Post-endoscopic retrograde cholangiopancreatography pancreatitis: Risk factors and predictors of severity

Ayman El Nakeeb, Ehab El Hanafy, Tarek Salah, Ehab Atef, Hosam Hamed, Ahmad M Sultan, Emad Hamdy, Mohamed Said, Ahmed A El Geidie, Tharwat Kandil, Mohamed El Shobari, Gamal El Ebidy

AIM
To detect risk factors for post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis (PEP) and investigate the predictors of its severity.

METHODS
This is a prospective cohort study of all patients who underwent ERCP. Pre-ERCP data, intraoperative data, and post-ERCP data were collected.

RESULTS
The study population consisted of 996 patients. Their mean age at presentation was 58.42 (± 14.72) years, and there were 454 male and 442 female patients. Overall, PEP occurred in 102 (10.2%) patients of the study population; eighty (78.4%) cases were of mild to moderate degree, while severe pancreatitis occurred in 22 (21.6%) patients. No hospital mortality was reported for any of PEP patients during the study duration. Age less than 35 years (P = 0.001, OR = 0.035), narrower median common bile duct (CBD) diameter (P = 0.0001) and increased number of pancreatic cannulations (P = 0.0001) were independent risk factors for the occurrence of PEP.

CONCLUSION
PEP is the most frequent and devastating complication after ERCP. Age less than 35 years, narrower median CBD diameter and increased number of pancreatic cannulations are independent risk factors for the occurrence of PEP.
cannulations are independent risk factors for the occurrence of PEP. Patients with these risk factors are candidates for prophylactic and preventive measures against PEP.

**Key words:** Pancreatitis; Obstructive jaundice; Endoscopic retrograde cholangiopancreatography

© The Author(s) 2016. Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Endoscopic retrograde cholangiopancreatography (ERCP) is increasingly used for therapeutic management of various biliary and pancreatic diseases. However, ERCP is not a procedure without morbidities. Post-ERCP pancreatitis (PEP) remains the most devastating and frequent complication after ERCP. Identification of risk factors for PEP helps adopt prophylactic measures in high risk patients and early discharge in low risk patients. Age less than 35 years, narrower median common bile duct diameter and increased number of pancreatic cannulations were identified to be independent risk factors for the occurrence of PEP.

El Nakeeb A, El Hanafy E, Salah T, Atef E, Hamed H, Sultan AM, Hamdy E, Said M, El Geidie AA, Kandil T, El Shobari M, El Ebidy G. Post-endoscopic retrograde cholangiopancreatography pancreatitis: Risk factors and predictors of severity. *World J Gastrointest Endosc.* 2016; 8(19): 709-715. Available from: URL: http://www.wjgnet.com/1948-5190/full/v8/i19/709.htm DOI: http://dx.doi.org/10.4253/wjge.v8.i19.709

**INTRODUCTION**

Endoscopic retrograde cholangiopancreatography (ERCP) is increasingly used for therapeutic management of various biliary and pancreatic diseases[1]. However, ERCP is not a procedure without morbidities[2]. Post-ERCP pancreatitis (PEP) remains the most common and serious complication after ERCP[3]. The reported incidence of PEP is around 5%[4,5]. This rate may increase up to 20%-40% in high risk patients. Although the majority of PEP cases are of mild degree, it can be severe and life threatening in a substantial proportion of cases[6].

Identification of risk factors for PEP helps adopt prophylactic measures in high risk patients and early discharge in low risk patients[1,7,8]. Being convinced with a number of patient-related risk factors, some gastroenterologists and surgeons prefer adoption of alternative management strategies for ERCP whenever possible in high risk patients. Similarly, some endoscopists try to avoid procedure-related risk factors to increases the safety of the procedure. All these factors make identification of risk factors for PEP be of paramount importance for the practice of ERCP.

Many patient and procedure related factors have been suggested to be associated with increased likelihood of PEP[8]. The trigger mechanism and pathogenesis for PEP remain unclear[9]. The aim of this study was to detect risk factors for PEP and investigate the predictors of its severity in a tertiary high volume referral surgical center in Middle East in Egypt.

