

Does timing matter? Endoscopic retrograde cholangiopancreatography performed during acute versus post-acute pancreatitis: a 25-year real-world comparative study from 2 high-volume centers

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Abstract

Background The optimal timing of endoscopic retrograde cholangiopancreatography (ERCP) in acute pancreatitis remains uncertain, particularly in the absence of cholangitis or persistent biliary obstruction. We compared the technical outcomes, procedural complexity and adverse events of ERCP performed during the acute phase, vs. after clinical and biochemical resolution.

Methods This retrospective real-world study reviewed consecutive ERCPs performed for pancreatitis at 2 high-volume hepatopancreatobiliary centers between January 2001 and July 2025. Of 5983 ERCPs, 344 met the inclusion criteria. Group A underwent ERCP during acute pancreatitis for cholangitis and/or rising or persistently elevated bilirubin suggestive of ongoing biliary obstruction (n=114), whereas Group B underwent ERCP after resolution of abdominal pain and serum amylase reduction to <3 times the upper limit of normal (n=230). Primary outcomes were biliary cannulation success, duct clearance and ERCP-related adverse events.

Results Successful biliary cannulation was achieved in 309/344 patients (89.8%) and in 309/329 (93.9%) after excluding cases in which the papilla could not be reached, without any significant between-group difference (93.0% vs. 88.3%; $P=0.114$). Group B more frequently required precut fistulotomy (33.8% vs. 25.2%; $P=0.04$) and >5 cannulation attempts (54.1% vs. 41.4%; $P=0.017$). Complete duct clearance was achieved in 90.9%, with no between-group difference. ERCP-related adverse events were uncommon (4.9%) and similar between groups, whereas intraprocedural bleeding was more frequent in Group B (37.8% vs. 28.1%; $P=0.047$).

Conclusions In high-volume centers, ERCP was effective and safe overall, both during acute pancreatitis and after resolution. Procedural complexity, rather than timing alone, may be a key determinant of risk.

Keywords Endoscopic retrograde cholangiopancreatography, acute biliary pancreatitis, ERCP timing, choledocholithiasis, post-ERCP adverse events

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Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is a fundamental therapeutic procedure for the management of biliary obstruction, choledocholithiasis and cholangitis. Despite its widespread use, ERCP remains an invasive intervention with a well-recognized risk of clinically significant adverse events. Among these, post-ERCP pancreatitis (PEP) is the most frequent complication, with incidence rates generally reported at between approximately 2% and 10% in unselected populations, and higher rates observed in high-risk groups [1,2].

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Over the past 2 decades, numerous studies and meta-analyses have clarified both patient-related and procedure-related risk factors for PEP. A meta-analysis by Ding *et al* demonstrated that female sex, prior pancreatitis, prior PEP, and sphincter of Oddi dysfunction significantly increase the likelihood of PEP [3]. Procedure-related factors, including difficult or prolonged cannulation, unintended pancreatic duct instrumentation or contrast injection, and the use of precut sphincterotomy have also consistently been identified as independent predictors [3,4]. These findings underscore that the interplay between patient susceptibility and technical difficulty is crucial to PEP risk.

The optimal timing of ERCP in the setting of acute biliary pancreatitis continues to be an area of active investigation. In the presence of cholangitis or persistent biliary obstruction, urgent ERCP is recommended by international guidelines [5]. However, in patients who have acute biliary pancreatitis without these features, the benefit of early ERCP (typically within 24–72 h) remains uncertain. Recent evidence suggests that delayed ERCP may be comparable to early ERCP in terms of safety and outcomes in selected cases without severe cholangitis or ongoing obstruction [6]. Other analyses indicate possible advantages of earlier intervention in specific subgroups, but the overall conclusions remain heterogeneous [7]. The variability in study designs, patient selection and definitions of “early” vs. “delayed” ERCP contributes to the ongoing debate.

Despite the extensive literature on ERCP-related complications and timing, there are still only limited long-term real-world data comparing ERCP performed during the acute phase of pancreatitis with ERCP performed after complete clinical resolution. Moreover, relatively few large cohorts have evaluated how papillary inflammation, the presence of periampullary diverticula (PAD), cannulation difficulty, stone characteristics and procedural strategies influence success rates and adverse events, specifically in the context of pancreatitis-related ERCP indications.

