Diagnostic and Interventional Endoscopy

Research Article

Early Fistulotomy or Late Fistulotomy: Which Is More Risky for Post-Endoscopic Retrograde Cholangiopancreatography Pancreatitis?

Altay Kandemir, İsmail Taşkıran, Adil Coşkun, Mehmet Hadi Yasa

Department of Gastroenterology, Aydın Adnan Menderes University, Faculty of Medicine, Aydın, Turkey

Cite this article as: Kandemir A, Taşkıran İ, Coşkun A, Yasa MH. Early fistulotomy or late fistulotomy: Which is more risky for post-endoscopic retrograde cholangiopancreatography pancreatitis?. *Diagn Interv Endosc.* 2023;2(1):5-8.

Corresponding author: Altay Kandemir, e-mail: altaykandemir@yahoo.com

Received: February 24, 2023 **Accepted:** March 22, 2023 **Publication date:** March 28, 2023 **DOI:** 10.5152/DiagnIntervEndosc.2023.223941

Abstract

Objective: The precut sphincterotomy technique is widely used for difficult biliary cannulation during the endoscopic retrograde cholangiopancreatography procedure. Even though an accepted risk factor for post-endoscopic retrograde cholangiopancreatography is a risk factor for pancreatitis, there are numerous studies showing whether this risk is technique-related or due to prolonged procedure time and recurrent cannulation attempts. The study's primary aim was to evaluate the incidence of post-endoscopic retrograde cholangiopancreatography pancreatitis in early precut procedures compared to the standard technique in patients with difficult biliary cannulation. The secondary aim was to compare complications and cannulation success.

Methods: In this prospective, single-center, randomized clinical trial, patients referred for therapeutic biliary endoscopic retrograde cholangiopancreatography and difficult biliary cannulation were divided into 2 groups. The first group was the early precut group (group A) and the second group was the late precut group (group B). Post-endoscopic retrograde cholangiopancreatography pancreatitis was defined as upper abdominal pain associated with at least a 3-fold rise in serum pancreatic enzymes above the normal level more than 24 hours after the procedure.

Results: Three hundred patients were enrolled in the study. Nine of 150 patients (6%) in group A and 21 of 150 patients (14%) in group B developed post-endoscopic retrograde cholangiopancreatography pancreatitis (odds ratio 2.33). Successful biliary cannulation without precutting was performed in 25 patients in group B, whereas delayed precutting was required in the remaining 125 patients. Compared to the delayed precut group (19/125, 15.2%), the incidence of post-endoscopic retrograde cholangiopancreatography pancreatitis was significantly lower in the early precut group (9/150, 6%) (odds ratio 3.3). The "late precut" subgroup had a post-endoscopic retrograde cholangiopancreatography pancreatitis rate with an odds ratio of 2.5 compared to the group with cannulation without precut. These data suggest that the post-endoscopic retrograde cholangiopancreatography pancreatitis risk among patients who received a late precut was higher than among patients who had an early precut or could be cannulated after repetitive efforts.

Conclusion: Early precutting is an effective technique for patients with challenging biliary tract cannulation and can significantly reduce post-endoscopic retrograde cholangiopancreatography pancreatitis incidence. Recurrent biliary cannulation attempts constitute a real risk factor for this complication.

Keywords: Endoscopic retrograde cholangiopancreatography, post-ERCP pancreatitis, precut sphincterotomy technique

INTRODUCTION

Successful biliary cannulation is the critical step in endoscopic retrograde cholangiopancreatography (ERCP). Unfortunately, cannulation fails in 5%-15% of cases when standard cannulation techniques are used.[1-3] Precut sphincterotomy has been associated with a success rate of up to 100% in complex biliary access cases.[3] Papillary trauma due to repetitive cannulation efforts increases the risk of post-ERCP pancreatitis (PEP).[4]

The incidence of pancreatitis ranges from 1%-7% and can rise to 25% in high-risk patient groups. Most PEP cases are mild or moderate in severity. However, 1%-5% of patients might experience severe pancreatitis. The outcome of PEP can be catastrophic, resulting in significant morbidity, prolonged hospitalization, and, rarely, mortality.[5] Prior use of precut sphincterotomy during ERCP may increase the probability of cannulation success but is also associated with elevated PEP risk. Precut sphincterotomy is a technique that can be used in such an endoscopic scenario but has been associated with a non-negligible incidence rate of adverse events. Regarding complications following precut sphincterotomy (especially PEP), some authors have proposed that they might be due to papillary trauma as a result of multiple attempts to cannulate the biliary duct or inadvertent pancreatic duct cannulation. Early rather than delayed use of precut sphincterotomy may reduce this risk in cases with challenging biliary access.[6]

The study's primary aim was to evaluate the incidence of PEP in early and late precut cases compared to the standard technique in patients with difficult biliary cannulation. The study's secondary aim was to compare complications and cannulation success.