**MATERIALS AND METHODS**

This is a prospective cohort study of all patients who underwent ERCP between August 2012 and September 2014. Excluded patients were those who presented with obstructed stent, active pancreatitis, previous endoscopic sphincterotomy, biliary complications after liver transplantation, dye allergy, pregnancy, or mental disability.

Patients were admitted 24 h before the procedure. Baseline laboratory assessment of liver functions, blood count and serum amylase level were done prior to ERCP. No pre-ERCP treatment was used to decrease the risk of PEP. In our center, ERCP is performed under general anesthesia with endotracheal intubation in left semi prone position with monitoring of oxygen saturation, heart rate, and blood pressure. The procedure was performed by experienced endoscopists who had performed at least 1500 ERCPs over the last 10 years. Selective bile duct cannulation was carried out in all patients, but pancreatic duct cannulation was performed when necessary. When three or more attempts were needed due to difficulty in cannulation, precut papillotomy was selectively performed. In addition, endoscopic papillotomy for stone extraction using balloon, basket and mechanical lithotripsy, bile duct placement of either plastic or self-expanding metallic stent, as well as brush cytology and dilation, were performed when indicated. Pancreatic duct stenting was not used to minimize PEP in our practice.

ERCP data were recorded in a standardized manner including all potential risk factors for PEP. Patients were hospitalized for 24 h after the procedure and observed for symptoms and signs of post-ERCP complications. Complete blood picture and serum amylase level were determined routinely after 6 h and 24 h.

PEP was defined and classified according to the consensus definition and grading system[10]. PEP was defined as new or worsened abdominal pain together with a serum amylase level at least three times normal at more than 24 h after ERCP and necessitating hospitalization for more than one night. PEP was graded according to the length of hospital stay and the need for intervention. Mild PEP required hospitalization for 2-3 days, moderate PEP required hospitalization for 4-10 nights, and severe pancreatitis required hospitalization for more than 10 d, or required intervention or was complicated by pseudocyst[10].

Descriptive data are presented as means and standard deviation or medians with range according to the data distribution. Comparison of means was done by \( t \)-test for categorical data or Student’s \( t \)-test for continuous data. Difference was considered significant when a \( P \)-value was less than 0.05. Independent risk factors for PEP were assessed by multiple logistic
Pancreatitis presented with obstructed stent (n = 24), previous endoscopic sphincterotomy (n = 110), biliary complications after liver transplantation (n = 36), dye allergy (n = 10), pregnancy (n = 14), or mental disability (n = 10).

Indications for ERCP were malignant obstructive jaundice due to peripapillary tumor (n = 460, 46.2%) or hilar cholangiocarcinoma (n = 2, 0.2%), calculi obstructive jaundice (n = 512, 51.4%), benign biliary stricture (n = 10, 1.0%), and post-cholecystectomy biliary leakage (n = 12, 1.2%). The mean age at presentation was 58.42 (± 14.727) years. There were 554 male in comparison to 442 female patients, with a male to female ratio of 1.3:1.

Overall, PEP occurred in 102 (10.2%) patients of the study population. Eighty (78.4%) cases were of mild to moderate degree, while severe pancreatitis occurred in 22 (21.6%) patients. The median length of hospital stay in patients with pancreatitis was 3 d (range, 2-15 d). No hospital mortality was reported for any of PEP patients during the study duration. Univariate analysis showed that patient age and narrower CBD diameter are statistically significant patient-related risk factors associated with occurrence and severity of PEP, while increased number of cannulation attempts and pancreatic cannulation more than three times were significant procedure-related risk factors associated with occurrence and severity of PEP. Indication for ERCP was not significantly associated with occurrence of pancreatitis (P = 0.4), but it was significantly associated with the severity of PEP (P = 0.009) (Tables 1 and 2).

Multivariate analysis after binary logistic regression analysis revealed that patient age less than 35 years (P = 0.001, OR = 0.035), narrower median CBD diameter (P = 0.001) were independent risk factors for the occurrence of PEP (Table 3).