In our 25-year, 2-center retrospective study from high-volume hepatopancreatobiliary (HPB) units, we compared clinical characteristics, imaging findings, ampullary morphology, technical success parameters and complication profiles between patients undergoing ERCP during acute pancreatitis and those treated after resolution of the episode. By analyzing real-world outcomes across a large and diverse population, this study aims to clarify how timing, anatomy and procedural complexity affect ERCP performance and safety in patients with pancreatitis.

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Patients and methods

Study design

This was a real-world, retrospective study of consecutive ERCP procedures performed at 2 high-volume HPB centers in Athens, Greece: Tzaneio General Hospital and Aretaieion Hospital. Procedures were conducted by a senior endoscopist (AV) or supervised trainees under AV's oversight. The study period spanned 25 years (January 2001 to July 2025). Among 5983 patients who underwent ERCP during the study period, 379 were eligible for inclusion, after exclusion of patients whose ERCP was not performed for the ongoing episode of acute pancreatitis. Of the 379 initially included patients, 35 were subsequently excluded from the analysis: 15 with pancreatitis attributed to an ampullary adenoma, 9 with pancreatic carcinoma, and 11 in whom a previously undetected stricture was identified on fluoroscopy during ERCP. Eligible patients were stratified according to the timing of ERCP in relation to the index episode of acute pancreatitis. More specifically, Group A included patients who underwent ERCP during the acute phase, within 7 days of admission and during the same hospitalization, in the presence of concomitant cholangitis and/or rising or persistently elevated bilirubin levels suggestive of ongoing biliary obstruction, whereas Group B included patients who underwent ERCP after resolution of the acute episode of pancreatitis, defined as absence of abdominal pain and serum amylase levels below 3 times the upper limit of normal. Patients in Group B had persistent evidence of common bile duct (CBD) stone on magnetic resonance cholangiopancreatography (MRCP) or endoscopic ultrasound (EUS), and/or clinical/laboratory findings compatible with persistent choledocholithiasis.

Data collection

Procedural data were recorded on standardized ERCP forms at the time of the procedure and were retrospectively analyzed in 2025. Variables included demographic, clinical, laboratory and radiological data, and postprocedural follow-up information.

ERCP procedure

Cannulation of the CBD was attempted with a sphincterotome and guidewire. No contrast was injected into the pancreatic duct unless necessary. Needle-knife precut was performed after 5–10 min of failed cannulation or multiple unsuccessful attempts. Once cannulation was achieved, sphincterotomy was performed. CBD clearance including the use of a balloon, basket, or both for stone extraction, and the decision to place a stent was left to the discretion of the endoscopist. When clinically indicated, plastic stents—straight (Amsterdam) or pigtail, 7–10 Fr, 7–10 cm—or covered metal

stents (4-6 cm) were placed. Stent removal was scheduled within 90 days.

Fluoroscopy was routinely used during ERCP, including assessment for retroperitoneal gas when clinically suspected. No patient received prophylactic pancreatic duct stents or rectal nonsteroidal anti-inflammatory drugs. Prophylactic pancreatic duct stenting was not adopted as a routine or systematic preventive strategy in the participating centers during the study period, including the more recent years. Instead, the procedural strategy primarily focused on minimizing pancreatic duct manipulation, including guidewire-assisted biliary cannulation, avoidance of pancreatic duct contrast injection unless strictly necessary, and early transition to needle-knife precut fistulotomy in cases of difficult cannulation. All patients received periprocedural intravenous fluids before and after ERCP, initially with 1 L of either normal saline or Ringer's lactate, according to clinical status. All patients received prophylactic intravenous antibiotics (cefuroxime, ciprofloxacin or piperacillin/tazobactam) tailored to allergies and previous exposures. Antiplatelet and anticoagulant management evolved over time. Until 2010, aspirin and clopidogrel were discontinued 5 days before ERCP, and warfarin was managed with bridging therapy. After 2010, aspirin was generally continued, direct oral anticoagulants were withheld 48-72 h before ERCP, and the international normalized ratio was monitored to ensure values below 1.5. Sedation initially consisted of midazolam, with or without fentanyl, and later evolved to titrated propofol administration according to patient status.

