Needle-knife precut sphincterotomy, repeated cannulation and post-ERCP pancreatitis in patients with bile duct stone disease

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Abstract

Background: Pancreatitis is the most common and serious complication to occur after endoscopic retrograde cholangiopancreatography (ERCP) resulting in substantial morbidity and occasional mortality. Biliary cannulation is unsuccessful during 5%–10% of ERCP procedures. Needle knife sphincterotomy (NKS) can improve success of cannulation but is often used as a last resort. Repeated attempts at cannulating the papilla of Vater and "needle-knief" precut sphincterotomy are independent risk factors for post-ERCP pancreatitis (PEP). Whether precut alone or repeated attempts at cannulation are the culprit factor in the development of post-ERCP pancreatitis remains controversial.

Aim: The aim of this study is to assess the role of precutting and multiple cannulations in the occurrence of post-ERCP pancreatitis in patients with bile duct stone disease.

Patients and methods: This prospective randomized study was performed at two referral centers, between June 2010 and June 2013. It included 515 patients with bile duct stone disease who subjected to ERCP. Pancreatitis rate was assessed in relation to the number of cannulation attempts (<10 and ≥10) and precutting.

Results: Cannulation was done without precutting in 467 cases (90.68%) and with precutting in 48 cases (9.32%). Pancreatitis occurred in 9.21% of patients who had undergone biliary cannulation without precutting and in 18.75% of patients who had undergone biliary cannulation with precutting (p=0.006). It was lower with <10 attempts than with ≥10 (p < 0.0001), either without (p < 0.0001) or with precutting (p < 0.01). Pancreatitis rate did not differ without and with precutting when <10 attempts at cannulation were done, whilst it was lower when precut was done before 10 attempts than when 10 or more attempts were made without precutting (p = 0.02).

Conclusions: Pancreatitis rate was lower when precut was done with <10 attempts than when ≥10 attempts were made without precutting. In experienced hands precut biliary sphincterotomy does not seem to be an independent risk factor for post-ERCP pancreatitis in patients undergoing endoscopic retrograde cholangio-pancreatography for bile duct stones.

Keywords: Precut Sphincterotomy; repeated cannulations; ERCP.

Introduction

ERCP is one of the most complex endoscopic procedures [1]. The reported incidence of ERCP-specific complications ranges from 5% to 15%, depending on the complexity of the procedure, the underlying diagnosis, and the patient co-morbidities [2,3]. Acute pancreatitis remains the most common and serious complication after ERCP with reported incidence ranging from 1.3% to 15.1% in most prospective series, resulting in substantial morbidity and occasional mortality [4-10]. PEP is defined as acute pancreatitis that has developed de novo following ERCP [9,11]. The mechanisms that lead to PEP are complex and not fully understood. Rather than having a single pathogenesis, PEP is believed to be multi-factorial, involving a combination of chemical, hydrostatic, enzymatic, mechanical, microbiologic and thermal factors [12].

Prospective studies have identified specific risk factors, either patient- or procedure-related, associated with a higher incidence of post-ERCP pancreatitis (PEP) [9-13]. Repeated attempts at cannulating the papilla and "needle-knife" precut sphincterotomy are recognized procedure-related risk factors and occur frequently because biliary cannulation may fail in up to 15% of cases, even in experienced hands; they therefore have a substantial impact on PEP rate. Although multiple cannulations has been widely considered as an independent risk factor for post-procedure pancreatitis, there are still conflicting data on the risk related to needle knife sphincterotomy. In a recent prospective Italian multicenter study conducted in high- and low-volume centres for ERCP procedures, the PEP rate was found significantly increased when ten or more attempts at cannulation were done [14].A cut-off of ten attempts at cannulation for significant increased risk of PEP was also found in a previous study that proposed a four-point risk score for the number of cannulations [15].

Since precutting generally follows a number of failed cannulation attempts, it is hard to clarify whether precutting as such or repeated cannulation is the prime culprit in post-procedure pancreatitis. There are few studies comparing the risk of PEP after "needle-knife" precut sphincterotomy or persistent attempts at biliary cannulation with the standard technique [16-19].

Aim of the work

The aim of this study was to assess the role of precutting and multiple attempts of cannulation of papilla of Vater, adjusted for the number of attempts at cannulation (fewer than ten and ten or more), in the occurrence of post-procedure pancreatitis, in a prospective evaluation of a consecutive series of patients who had undergone biliary cannulation and sphincterotomy for bile duct stones.