**DISCUSSION**

PEP is the most common and serious complication after ERCP\[8\]. PEP is associated with higher morbidity and mortality beside its effect in increasing the consumption of hospital resources\[111\]. Identification of clinical and procedural correlates for PEP is of crucial importance in the practice of ERCP. It affects the medical decision regarding patient choice, adoption of pharmacological prophylactic measures, avoidance of procedural risk factors, and determination of the time of discharge after the procedure\[1,7,8,11\]. Risk factors for PEP have been a matter of controversy and the pathogenesis of PEP is not fully understood yet\[9,11\]. This study reports risk factors for PEP according to the experience of a tertiary high volume surgical center in Egypt.

Despite advanced accessories and novel techniques in ERCP, complication rate after ERCP remained unchanged over the last decade\[7,12\]. According to previous reports, the incidence of PEP ranges from 5% to 40%. This great discrepancy in the reported rates can be attributed to heterogeneity of the definition of PEP and its grading system, variability in data collection, inclusion of diagnostic ERCP in the study, and difference in expertise among endoscopists\[13\]. The incidence of PEP in this cohort was 10.2% with adoption of the consensus definition of PEP\[10\]. Mild to moderate PEP occurred in 80

---

**Table 1** Risk factors for pancreatitis after endoscopic retrograde cholangiopancreatography n (%)  

| No pancreatitis | Pancreatitis | P-value |
|-----------------|--------------|---------|
| Patient related factors | | |
| Median age (yr) | 60 | 48 | 0.0001 |
| < 35 | 29 (7.2) | 20 (39.2) | 0.0001 |
| ≥ 35 | 415 (92.8) | 31 (60.8) | |
| Sex | | |
| Male | 510 (57) | 44 (43.1) | 0.05 |
| Female | 384 (43) | 58 (56.9) | |
| Median serum bilirubin (mg%) | | |
| < 2 | 124 (88.6) | 16 (11.4) | |
| ≥ 2 | 770 (90) | 86 (10) | 0.72 |
| Median CBD diameter (mm) | | |
| < 10 | 10 | 660 (89.5) | 0.0001 |
| ≥ 10 | 70 (7.8) | 58 (56.9) | |
| Indication for ERCP | | |
| Malignant | 402 (45) | 40 (39.2) | 0.43 |
| Benign | 452 (55) | 62 (60.8) | |
| Type of papilla | | |
| Normal | 540 (60.4) | 56 (54.9) | 0.01 |
| Atrophic | 18 (2) | 8 (7.8) | |
| Pregnant | 68 (7.6) | 2 (2) | |
| Tumour | 64 (7.2) | 4 (3.9) | |
| Redundant | 66(7.4) | 12 (11.8) | |
| Juxtaduvericular | 68 (7.6) | 16 (15.7) | |
| Small | 60 (6.6) | 2 (2) | |
| Long | 10 (1.1) | 2 (2) | |
| Procedure related factors | | |
| Number of cannulation attempts | | |
| < 5 | 600 (73.9) | 58 (56.9) | 0.01 |
| ≥ 6 | 234 (26.1) | 44 (43.1) | |
| Number of pancreatic cannulations | | |
| < 3 times | 864 (96.6) | 60 (58.8) | |
| ≥ 3 times | 28 (3.4) | 42 (41.2) | 0.0001 |
| Method of cannulation | | |
| Conventional | 640 (89.4) | 76 (10.6) | 0.7 |
| Precut | 252 (90.6) | 26 (9.4) | |
| Biliary sphincter balloon dilatation | No | 654 (73.2) | 86 (84.3) | 0.08 |
| Yes | 240 (26.8) | 16 (15.7) | |

CBD: Common bile duct; ERCP: Endoscopic retrograde cholangiopancreatography

regression. Statistical analyses of the data in this study were performed using SPSS software, version 17 (Chicago, IL).

**RESULTS**

From August 2012 to September 2014, a total of 1296 patients underwent ERCP at Gastrointestinal Surgical Center, Mansoura University, Egypt. The study population consisted of 996 cases after exclusion of those who presented with obstructed stent (n = 66), active pancreatitis (n = 24), previous endoscopic sphincterotomy (n = 110), biliary complications after liver transplantation (n = 36), dye allergy (n = 10), pregnancy (n = 14), or mental disability (n = 10).