Definition of complications

Acute pancreatitis was diagnosed according to standard criteria, and required at least 2 of the following: typical abdominal pain, serum amylase/lipase >3 times the upper limit of normal, and imaging findings consistent with pancreatitis [8]. PEP was defined as new or worsened abdominal pain with serum amylase and/or lipase elevation >3 times the upper limit of normal at >24 h after ERCP, requiring hospitalization or prolongation of hospital stay, according to the consensus criteria of Cotton *et al* [9]. Because patients in Group A underwent ERCP during an ongoing episode of acute pancreatitis, post-ERCP pancreatitis could not be reliably assessed in this group and was therefore evaluated descriptively only in Group B. In addition, ERCP-related perforation was defined by the presence of clinically significant free air collection in the abdomen or retroperitoneal space, or contrast extravasation and/or clinical findings suggestive of perforation, including subcutaneous emphysema or severe procedure-related deterioration requiring intervention [1]. Intraprocedural bleeding was defined as immediate endoscopically visible bleeding requiring endoscopic hemostasis during the procedure, without necessarily fulfilling the criteria for clinically significant post-procedural bleeding.

Statistical analysis

Categorical variables are presented as counts and percentages, while continuous variables are expressed as mean $\pm$ standard deviation or median with interquartile range, as appropriate. Comparisons between patients undergoing ERCP during the acute phase of pancreatitis (Group A) and those undergoing ERCP after clinical and biochemical resolution (Group B) were performed using Student's *t*-test or the Mann-Whitney *U* test for continuous variables, and the chi-square test or Fisher's exact test for categorical variables, as appropriate. All tests were 2-sided, and a *P*-value <0.05 was considered statistically significant. Analyses of complication subtypes were deemed descriptive, given the small number of individual adverse events, and no significant inferential comparisons were attempted for those categories. IBM SPSS Statistics for Windows, version 27.0 (IBM Corp., Armonk, NY, USA) was used to perform statistical analyses.

Results

Study population characteristics

A total of 344 patients underwent ERCP for pancreatitis (Table 1). The study population comprised 45.6% men and 54.4% women, with a mean age of 67 ± 18 years. ERCP was performed during the acute phase of pancreatitis in 114 patients (33.1%), within 7 days of admission during the index hospitalization (Group A), owing to concomitant cholangitis and/or rising or persistently elevated bilirubin levels suggestive of ongoing biliary obstruction. In contrast, 230 patients (66.9%) underwent ERCP after resolution of the pancreatitis episode (Group B), defined by the absence of abdominal pain and serum amylase levels below 3 times the upper limit of normal (Fig. 1). In this group, the mean time from symptom resolution to ERCP was 45 ± 30 days.

No significant between-group differences were observed in either age or sex distribution. The mean age was 66 ± 18 years in Group A compared with 68 ± 18 years in Group B (*P*=0.333). Similarly, sex distribution was comparable between the groups, with a male/female ratio of 49.1%/50.9% in Group A and 43.9%/56.1% in Group B (*P*=0.212).

Among the included patients, 44 (12.8%) had experienced at least 1 previous episode of pancreatitis without having undergone ERCP for that indication, consistent with relapsing pancreatitis. This was significantly more frequent in the non-acute group than in the acute group (40/230 [17.4%] vs. 4/114 [3.5%], *P*<0.001).

Overall, 18 of 344 patients (5.2%) had undergone ERCP previously, with no significant difference between Group A and Group B (4/114 [3.5%] vs. 14/230 [6.1%], *P*=0.141). In addition, 104 of 344 patients (30.2%) had a history of cholecystectomy, which tended to be more common in Group B, although the difference did not reach statistical significance (28/114 [24.6%] vs. 76/230 [33.0%], *P*=0.067). Use of antiplatelet agents was

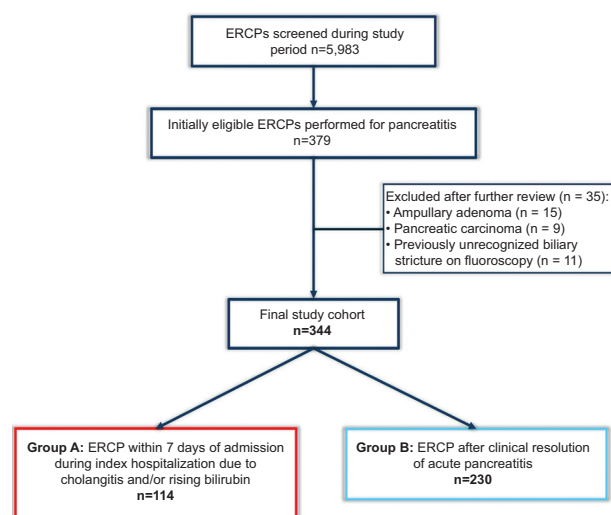
Table 1 Baseline characteristics, anatomical and pre-procedural findings, and procedural and safety outcomes in patients undergoing ERCP during the acute phase of pancreatitis (Group A) vs after clinical resolution (Group B)