Patients and methods

This prospective study was performed on 515 patients referred to gastro-intestinal endoscopy unit of Assuit University hospital (404 patients) and the gastro-intestinal endoscopy unit of surgery department of Sohag University hospital (111 patients), between June 2010 and June 2013.

The inclusion criteria were: (1) patients having bile duct stone disease pre-endoscopically evidenced by clinical manifestations, elevated direct serum bilirubin and abdominal imaging or patients with bile duct stone disease demonstrated by cholangiography during ERCP (Fig. 1), and (2) successful biliary cannulation and sphincterotomy.

Patients were excluded for any of the following reasons: (1) Pregnancy, (2) Patients with contraindication to ERCP (coagulopathy, history of contrast dye anaphylaxis, severe cardiopulmonary disease, recent myocardial infarction), (3) Acute pancreatitis, cholangitis or hyperamylasaemia at the time of the procedure, (4) previous biliary sphincterotomy, or (5) need for urgent ERCP within 12 hours. Ethical committee and informed written consent were taken before conducting the study.

All patients subjected to complete assessment including proper history, clinical examination, laboratory investigations (CBC, serum bilirubin, ALT, AST, ALP, serum albumin, PT, PC, urea and creatinine, blood sugar, and serum amylase), and imaging studies (US,CT, MRI or MRCP).