Indications for ERCP were malignant obstructive jaundice due to peripapillary tumor (n = 460, 46.2%) or hilar cholangiocarcinoma (n = 2, 0.2%), calculi obstructive jaundice (n = 512, 51.4%), benign biliary stricture (n = 10, 1.0%), and post-cholecystectomy biliary leakage (n = 12, 1.2%). The mean age at presentation was 58.42 (± 14.727) years. There were 554 male in comparison to 442 female patients, with a male to female ratio of 1.3:1.

Overall, PEP occurred in 102 (10.2%) patients of the study population. Eighty (78.4%) cases were of mild to moderate degree, while severe pancreatitis occurred in 22 (21.6%) patients. The median length of hospital stay in patients with pancreatitis was 3 d (range, 2-15 d). No hospital mortality was reported for any of PEP patients during the study duration. Univariate analysis showed that patient age and narrower CBD diameter are statistically significant patient-related risk factors associated with occurrence and severity of PEP, while increased number of cannulation attempts and pancreatic cannulation more than three times were significant procedure-related risk factors associated with occurrence and severity of PEP. Indication for ERCP was not significantly associated with occurrence of pancreatitis (P = 0.4), but it was significantly associated with the severity of PEP (P = 0.009) (Tables 1 and 2).

Multivariate analysis after binary logistic regression analysis revealed that patient age less than 35 years (P = 0.001, OR = 0.035), narrower median CBD diameter (P = 0.001) and increased number of pancreatic cannulations (P = 0.0001) were independent risk factors for the occurrence of PEP (Table 3).

---

**El Nakeeb et al.** Post-ERCP pancreatitis
(8%) patients, while severe PEP occurred in 22 (2.2%) patients. These ratios are concordant with data reported by previous studies [14-16].

Among different patient related risk factors, younger age and non-dilated extrahepatic biliary radicals were independent risk factors for PEP on multivariate analysis.

| Table 2  Predictors of severity of pancreatitis after endoscopic retrograde cholangiopancreatography n (%) | Mild to moderate pancreatitis (80) | Severe pancreatitis (22) | P-value |
|------------------------------------------------|----------------------------------|------------------------|---------|
| Patient related factors | | | |
| Median age (yr) | 52 | 30 | 0.0001 |
| Age | | | |
| < 35 | 26 (32.5) | 14 (63.6) | 0.0001 |
| > 35 | 54 (67.5) | 8 (36.4) | |
| Sex | | | |
| Male | 38 (47.5) | 6 (27.3) | 0.08 |
| Female | 42 (52.5) | 16 (72.7) | |
| Median serum bilirubin (mg%) | | | |
| < 2 | 14.1 | 9.9 | 0.3 |
| > 2 | 8 (50) | 8 (50) | |
| Median CBD diameter (mm) | | | |
| < 10 | 72 (85.7) | 14 (14.3) | 0.07 |
| > 10 | 10 (27.3) | 6 (27.3) | 0.0001 |
| Indication for ERCP | | | |
| Malignant | 39 (97.5) | 1 (2.5) | 0.009 |
| Benign | 41 (66.1) | 21 (33.9) | |
| Type of papilla | | | |
| Normal | 39 | 17 | 0.06 |
| Atrophic | 6 | 2 | |
| Pregnant | 0 | 2 | |
| Tumour | 4 | 0 | |
| Redundant | 9 | 3 | |
| Juxtadivericular | 15 | 1 | |
| Small | 2 | 0 | |
| Long | 2 | 0 | |
| Procedure related factors | | | |
| No. of cannulation attempts | | | |
| < 5 | 46 (57.5) | 12 (54.5) | 0.03 |
| ≥ 6 | 34 (27.5) | 10 (45.5) | |
| Median number of pancreatic cannulations | | | |
| < 3 times | 2 | 4 | 0.0001 |
| > 3 times | 58 (72.5) | 2 (9.1) | 0.0001 |
| Method of cannulation | | | |
| Conventional | 58 (72.5) | 18 (81.8) | 0.07 |
| Precut | 22 (52.4) | 4 (18.2) | |
| Biliary sphincter balloon dilatation | | | |
| No | 70 (87.5) | 16 (72.7) | 0.1 |
| Yes | 10 (12.5) | 6 (27.3) | |