	Overall (n=344)	Group A (n=114)	Group B (n=230)	P-value (Group A vs. Group B)
Baseline characteristics				
Age, years	67±18	66±18	68±18	0.333
Male sex, %	45.6	49.1	43.9	0.212
Previous pancreatitis without prior ERCP (relapsing pancreatitis), n/N (%)	44/344 (12.8)	4/114 (3.5)	40/230 (17.4)	<0.001
Prior ERCP, n/N (%)	18/344 (5.2)	4/114 (3.5)	14/230 (6.1)	0.141
Prior cholecystectomy, n/N (%)	104/344 (30.2)	28/114 (24.6)	76/230 (33.0)	0.067
Antiplatelet use, n/N (%)	27/344 (7.8)	7/114 (6.1)	20/230 (8.7)	0.456
Anticoagulant use, n/N (%)	27/344 (7.8)	6/114 (5.3)	21/230 (9.1)	0.354
Anatomical and preprocedural findings				
Ampulla not accessible/identifiable, n/N (%)	167/344 (48.5)	41/114 (36.0)	126/230 (54.8)	<0.001
CBD stones on pre-procedural imaging, n/N (%)	71/339 (20.9)	14/113 (12.4)	57/226 (25.2)	0.015
Periampullary diverticula, n/N (%)	60/329 (18.2)	40/111 (36)	20/218 (9.2)	<0.001
Inflamed papilla, n/N (%)				
Procedural outcomes				
Successful CBD cannulation at index ERCP, n/N (%)	309/344 (89.8)	106/114 (93.0)	203/230 (88.3)	0.114
Successful CBD cannulation among attempted cases, n/N (%)	309/329 (93.9)	106/111 (95.5)	203/218 (93.1)	0.342
Precut fistulotomy, n/N (%)	99/329 (30.1)	28/111 (25.2)	71/218 (33.8)	0.040
>5 cannulation attempts, n/N (%)	164/329 (49.8)	46/111 (41.4)	118/218 (54.1)	0.017
Stones detected on cholangiography, n/N (%)	154/329 (46.8)	55/111 (49.5)	99/218 (45.4)	0.274
Stones >1.5 cm, n/N (%)	11/154 (7.1)	5/55 (9.1)	6/99 (6.1)	0.347
Complete CBD stones clearance, n/N (%)	140/154 (90.9)	51/55 (92.7)	89/99 (89.9)	0.468
Biliary stent placement, n/N (%)	23/344 (6.7)	8/114 (7.0)	15/230 (6.5)	0.682
Safety outcomes				
Intraprocedural bleeding, n/N (%)	119/344 (34.6)	32/114 (28.1)	87/230 (37.8)	0.047
Remaining ERCP-related adverse events, n/N (%)	17/344 (4.9)	5/114 (4.4)	12/230 (5.2)	0.340
Post-ERCP pancreatitis, n/N (%)	6/230 (2.6)	NA	6/230 (2.6)	NA
Post-ERCP cholangitis, n/N (%)	1/230 (0.4)	NA	1/230 (0.4)	NA
All-cause mortality during index clinical course, n/N (%)	4/344 (1.2)	4/114 (3.5)	0/230 (0)	0.012
Procedure-related mortality, n/N (%)	1/344 (0.3)	1/114 (0.9)	0/230 (0)	NA

Percentages were calculated using the number of evaluable patients for each variable. Cannulation-related outcomes were calculated among patients in whom CBD cannulation was attempted (n=329), whereas stone size and complete duct clearance were calculated among patients with stones detected on cholangiography (n=154). Periampullary diverticula and inflamed papilla were analyzed according to available endoscopic data

Group A, ERCP during the acute phase of pancreatitis; Group B, ERCP after clinical resolution of pancreatitis

CBD, common bile duct; ERCP, endoscopic retrograde cholangiopancreatography; n/N, number of patients with the event/number of evaluable patients; NA, not applicable

**Figure 1** Study flowchart

ERCP, endoscopic retrograde cholangiopancreatography; n, number of cases

similar between Group A and B (7/114 [6.1%] vs. 20/230 [8.7%], $P=0.456$). Likewise, anticoagulant use did not differ significantly between the 2 groups (6/114 [5.3%] vs. 21/230 [9.1%], $P=0.354$).