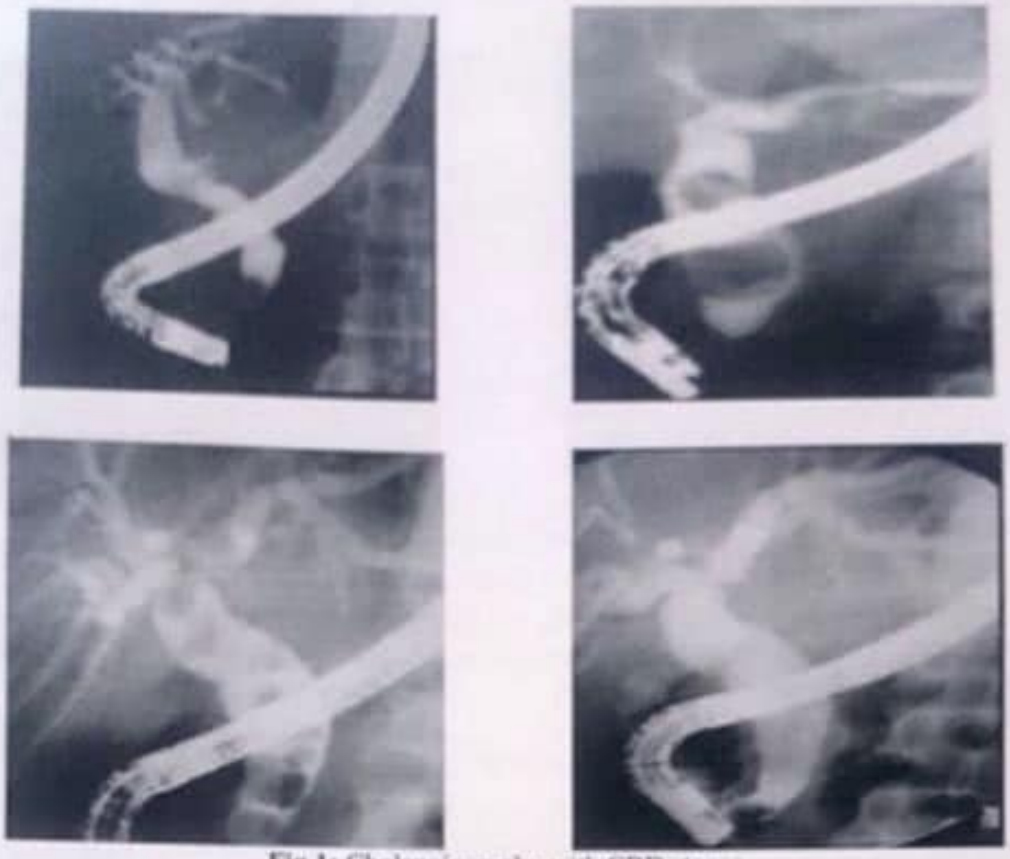

Fig.1: Cholangiography with CBD stones

Endoscopic procedure

All ERCP procedures were performed by high volume endoscopist using the Pentax lateral view endoscope ED-3440T and ED-3485T. Patients were placed in prone position and sedated with midazolam and propofol in conjunction with a topical anesthetic applied to the posterior oropharynx under the supervision of an anesthesiologist. Deep biliary cannulation was evidenced by direct injection of the contrast agent or by advancing a hydrophilic guide wire, preloaded into the sphincterotome. The decision whether and when to make the precut was decided by the operator. The precut was done using the freehand technique, starting approximately 5 mm above the papillary orifice, with a bottom up cut (fistulotomy) (Fig. 2). In all cases, a low-osmolality non-ionic radiological contrast medium (urografin 76%) was injected for ductal opacification.

Trainees completed at least part of the procedure in about 20% of cases, but did not carry out "needle-knife" precut.

All patients were admitted to the hospital at least for 24 hours following the procedure to detect early complications. All patients were monitored at least for 6 hours after the procedure to detect symptoms and signs of pancreatitis (e.g. abdominal pain, tachycardia, hypotension, fever and vomiting). Measurement of serum amylase was done by sampling of blood at four hours post-ERCP. Abdominal ultrasonography was routinely performed in all patients suffering from pancreatic-like pain lasting at least 24 hours. In cases of doubt of developing PEP, abdominal CT scan was done. If complications arose, patients stayed in the hospital until they recovered (from 2 days up to 14 days).

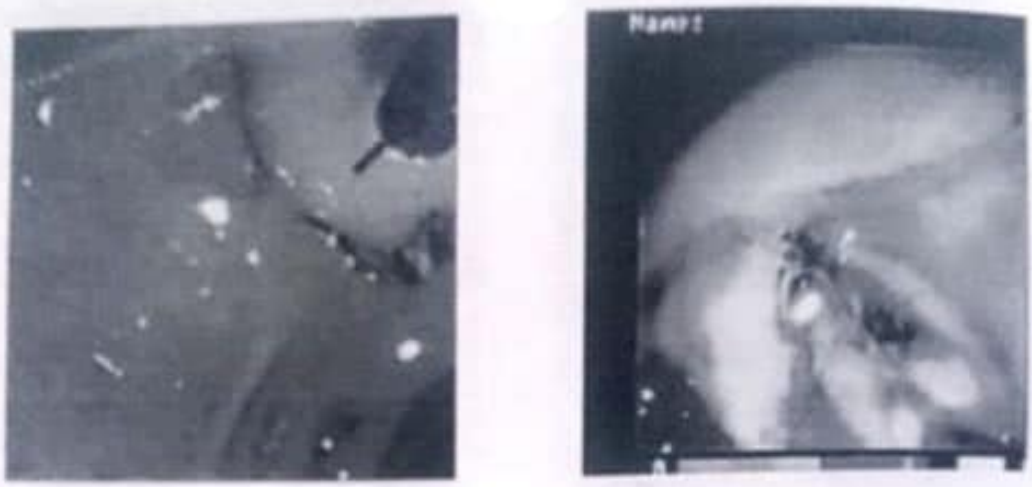

Fig. 2: Precut sphincterotomy

Successful cannulation was defined as free and deep instrumentation of the biliary tree. A cannulation attempts was defined as sustained contact between the cannulating device and the papilla for at least 5 seconds [20].

Pancreatitis was defined as post-procedure, new-onset or increased abdominal pain persisting for at least 24 hours, with serum amylase at least three times the upper limit of normal [21]. Amylase values have been found to peak between 90 minutes and 4 hours post-ERCP [22]. The serum amylase level measured 4 hours after the procedure is the most reliable predictor of PEP [23,24]. We therefore hypothesized and used the 4 hours amylase level as the most accurate amylase value for predicting subsequent pancreatitis. Pancreatitis was classified as mild, moderate or severe according to the criteria of the Atlanta International Symposium of 1992 [25]. In all cases the severity of the pancreatic damage was established on the basis of CT scans 48 hours after the onset of pancreatitis.

Statistical analysis

Data were analyzed using the software package SPSS 15 (Chicago, IL, USA). Groups were compared by the Mann–Whitney U-test and the chi-square ($\chi 2$) test, as appropriate. *P* value of less than 0.05 was considered significant.