CBD: Common bile duct; ERCP: Endoscopic retrograde cholangiopancreatography.

| Table 3  Multivariate logistic regression for analysis of pancreatitis after endoscopic retrograde cholangiopancreatography | P-value | Odds ratio | 95%CI for EXP(B) |
|------------------------------------------------|---------|------------|------------------|
| | | | Lower | Upper |
| Variable | P-value | Odds ratio | 95% CI for EXP(B) | |
| Age group | 0.001 | 0.035 | 0.005 | 0.259 |
| Age | 0.519 | 1.012 | 0.976 | 1.050 |
| Sex | 0.362 | 0.143 | 0.075 | 0.270 |
| CBD diameter below 10 mm | 0.609 | 0.726 | 0.212 | 2.481 |
| CBD diameter | 0.010 | 0.612 | 0.409 | 0.757 |
| Difficult cannulation | 0.207 | 0.476 | 0.150 | 1.506 |
| No. of pancreatic cannulations below 3 | 0.117 | 0.219 | 0.033 | 1.460 |
| No. of pancreatic cannulations | 0.080 | 5.258 | 2.665 | 10.370 |
| Papilla | 0.964 | | |

CBD: Common bile duct.
in this study. Also, using a cutoff value of 35 years to divide patients into two groups, the rate of PEP was significantly higher in the younger group by univariate analysis. Younger age has been a subject of controversy regarding its association with PEP\cite{21-23}. Many studies reported an insignificant relation between patient age and likelihood of PEP\cite{21,27}. However, Freeman et al\cite{21} first reported relatively younger age as a predictor of PEP on multivariate analysis. This finding was confirmed by later studies\cite{21,25-27}. High incidence of PEP in younger age was explained by the aging effect on pancreatic exocrine function, smaller common bile duct diameter and the higher incidence of sphincter of Oddi dysfunction in younger age\cite{17,18,19}.

Management of CBD stones in case of non-dilated extrahepatic biliary system represents a surgical challenge\cite{20}. Laparoscopic transcholedochal CBD exploration mandates a CBD diameter of at least 6-8 mm\cite{21-23}. According to many studies including this one, normal caliber CBD is associated with increased difficulty of the ERCP procedure\cite{24-26}. However, most of recent studies reported absence of association between narrower CBD diameter and PEP\cite{13}. Laparoscopic management for surgically fit patients with concomitant gall bladder and CBD stones in case of non-dilated CBD through transcystic CBD exploration or laparoscopic Rendezvous is better to avoid or minimize the risk of PEP\cite{21}. In case of isolated choledocholithiasis or in patients who are unfit for surgery, prophylactic measures against PEP should be adopted.

In this cohort, difficult cannulation, denoted by frequent cannulation attempts and pancreatic cannulation more than three times, was associated with a higher risk of PEP. The effect of pancreatic duct injection with contrast dye on PEP could not be evaluated because we did not use the conventional contrast cannulation method. The effect of precut sphincterotomy on PEP is controversial\cite{11}. Some authors advocate that precut sphincterotomy causes papillary oedema which retains pancreatic secretion resulting in PEP\cite{8}. However, Freeman et al\cite{21} reported an insignificant relation between patient age and CBD stones in case of non-dilated CBD through transcystic CBD exploration or laparoscopic Rendezvous.

In conclusion, PEP is the most frequent and devastating complication after ERCP. PEP is associated with higher morbidity and mortality beside its effect in increasing the consumption of hospital resources. Age less than 35 years, narrower median CBD diameter and increased number of pancreatic cannulations are independent risk factors for the occurrence of PEP. Patients with these risk factors are candidates for prophylactic and preventive measures against PEP.

**COMMENTS**

**Background**

Endoscopic retrograde cholangiopancreatography (ERCP) is increasingly used for therapeutic management of various biliary and pancreatic diseases. However, ERCP is not a procedure without morbidities. Post-ERCP pancreatitis (PEP) remains the most common and serious complication after ERCP. The reported incidence of PEP is around 5%. This rate may increase up to 20%-40% in high risk patients. Identification of risk factors for PEP helps adopt prophylactic measures in high risk patients and early discharge in low risk patients.

