

Original Article

## Fistulotomy-First Approach is Safe and Effective in Endoscopic Retrograde Cholangiography: Results of a Prospective Case Series

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### Abstract

**Background and Aims:** The aim of this study was to assess the safety and efficacy of using needle-knife fistulotomy (NKF) as a primary cannulation technique in patients undergoing endoscopic retrograde cholangiopancreatography (ERCP) with a native papilla.

**Patients and Methods:** This prospective feasibility study enrolled 50 patients between December 2018 and June 2019. The procedure was performed by two expert endoscopists (R.B. and L.H.). The primary outcome was the incidence of post-ERCP pancreatitis. Other variables assessed included the success rate of cannulation of the common bile duct (CBD), time to successful cannulation, and incidence of adverse events.

**Results:** Between December 2018 and June 2019, 50 patients enrolled in the study. The mean age was 63.4 years (standard deviation 18.1), and there were 26 females. Indications included biliary obstruction secondary to malignancy ( $n = 14$ ) and choledocholithiasis ( $n = 36$ ). Successful cannulation of the CBD through the fistulotomy occurred in 49/50 cases. The time to successful cannulation was 5.1 minutes (range 0.5 to 23 minutes). Mild acute pancreatitis occurred in two cases (4%). Post-ERCP bleeding occurred in three patients (6%)

**Conclusions:** In this pilot study, NKF was used as the primary biliary access technique and it was demonstrated that it appears to be at least as safe as the traditional access technique with a sphinctertome. However, its role as a primary cannulation technique requires further investigation with multicenter, randomized control studies.

**Keywords:** *Endoscopy; Gastroenterology; Hepatology*

### Introduction

Since its inception in 1968, endoscopic retrograde cholangiopancreatography (ERCP) has become an indispensable procedure for the diagnosis and treatment of pancreaticobiliary diseases (1). Six years later, the first endoscopic sphincterotomies were completed by Kawai and Claussen, and it is now used in the management of

choledocholithiasis, papillary stenosis, and other benign and malignant pancreaticobiliary diseases (1).

Despite the essential nature of the procedure, ERCPs continue to result in significant morbidity in a small but significant number of patients (1). Post-procedure pancreatitis (PEP), is the major source of this, affecting between 5–7% and up to 25% in high-risk patients (2, 3). For 10% of patients who experience

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post-ERCP pancreatitis, it can be severe and even fatal (4). Therefore, the pursuit of an intervention or technique that can minimize or even eliminate PEP is highly desired.

Medical interventions, such as intravenous volume expansion, pancreatic protease inhibitors, and Nonsteroidal anti-inflammatory drugs (NSAIDs), have shown promise or even benefit; nevertheless, the risk of PEP persists (5–12). Attention has therefore turned to the use of alternative procedural techniques; these, however, present a concatenation of questions regarding safety and adverse events requiring evaluation.

The conventional sphincterotomy technique, involving the cannulation of the bile duct via the ampulla of Vater, followed by sphincter incision using electrocautery, has been reported to fail between 5–10% of the time (13). When the standard approach fails, then precut techniques have been utilized as an alternative means of gaining biliary access.

The precut, provides access to the biliary system via incision of the ampulla without initial cannulation of the bile duct via the native orifice. There are various precut techniques used to gain access to the common bile duct (CBD), which include needle-knife fistulotomy (NKF), needle-knife sphincterotomy (NKS), and trans-pancreatic precut sphincterotomy (TPS) (14, 15). All of these techniques can be performed either as a primary access or secondary (rescue) technique (16), and all are done after careful inspection of the ampulla for anatomical landmarks. The NKF involves identifying the intra-duodenal segment of the bile duct and uses a needle knife to incise directly into the bile duct, thus minimizing thermal damage to the native orifice. The fistula is further away from the pancreatic duct compared with the native orifice of the papilla. NKS involves using a needle knife to cut starting at the native orifice and incising upwards to expose the bile duct opening. A TPS involves incising the pancreatic sphincter, which lies adjacent to the biliary sphincter (within the native orifice), to expose the biliary opening. This is usually done when the catheter has been inserted into the pancreatic duct several times, without accessing the bile duct.

