

## Patient And Procedure Related Risk Factors of Post-ERCP Pancreatitis In Assiut University Hospital

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### ABSTRACT

**Background:** Post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis (PEP) one of the most common and serious complications causing morbidity and mortality

**Aim of study:** This study aimed to assess patient and technical factors that may be related to PEP

**Patient and methods:** We observed 120 patients who developed signs of pancreatitis after ERCP, clinical data and procedural details were recorded in these patients to be evaluated

**Results:** A total of 120 studied patients, their mean age was  $37.38 \pm 12.51$  years, 63.3% were females, the most noted indication of ERCP was choledocholithiasis, 24.2% of patient have history of pancreatitis, long time of procedure was noted in these cases, precut sphincterotomy in 55% and pancreatic duct cannulation was noted in 53.3% of cases, moreover increased difficulty of cannulation occur more in our patients.

**Conclusion:** Patients' related factors as young age, female sex and indication of ERCP, and technical-related factors as precut sphincterotomy and pancreatic cannulation may contribute to PEP.

**Keywords:** ERCP, Pancreatitis, Risk factors.

### INTRODUCTION

Post ERCP pancreatitis (PEP) is increasing nowadays because of increased use of ERCP and may be complexity of the procedure. However it is used as diagnostic tool that may be decreased as MRCP and EUS may replace it. PEP may be considered one of the most common adverse events of ERCP <sup>(1)</sup>. The incidence of PEP ranged between 3.5% and 9.5%, however mortality may reach to 0.7% <sup>(2)</sup>. Pathogenesis of PEP was not fully understood and multiple mechanisms were implicated in this. However PEP is considered to be multifactorial including chemical, enzymatic and mechanical factors <sup>(3)</sup>.

Risk factors may be patient-related as age, sex and indication of disease and may be procedure-related but there is conflicting data about these factors. These discrepancies between studies may be attributed to differences in patients' population, endoscopic technique, and practical experience and use of preventive measures <sup>(4)</sup>. Thus, awareness of these risk factors can prevent the development of PEP. So, this research attempted to ascertain the patient's and procedure's risk factors to increase the safety of ERCP so decreasing PEP morbidity and mortality.

### PATIENTS AND METHODS

This prospective descriptive observational study was conducted through the period from May 2021 to April 2023 including patients who underwent ERCP by skilled endoscopist (who completed more than two effective ERCP procedures each week). The patient who developed manifestations suggesting pancreatitis as abdominal pain post ERCP and increase in serum amylase 3 fold 4 hours post ERCP was diagnosed as PEP and was included in the study then abdominal ultrasound and CT abdomen were performed to confirm diagnosis and asses severity of disease according to

Balthazar scoring system (0-3: mild acute pancreatitis, 4-6: moderate acute pancreatitis, and 7-10: sever acute pancreatitis) <sup>(5)</sup>. All patients were hospitalized for close monitoring.

**Exclusion criteria:** Age less than 18 years, mental disability, pregnancy, diagnosis of acute pancreatitis at time of endoscopy, structural gastrointestinal abnormalities as oesophageal stricture, contraindication to endoscopy as coagulopathy and biliary stent removal.

### Definitions:

Cannulation time is measured when the sphincterotomy came out of endoscope to reach papilla and where deep cannulation is achieved as evidenced by contrast injection. The total procedure time was the duration measured from the moment the endoscope is inserted into the mouth until it is removed <sup>(6)</sup>. Pancreatic cannulation refers to the insertion of a device into the pancreatic duct at a significant depth <sup>(7)</sup>.

Successful cannulation refers to the thorough and unrestricted insertion of instruments into the biliary channels. A cannulation attempt is considered when the cannulating device maintains contact with the papilla for a minimum of 5 seconds, difficult cannulation was defined as number of attempts to papilla before final cannulation [easy (one to five attempts), moderate (six to 15 attempts), and difficult (>15 attempts)] <sup>(8)</sup>.

Three categories were used to classify the difficulty of stone extraction: easy, which denotes little resistance to stone extraction; moderate, which denotes resistance to stone extraction with some degree of resistance; and difficult, which denotes resistance to stone extraction following lithotripsy or unsuccessful efforts at stone extraction.

Post-ERCP pancreatitis was diagnosed by presence of abdominal pain following an ERCP procedure, lasting for more than 24 hours. Additionally, their serum amylase level was elevated to at least three times the upper limit of normal confirmed by abdominal ultrasound and CT scan <sup>(9)</sup>.

**Statistical analysis**

IBM-SPSS version 26.0 software, a statistical tool for the social sciences, was used to analyse the data. Frequencies and percentages represented the category data were displayed. The Shapiro-Wilk test was used to determine if the data for all numerical variables were normal, and the results were presented using the means ± standard deviation (SD) to describe the quantitative data. P value ≤ 0.05 was deemed significant.