METHODS

These procedures were performed only by a single expert endoscopist with sufficient experience (>300 ERCPs/year). In this prospective, single-center, randomized clinical trial, patients who underwent therapeutic ERCP and were considered to have a difficult biliary cannulation (5 minutes and 3 guide wires into the main pancreatic duct (MPD)) were divided into 2 groups: the early precut group (n: 150) and the late precut group (n: 150) in the event of failed cannulation efforts. Group A patients were precut immediately (early precut), and group B patients were precut if efforts for cannulation lasted for 10 minutes and then failed or if the guidewire was entered into the MPD 3 times (late precut). A second ERCP was scheduled for 2-4 days later in patients with unsuccessful ERCP.

The PEP was defined as the onset of upper abdominal pain associated with increased serum pancreatic enzymes at least 3-fold the normal level 24 hours following the procedure.

Neither pancreatic stent placement nor rectal diclofenac or indomethacin for PEP prophylaxis was planned in this study; however, they were recommended, especially in high-risk patients. In addition, these treatments were not included to avoid possible confounding based on an expected higher rate of stent placement in patients randomized to the repeated cannulation attempts group than the early precut group.

Hemorrhage was defined as clinical evidence of bleeding with a decrease of at least 2 g/dL in hemoglobin level. Based on clinical findings, perforation was defined as definite if contrast leakage was endoscopically observed. Cholangitis was considered the presence of a fever of 38°C for more than 24 hours without an alternative explanation. Patients aged 18-85 years scheduled for therapeutic biliary ERCP were enrolled in the study. Exclusion criteria were a history of previous sphincterotomy, previous gastric surgery, chronic pancreatitis, active cholangitis or pancreatitis, coagulopathy, severe comorbidity (patients possibly needing intubation), and those who did not give informed consent. In addition, patients with standard easy cannulation (choledochal cannulation within 5 minutes and less than 3 guide wire pass attempts into the MPD) and those with an ampulloma or periampullary diverticulum were also excluded from the study.

The study was approved by the ethics committee of the Aydin Adnan Menderes University Faculty of Medicine (Aug 25, 2022/138).

MAIN POINTS

- Papillary trauma due to repetitive cannulation efforts increases the risk of post-endoscopic retrograde cholangiopancreatography pancreatitis (PEP).
- Early precutting is an effective technique for patients with challenging biliary tract cannulation and can significantly reduce PEP incidence.
- Recurrent biliary cannulation attempts constitute a real risk factor for this complication.

Endoscopic Retrograde Cholangiopancreatography Technique

Common bile duct (CBD) was cannulated using a double-lumen pull-type sphincterotome loaded with a hydrophilic guidewire. The guidewire was placed deep into the papillary duct with the sphincterotome's tip and advanced accurately in the direction of the CBD under fluoroscopy. When the guidewire was considered to have entered the CBD, it was gently advanced over the sphincterotome, and a contrast medium was injected to confirm biliary cannulation. If the guidewire was inadvertently directed into the MPD, it was withdrawn, no contrast medium was injected, and attempts to cannulate the CBD were repeated. A needle knife was used for precut sphincterotomy. Conventional precut technique or the fistulotomy technique was used.

Conventional Precut Technique

The conventional precut technique is usually defined as the use of a needle-knife to perform a stepwise incision of the mucosa starting at the upper margin of the papillary orifice in the direction of the bile duct until the underlying biliary sphincter is visualized.

Fistulotomy

The needle-knife fistulotomy (NKF) technique is usually defined as the use of a needle-knife to perform a stepwise incision of the mucosa starting directly over the roof of the papilla followed by an upward or downward cut until the underlying biliary sphincter is visualized.[7]

A blended electrosurgical current with a BOWA ARC electrocautery (Germany) was used, setting the endocut mode at 120 W cut, 50 W coagulation, and level 1. After CBD cannulation, a wire-guided sphincterotomy was performed. No prophylactic drugs or pancreatic stents were used for PEP.