Anatomical and pre-procedural findings

In 15 of 344 patients (4.4%), the ampulla was not accessible or identifiable during ERCP, precluding an attempt at CBD cannulation. Among patients in whom the papilla was inaccessible, the mean interval from the pancreatitis episode to ERCP was shorter than in those with an accessible papilla (8.7 ± 4.0 vs. 40.4 ± 36.9 days, $P=0.04$).

Stones in the CBD were identified before the procedure in 167 of 344 patients (48.5%). Preprocedural imaging consisted of MRCP, with or without computed tomography (CT) and abdominal ultrasound, in 164 patients (47.7%); EUS, with or without MRCP, CT and abdominal ultrasound, in

4 patients (1.2%); CT, with or without abdominal ultrasound, in 80 patients (23.3%); and abdominal ultrasound alone in 96 patients (27.9%). Stones in the CBD were significantly ($P<0.001$) more frequent in Group B (126/230 [54.8%]) compared to Group A (41/114 [36%]).

Periampullary diverticula were identified in 71 of 339 patients (20.9%) overall, and were more frequently observed in Group B (non-acute setting) than in Group A (57/226 [25.2%] vs. 14/113 [12.4%], $P=0.015$). Conversely, an inflamed papilla was documented in 60 of 329 patients (18.2%) overall and was significantly more common in Group A (acute setting) than in Group B (40/111 [36%] vs. 20/218 [9.2%], $P<0.001$).

Cannulation success and cholangiographic findings (Fig. 2)

Successful CBD cannulation at the index ERCP was achieved in 309 of 344 patients (89.8%). Although the rate was numerically lower in Group B than in Group A (88.3% vs. 93.0%), the difference was not statistically significant ($P=0.114$). Excluding the 15 patients in whom cannulation was not attempted increased the overall success rate to 93.9% (309/329). Among patients in whom CBD cannulation was attempted, both the use of precut fistulotomy and the need for more than 5 cannulation attempts were more common in Group B than in Group A (33.8% vs. 25.2%, $P=0.04$, and 54.1% vs. 41.4%, $P=0.017$, respectively).

Stones were detected in 154 of 329 patients (46.8%) and were similarly distributed between the 2 groups (Group A: 55/111 [49.5%] vs. Group B: 99/218 [45.4%], $P=0.274$). Most stones were small, with stones larger than 1.5 cm identified in only 11

of 154 patients (7.1%). The proportion of stones >1.5 cm did not differ significantly between the 2 groups (Group A: 5/55 [9.1%] vs. Group B: 6/99 [6.1%], $P=0.347$). Complete clearance of CBD stones was achieved in 140 of 154 patients (90.9%), with no significant difference between group A and Group B (51/55 [92.7%] vs. 89/99 [89.9%], $P=0.468$). Biliary stents were placed in 23 of 344 patients (6.7%), with comparable rates between Group A and Group B (7.0% vs. 6.5%, $P=0.682$).

Procedure-related complications (Fig. 2)

Intraprocedural bleeding, mostly immediate and endoscopically controlled, was observed more frequently in patients who underwent ERCP in the non-acute setting than in those treated in the acute setting (Group A: 32/114 [28.1%] vs. Group B: 87/230 [37.8%], $P=0.047$), possibly reflecting the more frequent use of needle-knife fistulotomy in Group B. In all cases, bleeding was successfully managed with periampullary injection of adrenaline solution, and no patient required repeat endoscopy.

Other ERCP-related adverse events were uncommon overall, occurring in 17 of 344 patients (4.9%), and were numerically more frequent in the non-acute group, although the difference did not reach statistical significance (Group A: 5/114 [4.4%] vs. Group B: 12/230 [5.2%], $P=0.34$). Reported events included retroperitoneal perforation in 1 patient (0.3%), postprocedural bleeding in 3 (0.9%) and cholecystitis in 2 (0.6%). Among patients undergoing ERCP in the non-acute setting, PEP occurred in 6 of 230 cases (2.6%) and post-ERCP cholangitis in 1 of 230 (0.4%). Lastly, all-cause mortality during the index clinical course was observed only in patients

