PEP, such as papilla contact and unintended PD cannulation, were not addressed in this study. Furthermore, procedure-related factors, including decisions about switching cannulation techniques, were made at endoscopist discretion. This could have influenced clinical outcomes. This also implies that time alone has limitations as a predictive factor, despite statistical adjustments. However, we focused on procedure time because it is a variable that endoscopists can easily monitor and control during the procedure. The time we suggest is not an absolute threshold, but rather, a reference point to guide decisions about when to stop the procedure. Lastly, because all procedures were performed by expert endoscopists, the findings may not be fully applicable to settings where less-experienced endoscopists or trainees are involved, further limiting generalizability of the results.

Conclusions

In conclusion, determining optimal cannulation attempt time requires balancing risk of PEP with the success rate for SBC. Although stopping at approximately 8 minutes may minimize risk of PEP, extending attempts up to 12 minutes can be reasonable to achieve higher success rates. For cases with a higher likelihood of success, such as those with classic papilla or choledocholithiasis, it is advisable to consider alternative methods if cannulation is not achieved within 10 minutes, because extended attempts are unlikely to improve outcomes. In contrast, for more complex cases, including those with non-classic papillae or distal strictures, extending attempts up to 15 minutes may be justified.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

[1] Testoni PA, Mariani A, Aabakken L et al. Papillary cannulation and sphincterotomy techniques at ERCP: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. Endoscopy 2016; 48: 657–683 doi:10.1055/s-0042-108641

[2] Chen PH, Tung CF, Peng YC et al. Duodenal major papilla morphology can affect biliary cannulation and complications during ERCP, an observational study. BMC Gastroenterol 2020; 20: 310

[3] Fugazza A, Troncone E, Amato A et al. Difficult biliary cannulation in patients with distal malignant biliary obstruction: An underestimated problem? Dig Liver Dis 2022; 54: 529–536

[4] Tabak F, Ji GZ, Miao L. Impact of periampullary diverticulum on biliary cannulation and ERCP outcomes: a single-center experience. Surg Endosc 2021; 35: 5953–5961 doi:10.1007/s00464-020-08080-8

[5] Lou L, Wang X, Zhang Y et al. Prolonged cannulation time is an independent risk factor for moderate-to-severe post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis: a large cohort study. Ann Transl Med 2023; 11: 188 doi:10.21037/atm-22-4697

[6] Mandai K, Uno K, Fujii Y et al. Number of endoscopic retrograde cholangiopancreatography procedures required for short biliary cannulation time. Gastroenterol Res Pract 2017; 2017: 1515260 doi:10.1155/2017/1515260

[7] Cotton PB, Lehman G, Vennes J et al. Endoscopic sphincterotomy complications and their management: an attempt at consensus. Gastrointest Endosc 1991; 37: 383–393

[8] Kiriyama S, Kozaka K, Takada T et al. Tokyo Guidelines 2018: diagnostic criteria and severity grading of acute cholangitis (with videos). J Hepatobiliary Pancreat Sci 2018; 25: 17–30

[9] Wong Kee Song LM, Baron TH. Endoscopic management of procedure-related bleeding. Gastrointest Intervention 2012; 1: 43–52

[10] Haraldsson E, Lundell L, Swahn F et al. Endoscopic classification of the papilla of Vater. Results of an inter- and intraobserver agreement study. United European Gastroenterol J 2017; 5: 504–510 doi:10.1177/2050640616674837

[11] Domagk D, Oppong KW, Aabakken L et al. Performance measures for ERCP and endoscopic ultrasound: a European Society of Gastrointestinal Endoscopy (ESGE) Quality Improvement Initiative. Endoscopy 2018; 50: 1116–1127 doi:10.1055/a-0749-8767

[12] ASGE Standards of Practice Committee. Faulx AL, Lightdale JR et al. Guidelines for privileging, credentialing, and proctoring to perform GI endoscopy. Gastrointest Endosc 2017; 85: 273–281

[13] Saito H, Kadono Y, Shono T et al. Synergistic effect of independent risk factors for post-endoscopic retrograde cholangiopancreatography pancreatitis: a multicenter retrospective study in Japan. Clin Endosc 2024; 57: 508–514 doi:10.5946/ce.2023.203

[14] Lee YS, Cho CM, Cho KB et al. Difficult biliary cannulation from the perspective of post-endoscopic retrograde cholangiopancreatography pancreatitis: Identifying the optimal timing for the rescue cannulation technique. Gut Liver 2021; 15: 459–465

[15] Haraldsson E, Kylanpaa L, Gronroos J 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: 957–963 doi:10.1016/j.gie.2019.07.014

[16] Yue P, Zhu KX, Wang HP et al. Clinical significance of different periampullary diverticulum classifications for endoscopic retrograde cholangiopancreatography cannulation. World J Gastroenterol 2020; 26: 2403–2415 doi:10.3748/wjg.v26.i19.2403

[17] Cagir Y, Durak MB, Simsek C et al. Comparison of ERCP outcomes and complication risk between elderly and younger patients: A large single-center study. J Clin Med 2024; 13: 6112

[18] Tabak F, Wang HS, Li QP et al. Endoscopic retrograde cholangiopancreatography in elderly patients: Difficult cannulation and adverse events. World J Clin Cases 2020; 8: 2988–2999 doi:10.12998/wjcc.v8.i14.2988

[19] Day LW, Lin L, Somsouk M. Adverse events in older patients undergoing ERCP: a systematic review and meta-analysis. Endosc Int Open 2014; 2: E28–E36 doi:10.1055/s-0034-1365281

[20] Yang JH LW, Si XK, Zhang JX et al. Efficacy and safety of therapeutic ERCP in the elderly: A single center experience. Surg Laparosc Endosc Percutan Tech 2018; 28: e44–e48 doi:10.1097/SLE.0000000000000499

[21] Chan T-T, Chew M, Tang R. Troubleshooting difficult bile duct access: Advanced ERCP cannulation techniques, percutaneous biliary drainage, or EUS-guided rendezvous technique? Gastroenterology Insights 2021; 12: 405–422

[22] Dumonceau JM, Andriulli A, Elmunzer BJ et al. Prophylaxis of post-ERCP pancreatitis: European Society of Gastrointestinal Endoscopy (ESGE) Guideline – updated June 2014. Endoscopy 2014; 46: 799–815 doi:10.1055/s-0034-1377875