Data

Patient and procedural data were documented in detail during ERCP. The data entry form consisted of baseline patient characteristics, patient-related risk factors, indications for the procedure, technical details of the procedure, final diagnoses, and procedure-related complications. Data were analyzed using the statistical software package Statistical Package for the Social Sciences for Windows.

Statistical Analysis

Differences in the incidence of PEP, other complications, and success of the biliary cannulation in the 2 groups were compared using Student's *t*-test for continuous variables and Fisher's exact or chi-squared test for categorical variables. Means (SD) were computed for continuous variables, and percentages were calculated for categorical variables. All differences were considered significant at a 2-sided *P* value of less than .05. Differences between the 2 groups regarding biliary cannulation success, PEP incidence, and complication rates were analyzed using Student's *t*-test for continuous variables and Fisher's exact or chi-square test for categorical variables.

Means (SD) values were calculated for continuous variables and percentages for categorical variables. All differences were considered significant when *P* value was less than .05.

RESULTS

From November 2015 to February 2021, 300 patients were enrolled. Patients' mean age was 62.1 ± 17 years in group A (102/150 women (68%)) and 66.2 ± 16.0 years in group B (111/150 women (74%)). There was no statistical difference between these 2 groups regarding the patients' clinical indications and demographic characteristics.

Table 1. Indications for Endoscopic Retrograde Cholangiopancreatogr aphy with Early Precut (Group A) and Prolonged Cannulation Attempts (Group B) Strategies

Indication	Group A (%)	Group B (%)
Bile duct stones	90 (60)	86 (57.3)
Malignant biliary stricture	30 (20)	35 (23.3)
Cholangitis	13 (8.7)	15 (10)
Benign biliary stricture	8 (5.3)	7 (4.8)
Suspected sphincter of oddi dysfunction	4 (2.7)	3 (2)
Post-surgery biliary leakage	3 (2)	2 (1.3)
Other	2 (1.3)	2 (1.3)

Tables 1 and 2 show the procedural indications and clinical/technical risk factors. The overall success rate of CBD cannulation was similar in both groups: 90% (135/150) in group A and 92% (138/150) in group B (Table 3). The PEP developed in 10% of cases and was mild in 90% of the patients who experienced it. Severe pancreatitis was present in only 3 patients. Of these, 1 was in the early precut group, and 2 were in the late precut group. The PEP developed in 9 (6%) of 150 patients in group A and 21 (14%) of 150 patients in group B (odds ratio (OR) 2.33). Choledochal cannulation without precut was performed in 25 patients in group B, whereas precut (late precut) was required in the remaining 125 patients. The PEP incidence was significantly lower in the early precut subgroup (9/150, 6%) than in the late precut subgroup (19/125, 15.2%) (OR 3.33). The incidence of PEP was (2/25, 8%) in the subgroup with no precut. The incidence of PEP was higher in the late precut group (OR 2.5), comparing the non-precut subgroup with the late precut subgroup.

In group A, fistulotomy was used in 138 patients and conventional precut technique was used in 12 patients. In group B, fistulotomy was used in 115 patients and conventional precut technique was used in 10 patients. We applied the conventional precut technique using the transpancreatic precut sphincterotomy technique in all cases. There was no difference in complications between the conventional precut technique and the fistulotomy in both groups. When the indications for ERCP were analyzed, PEP rates were similar in both groups. The most typical indication was choledocholithiasis. Bleeding complications were similar in both groups; group A had 6.6% (10/150), and group B had 6% (9/150). Perforation was observed in 1 patient in each group; both patients had a type-2 perforation and were successfully treated with a partially covered metallic choledochal stent. Groups did not differ regarding biliary cannulation success, perforation, bleeding, and cholangitis (Table 4). No patient died due to ERCP complications.

Table 2. Clinical and Technical Risk Factors for Post-Endoscopic Retrograde Cholangiopancreatography Pancreatitis with Early Precut (Group A) and Prolonged Cannulation Attempts (Group B)

Risk Factors	Group A (%)	Group B (%)
Young age (<60 years)	31 (20.7)	34 (22.7)
Female	102 (68)	111 (74)
Previous PEP	1 (0.7)	0
Previous pancreatitis	8 (5.3)	7 (4.6)
>1 passage of guidewire into MPD	50 (30)	60 (40)
Contrast injection of the MPD	8 (5.3)	10 (6.7)
Biliary balloon dilation	0	1 (0.7)

MPD, main pancreatic duct; PEP, post-endoscopic retrograde cholangiopancreatography pancreatitis.