Results

This is a prospective study included 515 patients with bile duct stone disease who fulfilled the inclusion criteria. Attempted biliary cannulation without precut was performed in 467 patients (90.68%). Amongst these cases, 432 cases (92.51%) required less than 10 attempts whilst the remaining 35 cases (7.49%) required ten or more cannulation attempts (Table 1).

"Needle-knife" precut sphincterotomy was required to reach the CBD in the remaining 48 patients (9.32%). Precutting was associated with fewer than ten attempts at cannulation in 31 cases (64.58%), and with ten or more in the other 17 cases (35.42%) (Table 1).

Table 1: Technical details of the procedures

	Biliary cannulation without precutting		Biliary cannulation with Precutting	
No. of attempts	<10	≥10	<10	≥10
No. of procedures	432	35	31	17

Patients in both groups matched for age, sex, CBD dilation, serum bilirubin, pancreatic duct opacification, and cannulation technique, with the exception of patients who had undergone precutting, in whom cannulation was attempted mainly with guide wire assistance.

Post ERCP pancreatitis

The overall post-procedure pancreatitis rate was 10.1% (52/515 cases). Pancreatitis occurred in 43 patients (9.21%) in whom precutting was not done and in 9 patients (18.75%) in whom precutting was done, independently of the cannulation technique. The incidence of PEP was significantly higher after precutting ($p = 0.006$).

In cases without precutting, the pancreatitis rate was significantly lower ($p < 0.0001$) when fewer than ten attempts at cannulation were needed than when ten or more were made. Similarly, after the precut procedure, the pancreatitis rate appeared significantly lower with fewer than ten attempts than after ten or more ($p < 0.01$) (Table 2).

Table 2: Pancreatitis rates in relation to the number of attempts at cannulation, with and without precutting

	Cannulation attempts <10	Cannulation attempts ≥10	*P* value
Biliary cannulation without precutting	33/432 (7.64%)	10/35 (28.57%)	<0.0001
Biliary cannulation with Precutting	3/31 (9.68%)	6/17 (35.29%)	<0.01

Successful biliary cannulation needing ten or more attempts was associated with four times the risk of PEP in comparison with fewer than ten attempts. The risk of post-procedure pancreatitis was similar for cases in which the biliary ductal system was cannulated with or without precutting before ten attempts had been made.

When ten or more attempts were needed, with or without precutting, the pancreatitis rate was significantly higher; in these cases, precutting did not significantly affect the incidence ($p = 0.45$). However, precutting before ten attempts at cannulation was significantly less risky than ten or more attempts without precutting.

Discussion

A still unsettled question about "needle-knife" sphincterotomy is whether or not the reported procedure-related high risk of pancreatitis depends on the technique itself or merely reflects that fact the cannulation was difficult, with repeated attempts that may have caused papillary oedema, and/or repeated contrast injection into the pancreatic ductal system [26-28]. Two studies found that delaying the precut increased the risk of PEP [29,30], whilst four others did not [16,31-33].

Another four studies showed that the complication rate of early precut did not exceed that of the standard technique in experienced hands [17,34-36]. A recent prospective study stated that the timing of the precut procedure did not influence the complications rate for ERCPs [18], whilst a meta-analysis of six

randomized, controlled trials showed that the precut reduced the risk of pancreatitis compared with conventional technique [37]. Most of these studies were conducted in high-volume centres by experienced endoscopists and indicated that both precut sphincterotomy and repeated attempts give similar success and complication rates in cases of difficult biliary cannulation. In contrast, in prospective multicenter trials in tertiary referral centres and community-based practises with endoscopists of varying levels of expertise, the precut has been shown to be an independent risk factor for overall complications and pancreatitis, with adjusted odds ratios of respectively 3.61 and 4.34 [4] and relative risk of 1.87 and 2.80 [5].

Our study assessed the PEP rate in relation to a cut-off number of ten attempts at cannulation and the timing of precutting in a large series of consecutive patients undergoing therapeutic ERCP for documented bile duct stone disease. Repeated attempts at papillary cannulation, independently of pancreatic duct cannulation, were confirmed as a significant risk factor for post-procedure pancreatitis; ten or more attempts at cannulation increased the rate four fold, from 7.77% to 30.77%.