Numerous studies have demonstrated that adverse event rates are comparable between methods when precut sphincterotomy is conducted by an expert endoscopist (17) and that moving to precut techniques earlier in the procedure can be associated with fewer adverse events (16, 18, 19). A table summarizing several fistulotomy studies to date is available as an appendix to this article (Supplementary Table 1). The next step in this reasoning is moving to a precut technique directly, without attempting to cannulate the ampulla via the native orifice. This has been shown to be successful in various small case series (19–21). With respect to which of the three techniques to employ, the NKF theoretically offers the lowest risk of pancreatitis as the incision is performed directly into the intra-duodenal segment of the bile duct under direct visualization, minimizing

any contact or thermal damage to the pancreatic duct. This theory is supported by the results in the series by Jin et al., who observed a 0% incidence of pancreatitis using the NKF method as the initial technique for cannulation in high-risk patients (21). As a first step in this technique at our center, we embarked on a single-arm, non-blinded, feasibility study. A major difference between this study and the one by Jin et al., is the inclusion of all patients with a native papilla, not only those assessed pre-procedurally as high risk of PEP. The feasibility study format would allow us to garner information for employing this technique in this more general population and possibly lead to a larger randomized trial.

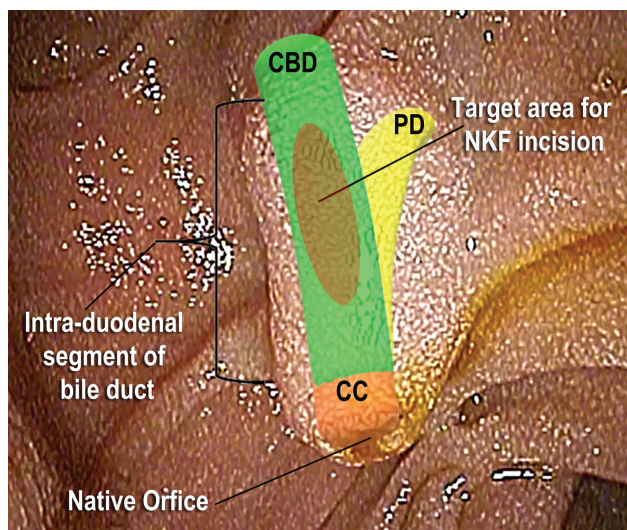
## METHODS

This prospective, single-arm, feasibility study was designed to assess the safety and efficacy of using NKF as a starting technique in a nonselective patient population. All patients booked for biliary ERCP were considered for inclusion. Patients were excluded for the following reasons: inability to provide consent, bleeding disorder (Von Willebrand disorder, platelet count <100,000, or international normalized ratio (INR) >1.5), therapeutic level anticoagulation with low molecular weight heparin, warfarin, or a direct-acting oral anticoagulant, prior biliary sphincterotomy, altered upper gastrointestinal tract anatomy, malignant infiltration of the ampulla or peri-ampullary area, and operator inability to identify the intra-duodenal portion of the bile duct (including deep peri-ampullary diverticulum). The study was approved by the Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board on October 25, 2018 and was registered at clinicaltrials.gov (NCT03698266).

## Interventions

Consent for the ERCP procedure was obtained by the treating physician in a routine manner. Patients meeting eligibility criteria were approached by a research coordinator, and, if agreeable, consented for the study. Preprocedure demographics, laboratory values, suspected diagnosis, and baseline location and severity of abdominal pain were recorded.