Table 3. Common Bile Duct (CBD) Cannulation Rate with Early Precut (Group A) and Prolonged Cannulation Attempts (Group B)

	n	CBD Cannulation Success, n (%)	*P* vs Group A
Group A	150	135 (90)	
Early precut			
Group B	150	138 (92)	.56
Prolonged cannulation attempts	25		
Delayed precut	125		

DISCUSSION

In patients with difficult biliary cannulation, early precut is an effective technique in experienced hands and can significantly reduce PEP incidence compared to continual cannulation attempts. At the same time, it may be equally effective in achieving successful biliary cannulation. The PEP was diagnosed in 10% of all cases, and 90% of these cases had mild pancreatitis. The incidence of pancreatitis was 6% in the early precut group and 14% in the prolonged cannulation attempts group ($P=.03$). In the study conducted by Manes et al.[8] while the overall complication rates were similar, the rate of pancreatitis was 2.6% in the early precut group and 14.9% in the late-access group ($P=.008$). However, according to a 966-patient meta-analysis of 6 randomized controlled trials by Cennamo et al.[9] PEP developed in 2.5% of patients randomized to the early precut groups compared to 5.3% of patients in the permanent intervention groups (OR 0.47; 95% CI 0.24-0.91). Considering the rates of pancreatitis, bleeding, cholangitis, and perforation, the overall complication rates were 5.0% in the early precut groups and 6.3% in the persistent intervention groups (OR 0.78; 95% CI 0.44-1.37). It shows that early precut and persistent cannulation attempts have similar cannulation rates; early precut may reduce the risk of PEP but has been shown not to reduce the overall complication rate.[9] Our data also show that performing a late precut (15.2%) sphincterotomy has a more significant effect on PEP than performing an early precut (6%) or successful cannulation with repetitive cannulation attempts (8%).

It is challenging to determine or standardize the optimal precut timing to limit PEP incidence. Our attitude inspired this design in routine ERCP practice that views the precut strategy as a "salvage" technique when cannulation attempts fail rather than as a direct approach to achieve CBD cannulation. A generally accepted indication for the early precut procedure is difficult papillary cannulation. However, a consensus on defining difficult biliary cannulation is still lacking. In this study, a time point was used to define difficult cannulation because even though the number of cannulation attempts might be more appropriate for determining the risk threshold for PEP, it is more compatible with ERCP practice. The 5-minute duration of cannulation attempts,

Table 4. Complications of Early Precut (Group A) and Prolonged Cannulation Attempts (Group B) Strategies

	Total (n=300), n (%)	Group A (n=150), n (%)	Group B (n=150), n (%)	*P*
Overall complications	44 (14.6)	16 (10.7)	28 (18.7)	.08
Pancreatitis	30 (10)	9 (6)	21 (14)	.03
Bleeding	9 (3)	5 (3.3)	4 (2.7)	1
Perforation	2 (1.3)	1 (0.7)	1 (0.7)	1
Cholangitis	3 (1)	1 (0.7)	2 (1.3)	1

which was arbitrarily applied in this study, has provided a reliable baseline. A maximum limit of 3 MPD cannulations was determined before randomization, and opaque material administration to the MPD was avoided to limit post-procedural pancreatic injury. In the present study, fistulotomy was the preferred primary approach because it protects the pancreatic orifice from diathermic injury with a cutting wire, except in patients with a small papilla, in whom it would be more challenging to cut the roof. The extensive use of fistulotomy in this study might have prevented trauma in the vicinity of the pancreatic orifice, and this would help to explain the lower PEP rate in the precut group since in the repetitive cannulation attempts group, there is a greater risk of injury to the early pancreatic orifice and consequent impairment of the pancreatic fluid outflow. Recurrent biliary cannulation attempts and/or delayed precut is a definite risk factor for PEP complications.[10] The early precut strategy may also offer the advantage of shortening ERCP time. In a study by Mariani et al.[11] early precut sphincterotomy was effective in complex biliary cannulation cases and significantly reduced PEP incidence. The NKF and conventional precut sphincterotomy (CPS) are widely used in difficult biliary cannulation. In the study by Başpinar et al.[12] PEP rate was higher in CPS (9.5%) than NKF group (3.0%, $P = .063$). Bleeding and cholangitis were similar in both groups. In our study, the rate of pancreatitis was similar between the fistulotomy group and CPS, but the statistical comparison could not be made because the number of patients in the CPS group was very small.