Whether the biliary precut was done before or after ten attempts at cannulation also significantly changed the post-procedure pancreatitis rate in our study, from 9.68% up to 35.29% - a four fold difference. The increase was similar to that between fewer and more than ten attempts at cannulation, without precutting (from 7.64% to 28.57%). Adding the precut to persistent cannulation attempts further increased the pancreatitis rate, from 28.57% to 35.29%, although the difference was not statistically significant. These data do not agree with three previous studies [16,18,30] that used the cannulation time instead of the number of attempts and found no difference between delayed precutting and persistence in cannulation.

A biliary precut done before ten attempts at cannulation did not significantly raise the pancreatitis risk in comparison to cases in which successful biliary cannulation was achieved with fewer than ten attempts and without precutting; this confirms that the precut per se should not be considered an independent risk factor for post-procedure pancreatitis in experienced hands.

Conclusions

In conclusion, this prospective analysis on a large series of patients undergoing ERCP for bile duct stones showed that a "needle-knife" precutting to access the biliary ductal system done before ten attempts have been made at cannulation did not increase the risk of post-procedure pancreatitis, compared with the standard cannulation technique, and it should be preferred rather than persisting at cannulation when up to nine cannulation attempts have already been made, because the risk of pancreatitis is significantly higher for either repeatedly trying for cannulation or adding a delayed precut.

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الملخص العربى

علاقة شق حلمة الأثنى عشر والمحاولات المتكررة لدخول القناة المرارية مع نسبة حدوث التهاب البنكرياس الحاد بعد تنظير القنوات المرارية و البنكرياسية فى مرضى حصوات القناة المرارية

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مقدمة:

يعتبر منظار القنوات المرارية و البنكرياسية من أفضل وسائل تشخيص و علاج أمراض البنكرياس و القنوات المرارية. ويعتبر التهاب البنكرياس الحاد من أهم و أخطر المضاعفات الناتجة عن تنظير القنوات المرارية و الذى يؤدي الى ارتفاع النسبة المرضية و معدل الوفيات. و قد أثبتت الدراسات الحديثة أن معدل التهاب البنكرياس الناتج عن تنظير القنوات المرارية يتراوح ما بين 1.3% : 15.1% و قد ترتفع هذة النسبة لتصل الى 40% حسب اختلاف تصميم الأبحاث و تعريف التهاب البنكرياس. ولقد هدفت هذه الدراسة إلى تقييم و دراسة العلاقة بين شق حلمة الأثنى عشر بالسكين والمحاولات المتكررة لدخول القناة المرارية ونسبة حدوث التهاب البنكرياس الحاد بعد تنظير القنوات المرارية و البنكرياسية فى مرضى حصوات القناة المرارية.

المرضى وأساليب العلاج:

أجريت هذة الرسالة على 515 مريضاً يعانون من حصوات بالقناة المرارية تم اجراء منظار علاجى للقنوات المرارية لهم بوحدة مناظير الجهاز الهضمى بقسم الجراحة العامة بكلية طب سوهاج و وحدة مناظير الجهاز الهضمى بالمستشفى الجامعى بأسيوط فى الفترة من يونيو 2010 الى يونيو 2013.

النتائج : أظهرت النتائج الآتى:

- 10.1% من اجمالى المرضى عانوا من التهاب حاد بالبنكرياس بعد اجراء المنظار وكانت نسبة حدوث التهاب البنكرياس فى المرضى الذين تم علاجهم بالمنظار بعد دخول القناة المرارية بدون استخدام السكين 9.21% بينما كانت 18.75 فى حالات استخدام السكين.
- وجود علاقة ذات دلالة احصائية بين عدد محاولات دخول القناة المرارية (<10أو ≤ 10) سواء باستخدام أو عدم استخدام السكين و نسبة حدوث التهاب بالبنكرياس.
- ارتفاع نسبة حدوث التهاب البنكرياس فى المرضى الذين تم علاجهم بالمنظار بعد ≤ 10 محاولات لدخول القناة المرارية الى أربعة أضعاف النسبة فى المرضى الذين تم علاجهم بالمنظار بعد<10 محاولات لدخول القناة المرارية سواء باستخدام أو عدم استخدام السكين.

الاستنتاج: نستنتج من النتائج السابقة:

- وجود علاقة طردية بين نسبة حدوث التهاب البنكرياس و عدد محاولات دخول القناة المرارية أيا كانت الطريقة المستخدمة لدخول القناة المرارية.
- يفضل استخدام السكين لشق حلمة الأثنى عشر لدخول القناة المرارية اذا زادت محاولات دخول القناة المرارية بالطريقة المعتادة عن تسع محاولات.