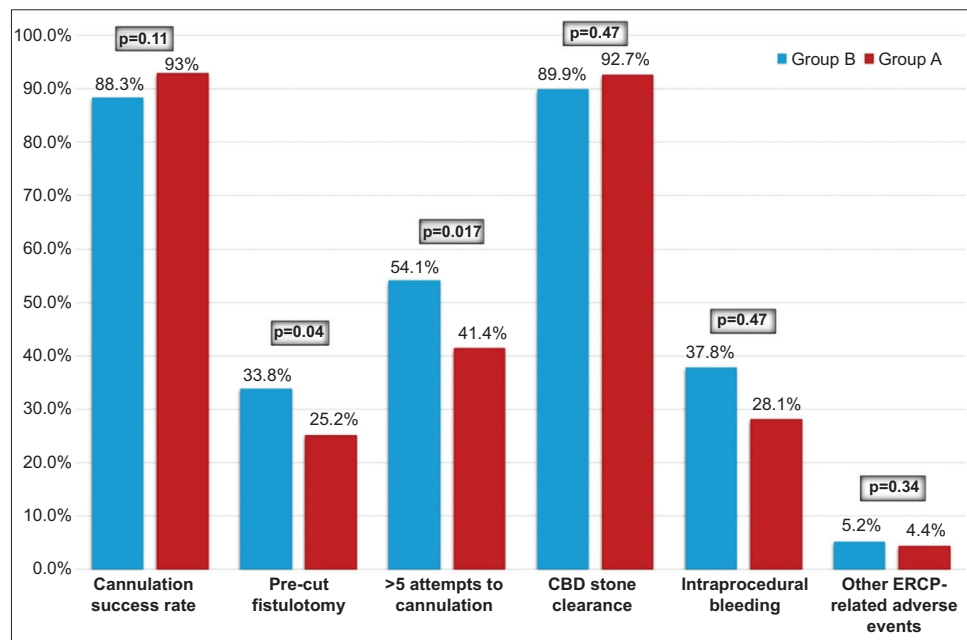


Figure 2 Comparison of major procedural outcomes and safety endpoints between patients undergoing ERCP during the acute phase of pancreatitis (Group A) vs. after clinical resolution (Group B)

CBD, common bile duct; ERCP, endoscopic retrograde cholangiopancreatography

undergoing ERCP in the acute setting (Group B: 0/230 vs. Group A: 4/114 [3.5%], $P=0.012$). However, only 1 death was considered to be procedure-related, whereas the remaining 3 occurred in patients already admitted to the intensive care unit because of severe pancreatitis. Given the very small number of events in each category, subgroup comparisons for individual adverse events were not considered informative.

Discussion

In this 25-year, real-world cohort from 2 high-volume HPB centers, we compared ERCP performed during the acute phase of pancreatitis with ERCP undertaken after clinical resolution. Overall technical performance was high, with successful biliary cannulation achieved in 89.8% of patients, and in 93.9% when cases in which the papilla could not be reached were excluded. These rates align with those reported from experienced centers, where cannulation success typically exceeds 90% [10]. Importantly, neither cannulation success nor stone clearance differed significantly between acute and post-acute interventions, indicating that timing relative to pancreatitis does not inherently compromise procedural success when ERCP is performed by expert endoscopists.

Several differences in anatomical characteristics and procedural complexity were noted. PAD were significantly more common in patients undergoing ERCP after resolution of pancreatitis, whereas papillary inflammation was markedly more frequent during acute presentations. Although PAD have historically been associated with increased cannulation difficulty and occasionally higher complication rates [11,12], more recent studies suggest that high success rates can be achieved in these patients in expert centers [13]. Our findings are consistent with this more contemporary evidence, as overall outcomes remained favorable despite a higher need for precut sphincterotomy and repeated cannulation attempts in the post-acute group. Additionally, we found that failure to reach the ampulla was associated with a shorter interval between the pancreatitis episode and ERCP. Together with the more frequent observation of papillary inflammation in the acute setting, this finding suggests that early ERCP may be technically more challenging. This potential limitation should be considered by endoscopists when planning ERCP timing in this context.

Adverse events were infrequent in our cohort (4.9%), consistent with large multicenter studies reporting ERCP-related complication rates from 2-10% [2]. Intraprocedural bleeding was significantly more common in the post-acute group, paralleling the greater procedural complexity observed in these patients. PEP occurred only in the post-acute group, and at a low rate, consistent with the lower end of reported PEP incidence in unselected populations [2]. All-cause mortality occurred only among patients undergoing ERCP during the acute episode; however, only 1 death was procedure-related, whereas the remaining deaths were attributable to severe underlying pancreatitis. This observation aligns with evidence indicating that mortality in severe acute pancreatitis is driven

primarily by the underlying systemic inflammatory response, rather than endoscopic treatment [5].