**Research frontiers**

Many studies have tried to identify the risk factors for pancreatitis after ERCP. Many patient and procedure related factors are suggested to be associated with increased likelihood of PEP. The trigger mechanism and pathogenesis for PEP remain unclear.

**Innovations and breakthroughs**

ERCP is not a procedure without morbidities. Identification of risk factors for PEP helps adopt prophylactic measures in high risk patients and early discharge in low risk patients.

**Applications**

The data in this study suggested risk factors for PEP and investigated the predictors of its severity in a tertiary high volume. Furthermore, this study also provided readers with important information regarding the risk factors for PEP.

**Terminology**

PEP remains the most devastating and frequent complication after ERCP. The reported incidence of PEP is around 5%. This rate may increase up to
20%-40% in high risk patients.

**Peer-review**

This is an interesting manuscript with a significant number of patients treating an important topic, and the aim of this study was to detect risk factors for PEP and investigate the predictors of its severity in a tertiary high volume referral surgical center in Egypt.

**REFERENCES**

1. Jurjank SM, Siersema PD, Steyerberg EW, Dees J, Poley JW, Harangozo J, Kuipers EJ. Predictors of complications after endoscopic retrograde cholangiopancreatography: a prognostic model for early discharge. Surg Endosc 2011; 25: 2892-2900 [PMID: 21455806 DOI: 10.1007/s00261-011-1638-9]

2. Cotton PB, Garrow DA, Gallagher J, Romagnuolo J. Risk factors for complications after ERCP: a multivariate analysis of 11,497 procedures over 12 years. Gastrointest Endosc 2009; 70: 88-88 [PMID: 19286178 DOI: 10.1016/j.gie.2008.10.039]

3. Yang D, Dragavon PV. Indomethacin for post-endoscopic retrograde cholangiopancreatography pancreatitis prophylaxis: is it the magic bullet? World J Gastroenterol 2012; 18: 4082-4085 [PMID: 22919238 DOI: 10.3748/wjg.v18.i3.4082]

4. Williams EJ, Taylor S, Fairclough P, Hamlyn A, Logan RF, Martin D, Riley SA, Veitch P, Wilkinson ML, Williamson PR, Lombard M. Risk factors for complication following ERCP; results of a large-scale, prospective multicenter study. Endoscopy 2007; 39: 793-801 [PMID: 17703388 DOI: 10.1055/s-2007-966723]

5. Cheng CL, Sherman S, Watkins JI, Barnett J, Freeman M, Geenen J, Ryan M, Parker H, Frakes JT, Fogel EL, Silverman WB, Dua KS, Alipperti G, Yakshe P, Zavos Z, Kountouras J. Risk factors for therapeutic ERCP-related complications: an analysis of 2,715 cases performed by a single endoscopist. Ann Gastroenterol Surg 2014; 27: 65-72 [PMID: 24714755]

6. Dumonceau JM, Andriulli A, Deviere J, Mariani A, Sigillito A, Leandro G, Leo P, De Marzio G, Peri P. Gastrointestinal biliary sphincterotomy. N Engl J Med 1996; 335: 909-918 [PMID: 8782497 DOI: 10.1161/NEJM199607023351301]

7. Wang P, Li ZS, Liu F, Ren X, Lu NH, Fan ZN, Huang Q, Zhang X, He LP, Sun WS, Zhao Q, Shi RH, Tian ZB, Li YQ, Li W, Zhi FC. Risk factors for ERCP-related complications: a prospective multicenter study. Am J Gastroenterol 2009; 104: 31-40 [PMID: 19098846 DOI: 10.1038/ajg.2008.55]

8. Sharma A, Daihya P, Khullar R, Soni V, Bailaj M, Chowbey PK. Management of common bile duct stone in the laparoscopic era. Indian Surg J 2012; 74: 264-269 [PMID: 23730054 DOI: 10.1007/s12262-012-0593-6]