Enrolled patients underwent preparation, sedation, and the first stages of the ERCP as per standard of care, including receiving sedation in the form of intravenous midazolam, fentanyl, diazepam and/or dimenhydrinate. After the ampulla was identified, it was closely examined to accurately delineate the infundibulum. A needle knife (Needlecut 3V, Olympus Medical Canada, Markham, Ontario, Canada) was used to make a 2 to 3 mm incision in the mid to proximal third of the vertical axis in the intra-duodenal segment (Figure 1). The needle was used to cut through the thin layers of mucosa with intermittent examination for the



**Figure 1.** Rudimentary luminal anatomy of ampulla noting the common bile duct (CBD), pancreatic duct (PD), common channel (CC), native orifice, intra-duodenal segment of the bile duct and the target area for the needle-knife fistulotomy (NKF) incision.

muscular ampulla complex and subsequent penetration into the bile duct usually signaled by bile flow. When bile was seen, the fistula was gently probed with a catheter and guidewire until the CBD was cannulated. Cannulation of the CBD was confirmed with proximal advancement of the guidewire and contrast injection with cholangiography. If the findings on the cholangiogram indicated that further interventions were necessary, then the fistulotomy site was extended with the use of the needle knife, standard sphincterotomy, or balloon sphincteroplasty. A video of a needle knife fistulotomy is available for reference ([Supplementary Video 1](#)). Further interventions may have included: placement of metal or plastic biliary stents, brushing of the ducts for cytology, balloon dilation of strictures, intra-ductal cholangioscopy basket retrieval of stones, and balloon sweeping of the CBD.

Intra-procedure data collection included time to successful cannulation, as measured from the time of identification of the ampulla to successful CBD cannulation as evident by the cholangiogram and total time of the procedure. Postprocedure data included abdominal pain and assessment for pain/pancreatitis at 1 and 24 hours postprocedure. Additionally, a postprocedure day 7 phone call was scheduled, and patients were questioned regarding abdominal pain, fevers or recent hospital admission.

### Outcomes

The primary outcome of the study was the incidence of PEP, defined as the occurrence of worsening abdominal pain persisting for 24 hours following the procedure and an elevation greater than three times the upper limit of normal of serum lipase levels (22).

Other study variables included the following: rate of successful cannulation of the CBD, with technical success determined by a cholangiogram following the NKF; time to successful cannulation, as measured from the time of identification of the ampulla to successful CBD cannulation as evident by the cholangiogram; and incidence of adverse events, notably, intra-procedural bleeding that required intervention (cautery, clips, or injection of epinephrine), as well as delayed or sustained bleeding requiring transfusion or repeat endoscopy.

### Sample Size and Statistical Analysis

This prospective feasibility pilot study enrolled 50 subjects. This allowed for an estimate of the success rate of NKF as a primary access technique, as well as an estimate of the rate of PEP. Data is presented using descriptive statistics, as the number of outcomes (PEP) was too low to allow for meaningful comparisons.

## RESULTS

Between December 2018 and June 2019, 50 patients enrolled in the study; 28 were inpatients and 22 were outpatients. One hundred and sixteen patients were screened during this period. Ten consented but did not undergo fistulotomy for (a) anatomic reasons ( $n = 5$ ; 4 had papilla within deep diverticuli and 1 had severe duodenal wall edema that precluded identification of the intra-duodenal portion of the CBD), (b) the ERCP was deemed unnecessary after concurrent endoscopic ultrasound ( $n = 1$ ), (c) they already had a sphincterotomy in a prior ERCP ( $n = 3$ ) or (d) they were unable to undergo the procedure due to sedation issues ( $n = 1$ ). Sixteen patients declined participation, and 40 were ineligible.

The mean age was 63.4 years (standard deviation [SD] 18.1) and there were 26 females. Indications included biliary obstruction secondary to malignancy ( $n = 14$ ) and choledocholithiasis ( $n = 36$ ). Pre-ERCP blood work is shown in [Table 1](#).

Two endoscopists performed the procedures (R.B.,  $n = 24$ ; L.H.,  $n = 26$ ) with conscious sedation using combinations of midazolam ( $n = 50$ ), fentanyl ( $n = 50$ ), dimenhydrinate ( $n = 18$ ), and diazepam ( $n = 3$ ; mean doses and range shown in [Table 2](#)).