The relationship between ERCP timing and clinical outcomes in acute biliary pancreatitis remains an area of active investigation. Several randomized trials and meta-analyses have shown no clear benefit to routine early ERCP in patients without cholangitis or persistent biliary obstruction [2,14], while early intervention is consistently recommended in cases of acute cholangitis or suspected ongoing obstruction [15]. Our findings reinforce this clinical distinction. In our cohort, the timing (acute vs. post-acute) did not significantly affect technical success or overall complication rates, suggesting that procedural factors, such as cannulation difficulty, papillary anatomy and the need for precut, may be stronger determinants of ERCP-related risk than timing alone.

This study had several limitations. Its retrospective design introduced inherent selection and information bias, as the decision to perform ERCP during the acute or post-acute phase was based on clinical judgment rather than predefined criteria. The long study period (2001-2025) also spanned major advances in endoscopic equipment, sedation practices, periprocedural anticoagulation management, and imaging modalities. Moreover, contemporary evidence-based prophylactic measures for post-ERCP pancreatitis were not systematically implemented in this cohort. No patient received rectal nonsteroidal anti-inflammatory drugs or prophylactic pancreatic duct stenting, including during the more recent years of the study. This reflected a long-standing institutional and operator-dependent practice focused on minimizing pancreatic duct manipulation. In our series, transpancreatic sphincterotomy and the double-guidewire cannulation technique were not used, repeated pancreatic duct access was avoided, and difficult biliary cannulation was managed by early transition to needle-knife precut fistulotomy rather than prolonged cannulation attempts. Therefore, the number of patients fulfilling the most specific contemporary criteria for prophylactic pancreatic duct stenting was probably limited. Nevertheless, because current guidelines recommend or consider prophylactic pancreatic duct stenting in selected high-risk settings, the absence of such prophylaxis remains an important limitation, and may reduce the comparability of our findings with contemporary ERCP practice. Furthermore, the relatively low number of adverse events limited the statistical power for subgroup analyses of specific complications. Lastly, because ERCP timing was determined by clinical judgment rather than random allocation, comparisons between the acute and post-acute groups should be interpreted as reflecting real-world timing strategies rather than the causal effect of ERCP timing alone. In particular, patients undergoing ERCP during the acute phase were more likely to have cholangitis and/or biochemical evidence of ongoing biliary obstruction, whereas those treated after resolution represented a more elective post-acute population. Therefore, residual confounding by indication cannot be excluded, despite the real-world value of this cohort.

In conclusion, in this large, long-term, real-world series, ERCP performed during either the acute or the post-acute

phase of pancreatitis achieved high cannulation and stone clearance rates, with low overall complication rates. Post-acute ERCP was associated with greater procedural complexity, as reflected by more frequent precut sphincterotomy, repeated cannulation attempts and intraprocedural bleeding; however, major adverse events were uncommon in both groups. These findings suggest that, when performed by experienced endoscopists, ERCP can be performed safely and effectively, irrespective of its timing relative to the pancreatitis episode, and that procedural difficulty and underlying disease severity may be more important determinants of outcomes than timing alone. Prospective studies incorporating contemporary post-ERCP pancreatitis prophylaxis strategies are needed to further refine risk stratification and optimal timing in pancreatitis-associated ERCP.

Summary Box

What is already known:

- Endoscopic retrograde cholangiopancreatography (ERCP) is an established therapeutic procedure for biliary obstruction, choledocholithiasis, and acute cholangitis
- In acute biliary pancreatitis, urgent ERCP is recommended for patients with cholangitis or persistent biliary obstruction, whereas the role of routine early ERCP in the absence of these features remains uncertain

What the new findings are:

- In this 25-year, 2-center real-world cohort of 344 patients, biliary cannulation success and complete common bile duct stone clearance were comparable between ERCP performed during acute pancreatitis and ERCP performed after clinical resolution
- Post-acute ERCP was associated with higher rates of precut fistulotomy, more than 5 cannulation attempts, and intraprocedural bleeding, while overall ERCP-related adverse events were uncommon and similar between groups

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