9. El Nakeeb A, El Geidie A, El Hanafy E, Atef E, Askar W, Sultan AM, Hamady E, El Shobary M, Hamed H, Abdelrafee A, Zeid MA. Management and Outcome of Borderline Common Bile Duct with Stones: A Prospective Randomized Study. J Laparoendosc Adv Surg Tech A 2016; 26: 161-167 [PMID: 26828596 DOI: 10.1089/ lap.2015.0493]

10. Shojaiefard A, Esmaeilezadeh M, Ghafouri A, Mehraei A. Various techniques for the surgical treatment of common bile duct stones: a meta review. Gastroenterol Res Pract 2009; 2009: 840208 [PMID: 19672460 DOI: 10.1155/2009/840208]

11. Lee HM, Min SK, Lee HK. Long-term results of laparoscopic common bile duct exploration by cholecdochojunostomy for choledochojunostomy: 15-year experience from a single center. Ann Surg Treat Res 2014; 86: 1-6 [PMID: 24761400 DOI: 10.4174/ astr.2014.86.1.1]

12. Sherman S, Ruffolo TA, Hawes RH, Lehman GA. Complications of endoscopic sphincterotomy. A prospective series with emphasis on the increased risk associated with sphincter of Oddi dysfunction and nondilated bile ducts. Gastroenterology 1991; 100: 1068-1075 [PMID: 1889690]

13. Khaled M, Freeman M. Prevention and management of post-endoscopic retrograde cholangiopancreatography complications. Clin Endosc 2012; 45: 305-312 [PMID: 22977824 DOI: 10.5946/ cc.2012.45.3.305]

14. Chen YK, Foliante RL, Santoro MJ, Walter MH, Collen MJ. Endoscopic sphincterotomy-induced pancreatitis: increased risk associated with nondilated bile ducts and sphincter of Oddi dysfunction. Am J Gastroenterol 1994; 89: 327-333 [PMID: 8122639]

15. Freeman ML, Guda NM. ERCP cannulation: a review of reported techniques. Gastrointest Endosc 2005; 61: 112-125 [PMID: 15672074 DOI: 10.1016/S0016-5107(04)02463-0]

16. Zhang QS, Han D, Xu JH, Gao P, Shen YC. Needle-knife
papillotomy and fistulotomy improved the treatment outcome of patients with difficult biliary cannulation. Surg Endosc 2016; Epub ahead of print [PMID: 27129550 DOI: 10.1007/s00464-016-4914-x]

29 Ayoubi M, Sansoè G, Leone N, Castellino F. Comparison between needle-knife fistulotomy and standard cannulation in ERCP. World J Gastrointest Endosc 2012; 4: 398-404 [PMID: 23125897 DOI: 10.4253/wjge.v4.i9.398]

30 Swan MP, Alexander S, Moss A, Williams SJ, Ruppin D, Hope R, Bourke MJ. Needle knife sphincterotomy does not increase the risk of pancreatitis in patients with difficult biliary cannulation. Clin Gastroenterol Hepatol 2013; 11: 430-436.e1 [PMID: 23313840 DOI: 10.1016/j.cgh.2012.12.017]

31 Jin YJ, Jeong S, Lee DH. Utility of needle-knife fistulotomy as an initial method of biliary cannulation to prevent post-ERCP pancreatitis in a highly selected at-risk group: a single-arm prospective feasibility study. Gastrointest Endosc 2016; 84: 808-813 [PMID: 27102829 DOI: 10.1016/j.gie.2016.04.011]

32 Mariani A, Di Leo M, Giardullo N, Giussani A, Marini M, Buffoli F, Cipolletta L, Radaelli F, Ravelli P, Lombardi G, D’Onofrio V, Macchiarelli R, Irritano E, Le Grazie M, Pantaleo G, Testoni P. Early precut sphincterotomy for difficult biliary access to reduce post-ERCP pancreatitis: a randomized trial. Endoscopy 2016; 48: 530-535 [PMID: 26990509 DOI: 10.1055/s-0042-102250]

33 Kim SJ, Kang DH, Kim HW, Choi CW, Park SB, Song BJ, Hong YM. Needle-knife fistulotomy vs double-guide-wire technique in patients with repetitive unintentional pancreatic cannulations.