Forty-two patients received 100 mg rectal diclofenac at the end of the procedure. Eight patients did not due to allergies ( $n = 1$ ), acute renal injury ( $n = 1$ ), no anus ( $n = 1$ ), active gastrointestinal (GI) bleeding ( $n = 1$ ), lactation ( $n = 1$ ), already existing pancreatitis ( $n = 1$ ), and no reason given ( $n = 3$ ). The mean inspection time of the papilla (time from first visualization to start of fistulotomy) was 2 minutes 3 seconds (range 10 seconds to 8 minutes).

Successful cannulation of the CBD through the fistulotomy occurred in 49/50 cases. The time to successful cannulation (as measured by time of visualization of the needle knife on the



**Table 1.** Patient demographics and baseline information

Factor		Results
Age (mean)		63.4 years, range 18–93
Sex		26 female
Indication for ERCP	Choledocholithiasis	36
	Malignancy	14
Preprocedure blood work	Alanine aminotransferase (mean $\pm$ SD)	280 $\mu$ /L, $\pm$ 254
	Bilirubin (mean $\pm$ SD)	92 $\mu$ mol/L $\pm$ 114
	INR (mean, range)	1.2, 1–1.5
	Hemoglobin (mean $\pm$ SD)	126 g/L $\pm$ SD 24
	Lipase (mean, range)	300 $\mu$ /L, 12–6706

ERCP, endoscopic retrograde cholangiopancreatography; SD, standard deviation.

**Table 2.** Sedation and technical aspects of ERCPs

Medication	Dose administered
Midazolam, mean total (SD; $n = 50$ )	3.6 mg (1.6)
Fentanyl, mean total (SD; $n = 50$ )	130 mcg (64)
Dimenhydrinate, mean total (SD; $n = 18$ )	44.4 mg (13.7)
Diazepam, mean total (SD; $n = 3$ )	9.2 mg (1.4)
Inspection time of papilla, mean (SD)	123.4 s (92.4)
Time to successful cannulation of CBD, mean (SD)	5.1 min, SD 4.7, range 0.5–23

CBD, common bile duct; ERCP, endoscopic retrograde cholangiopancreatography; SD, standard deviation.

screen to cannulation of the guidewire into the CBD) was 5.1 minutes (range 0.5 to 23 minutes). In one case, the endoscopist switched to the traditional papillary approach after attempting the fistulotomy for 6 minutes. The mean total procedure time was 23.6 minutes (SD 11.5).

The pancreas was cannulated with a wire in five cases, either through the native papilla ( $n = 1$ ) or through the fistulotomy ( $n = 4$ ). No pancreatic stents were placed. CBD stents were placed in 20 cases. The degree of difficulty of the fistulotomy was subjectively graded by the endoscopist as low in 16 cases, moderate in 26 cases, and high in 8 cases.

Acute pancreatitis occurred in two cases (4%). One of these was a 52-year-old female with malignant hilar biliary obstruction. She had a fistulotomy that was graded as high difficulty, and cannulation of the pancreas with a wire occurred through the native papilla after failure to cannulate the bile duct through the fistulotomy. She did not receive diclofenac as she had previously undergone total colectomy and abdominoperineal resection. The patient presented with abdominal pain 6 hours

postprocedure, had an elevated lipase, was admitted to hospital, and treated conservatively. She was pain free 48 hours later. The second patient, a 26-year-old female with choledocholithiasis, had a successful fistulotomy graded as moderately difficult without any cannulation of the pancreatic duct. She did not receive diclofenac due to breastfeeding. Eighteen hours after ERCP, she developed severe epigastric pain and elevated lipase. The pain settled within 72 hours and no further adverse events from the pancreatitis developed. A review of video of the fistulotomy revealed that the initial incision was in the distal third of the infundibulum and included the native orifice, which would be more accurately classified as an NKS.