**Ethical approval: All participants provided written informed consents, and the study received approval from The Research Ethical Committee of the Faculty of Medicine, Assiut University (IRB#300233). The study adhered to the Code of Ethics of the World Medical Association, specifically the Declaration of Helsinki, for research involving human subjects.**

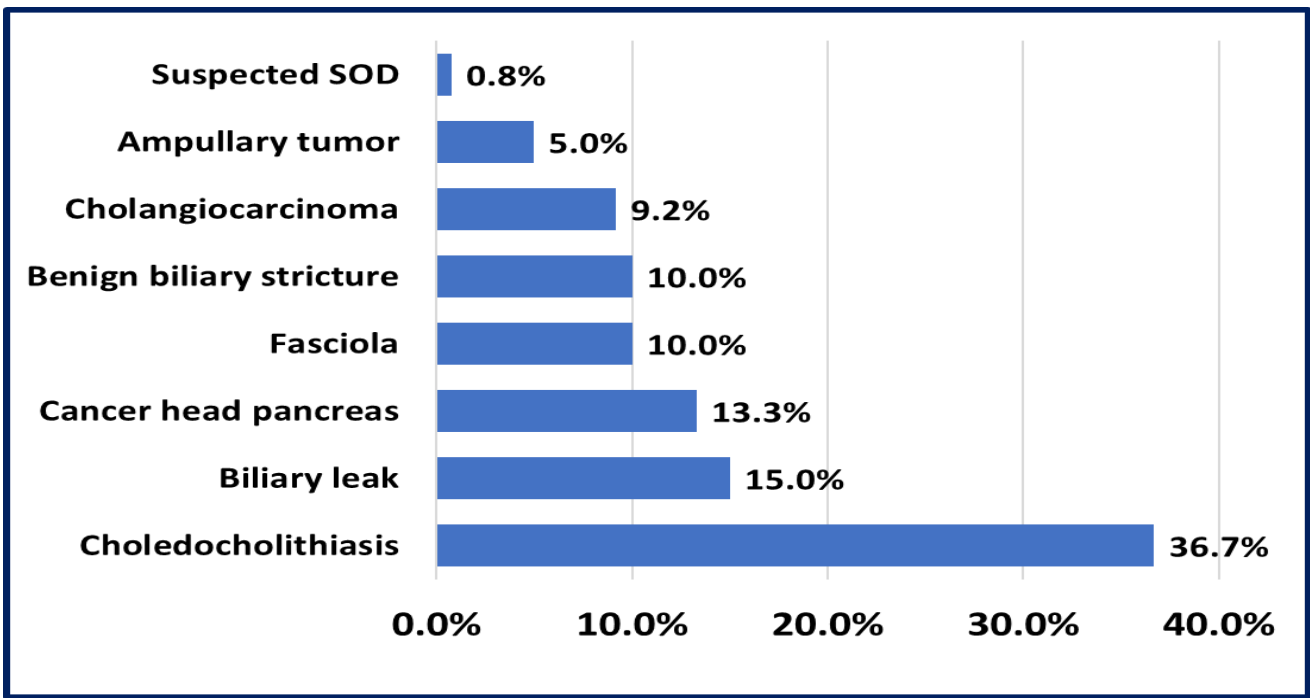
**RESULTS**

A total of 120 studied patients, their mean age was 37.38 ± 12.51 and ranged from 19 to 71 years, 63.3% were females and 36.7% were males. 19.2% of them had DM, 7.5% had hypertension and 1.7% had IHD. ERCP was indicated mainly due to choledocholithiasis, biliary leak, cancer head pancreas, fasciola, benign biliary stricture, cholangiocarcinoma, ampullary tumor and suspected sphincter of Oddi dysfunction (SOD) (36.7%, 15%, 13.3%, 10.0, 10.0, 9.2%, 5.0% and 0.8% respectively). 50.0% had previous history of cholecystectomy, 24.2% had history of pancreatitis, 12.5% had history of sphincterotomy and 10.8% had history of previous PEP. 63.3% of patients had total serum bilirubin less than 2 mg and 66.7% had diameter of common bile duct less than 10 mm. Regarding nature of the disease, 70.8% were benign and 29.2% were malignant (Table1 & figure 1)