In most reports, the standard approach of precut technique and CBD cannulation has been mainly performed by experienced endoscopists, as in the current study, in which ERCP was performed by a single physician with 10 years of experience with more than 800 ERCP procedures per year. The study's limitations are that it is unclear how early precutting by less experienced physicians would affect the incidence of PEP in real-life data. In addition, total ERCP procedure durations were not recorded in the study.

In conclusion, the present study suggests that in cases of difficult biliary cannulation, the early precut technique in experienced hands may reduce PEP risk compared to persistent cannulation attempts and may be equally effective for successful biliary cannulation. However, further prospective multicenter randomized controlled trials are needed to evaluate the risk of precut incision on PEP in patients with difficult biliary cannulation.

Ethics Committee Approval: Ethics committee approval was receives for this study from the ethics committee of Aydın Adnan Menderes University (Date: Aug 25, Number: 2022/138).

Informed Consent: Written informed consent was obtained from patients/ patients' parents/ the parents of the patients/patient who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – A.K.; Design – A.K.; Supervision – A.K.; Resources – İ.T.; Materials – A.K., İ.T.; Data Collection and/or Processing – İ.T.; Analysis and/or interpretation – A.C.; Literature Search – M.H.Y.; Writing Manuscript – A.K.; Critical Review – A.C.; Other – M.H.Y.

Declaration of Interests: The authors declare that they have no competing interest.

Funding: The authors declared that this study has received no financial support.

REFERENCES

1. Bailey AA, Bourke MJ, Williams SJ, et al. A prospective randomized trial of cannulation technique in ERCP: effects on technical success and post-ERCP pancreatitis. *Endoscopy*. 2008;40(4):296-301. [CrossRef]
2. Williams EJ, Taylor S, Fairclough P, et al. Are we meeting the standards set for endoscopy? Results of a large-scale prospective survey of endoscopic retrograde cholangio-pancreatograph practice. *Gut*. 2007;56(6):821-829. [CrossRef]
3. Freeman ML, Guda NM. ERCP cannulation: a review of reported techniques. *Gastrointest Endosc*. 2005;61(1):112-125. [CrossRef]
4. Freeman ML, DiSario JA, Nelson DB, et al. Risk factors for post-ERCP pancreatitis: a prospective, multicenter study. *Gastrointest Endosc*. 2001;54(4):425-434. [CrossRef]
5. Hwang HJ, Guidi MA, Curvale C, Lasa J, Matano R. Post-ERCP pancreatitis: early precut or pancreatic duct stent? A multicenter, randomized-controlled trial and cost-effectiveness analysis. *Rev Esp Enferm Dig*. 2017;109(3):174-179. [CrossRef]
6. Navaneethan U, Konjeti R, Venkatesh PG, Sanaka MR, Parsi MA. Early precut sphincterotomy and the risk of endoscopic retrograde cholangiop ancreatography related complications: an updated meta-analysis. *World J Gastrointest Endosc*. 2014;6(5):200-208. [CrossRef]
7. 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(7):657-683. [CrossRef]
8. Manes G, Di Giorgio P, Repici A, Macarri G, Ardizzone S, Porro GB. An analysis of the factors associated with the development of complications in patients undergoing precut sphincterotomy: a prospective, controlled, randomized, multicenter study. *Am J Gastroenterol*. 2009;104(10):2412-2417. [CrossRef]
9. Cennamo V, Fuccio L, Zagari RM, et al. Can early precut implementation reduce endoscopic retrograde cholangiopancreatography-related complication risk? Meta-analysis of randomized controlled trials. *Endoscopy*. 2010;42(5):381-388. [CrossRef]
10. Masci E, Mariani A, Curioni S, Testoni PA. Risk factors for pancreatitis following endoscopic retrograde cholangiopancreatography: a meta-analysis. *Endoscopy*. 2003;35(10):830-834. [CrossRef]
11. Mariani A, Di Leo M, Giardullo N, et al. Early precut sphincterotomy for difficult biliary access to reduce post-ERCP pancreatitis: a randomized trial. *Endoscopy*. 2016;48(6):530-535. [CrossRef]
12. Başpinar B , Ödemiş B, Erdoğan Ç, Yüksel M. Suprapapillary needle knife fistulotomy versus conventional precut sphincterotomy in difficult biliary cannulation: a retrospective comparative study. *Surg Laparosc Endosc Percutan Tech*. 2022;32(6):700-706. [CrossRef]