Post-ERCP bleeding occurred in three patients. One patient developed melena and a drop of hemoglobin from baseline 4 days post-ERCP, with subsequent endoscopy finding a clean-based ulcer in the duodenal cap and no other bleeding sites (the fistulotomy site appeared clear). The second patient was a 66-year-old female, with normal platelet count and INR. She presented with painless jaundice from metastatic colon cancer and portal lymphadenopathy resulting in biliary obstruction. The fistulotomy was rated as low in difficulty. At the end of the procedure oozing blood at the top of the fistulotomy was noted, and this was treated with topical epinephrine and soft coagulation delivered with a hemostatic grasper forceps (Coag-grasper, Olympus Medical Canada, Markham, Ontario, Canada). The patient then developed presyncope 24 hours later, accompanied with a drop in hemoglobin from 101 to 91  $\mu$ /L. Repeat endoscopy was undertaken and further oozing seen from the site. This was again treated with soft coagulation delivered through a hemostatic grasper with good effect and no further bleeding. The third patient underwent ERCP for choledocholithiasis, and the fistulotomy was rated as moderately difficult. Three days later, she had hematemesis and underwent endoscopy. A clot was found at the fistulotomy site, with blood oozing from the top when the clot was cold snared off. This was treated with injection of 1/10,000 epinephrine with excellent short- and long-term results.



## Discussion

Our study sought to build on the findings by Jin et al., by offering enrollment to all patients undergoing an ERCP with a native papilla. We additionally included patients with other indications for ERCP, such as malignant obstructions. Using these parameters, our prospective, single-arm, feasibility study was designed to assess the safety and efficacy of using NKF as a starting technique for a wide range of patients undergoing biliary ERCP.

Two of the 50 enrolled patients experienced postprocedure pancreatitis. This rate is in line or lower than other studies of standard sphincterotomy, although inferences from this finding are limited by the small sample size and the relative infrequency of PEP. Both cases of pancreatitis occurred in cases classified as high risk using established patient clinical risk factors for PEP (17). In the first patient, the fistulotomy was graded as a high difficulty, and cannulation of the pancreas with a wire occurred through the native papilla after failure to cannulate the bile duct through the fistulotomy. Furthermore, she did not receive diclofenac as she had previously undergone total colectomy and abdominoperineal resection. The second patient's PEP occurred following a moderately difficult fistulotomy; otherwise, the procedure went without difficulty and without pancreatic duct cannulation. Due to breastfeeding, she also did not receive diclofenac. It is noteworthy, however, that post hoc video review of the two patients with pancreatitis suggests that the fistulotomy was started at the native orifice rather than in the proximal mid/third portion of the infundibulum as per the protocol guidelines; thus, it is possible that the rate of PEP with fistulotomy could actually be lower than we found.

In addition to pancreatitis, there were three cases of postfistulotomy bleeding, both of which required endoscopic intervention. As definitions differ between studies, a direct comparison of bleeding rates is not feasible. This rate of bleeding following NKF in a nonselective population needs to be further assessed in a larger sample size and, preferably, in a randomized trial compared with standard sphincterotomy.

The rate of successful cannulation in our study was 98% (49/50 cases). This success rate is higher than that reported by Jin et al. (21). However, our study's time to successful cannulation was longer (5.1 minutes [range 0.5 to 23 minutes]).

Limitations in this study include the lack of a control group and small sample size. Additionally, the ERCPs were conducted by two expert endoscopists, thus limiting the generalizability of the findings.

In this study, NKF was used as the primary biliary access technique in a nonselective sample of patients undergoing ERCP. Our results suggest that, in expert hands, it appears at least as safe as the traditional access technique with a sphinctertome though the ampullary orifice. Additionally, the results support moving to a multicenter, randomized, controlled trial that

would address the limitations of the current study and compare NKF with the standard sphincterotomy technique in a nonselective population. Further studies examining which ampullary morphologies are more suitable for NKF versus traditional access techniques may also be necessary, as the ampullary anatomy can be quite variable.

## Supplementary data

Supplementary data are available at *Journal of the Canadian Association of Gastroenterology* online.

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## Conflict of Interest

Dr. R.B.: Olympus-consultant.

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