**Table (1): Patients related risk factors for post ERCP pancreatitis.**

Variables	Total	%
<b>Patients risk factors</b>		
Age (years): Mean ± SD	37.38±12.51 (19-71)	
<b>Gender</b>		
▪ Male	44	36.7%
▪ Female	76	63.3%
<b>Presence of comorbid</b>		
▪ DM	23	19.2%
▪ HTN	9	7.5%
▪ IHD	2	1.7%
<b>Indications of ERCP</b>		
▪ Choledocholithiasis	44	36.7%
▪ Biliary leak	18	15%
▪ Cancer head pancreas	16	13.3%
▪ Fasciola	12	10.0%
▪ Benign biliary stricture	12	10.0%
▪ Cholangiocarcinoma	11	9.2%
▪ Ampullary tumor	6	5.0%
▪ Suspected SOD	1	0.8%
<b>Previous history of:</b>		
▪ Cholecystectomy	60	50.0%
▪ Pancreatitis	29	24.2%
▪ Sphincterotomy	15	12.5%
▪ Previous PEP	13	10.8%
<b>Total serum bilirubin</b>		
▪ Less than 2 mg	76	63.3%
▪ More than 2 mg	44	36.7%
<b>Common bile duct (CBD)</b>		
▪ Less than 10 mm	80	66.7%
▪ 10 mm	10	8.3%
▪ More than 10mm	30	25.0%
<b>Nature of the disease</b>		
▪ Benign	85	70.8%
▪ Malignant	35	29.2%

Data were expressed as frequency (%) or mean ± SD



**Figure (1):** Indication of ERCP among patients with post ERCP pancreatitis.

The study recorded the different technical procedures during endoscopy even the duration of the procedure, and it was noticed that most of cases were with moderate to difficult cannulation (65% and 23.3% of cases respectively), cannulation time was more than 5 minute in 70.8% of studied patients.

Regarding choledocholithiasis as an indication of ERCP, results showed that about 77.3% of patients with moderate degree of difficulty of stone extraction and 9.1% of cases were difficult to be extracted, stone basket catheter was used in 21.7% of patients. Regarding the way to cannulate common bile duct it is revealed that 55% of cases were done by precut sphincterotomy so it might be prominent in this study.

Moreover pancreatic duct cannulation accidentally occurred in 53.3% of studied patients and pancreatic duct injection in 25%. Biliary sphincterotomy was done in 45%.

Also, other procedures as endoscopic papillary balloon dilatation that may be used for extraction of stones have been observed in 36.7% of cases, biopsy from papilla in 15% and endoscopic metal biliary endoprosthesis was shown in 14.2% of cases, parapapillary diverticulum was present in 31.7% of patients which may add to difficulty of cannulation and risk of PEP (Table 2).

**Table (2):** procedure related risk factors for post ERCP pancreatitis

Variables	Total (n=120)	%
<b>Parapapillary diverticulum</b>	38	31.7%
<b>Difficulty of cannulation</b>		
▪ Easy	14	11.7%
▪ Moderate	78	65.0%
▪ Difficult	28	23.3%
<b>Cannulation time (min)</b>		
▪ less than 5	35	29.2%
▪ More than 5	85	70.8%
<b>Total procedure time (min)</b>		
▪ Less than 30	45	37.5%
▪ More than 30	75	62.5%
<b>Difficulty of stone extraction</b>	<b>N=44</b>	
▪ Easy	6	13.6%
▪ Moderate	34	77.3%
▪ Difficult	4	9.1%
<b>Pancreatic duct cannulation</b>	64	53.3%
<b>Pancreatic duct injection</b>	30	25.0%
<b>Stone basket catheter</b>	26	21.7%
<b>Biopsy in the bile duct or papilla</b>	18	15.0%
<b>Endoscopic papillary balloon dilatation</b>	44	36.7%
<b>Endoscopic metal biliary endoprosthesis</b>	17	14.2%
<b>Precut sphincterotomy</b>	66	55%
<b>Biliary sphincterotomy</b>	54	45.0%

Data were expressed as frequency (%).

Regarding the score of pancreatitis among patients with post-ERCP pancreatitis, 44.2% were mild, 48.3% were moderate and 7.5% were severe (Table.3).

**Table (3):** Score of pancreatitis among patients with post ERCP pancreatitis

Variables	Total (n=120)	%
<b>Score of pancreatitis</b>		
▪ Mild	53	44.2%
▪ Moderate	58	48.3%
▪ Sever	9	7.5%

Data were expressed as frequency (%).

## DISCUSSION

ERCP is the best modality treating diseases of biliary channels, in spite of advances in technique of ERCP but still there is high incidence of PEP, which is the most prevalent and severe complication post-ERCP. Identification of risk factors can help in preventing occurrence of PEP, multiple studies showed some differences in these risk factors <sup>(10)</sup>.

In the current study it seems that younger age could be more correlated with PEP, as regarding sex female gender was more obvious in these cases. Moreover, the previous studies demonstrated that younger age usually is associated with increase in incidence of PEP. This finding can be explained by decreasing exocrine pancreatic function with old age, which protect them from PEP <sup>(11)</sup>. There are conflicting findings regarding sex, some studies revealed that female sex is associated with high risk of PEP, while other study showed that there was no difference regarding sex <sup>(12)</sup>.

Our study showed that 24.2% of patients had history of previous pancreatitis, some of them had previous history of PEP, and so it could be correlated with occurrence of recent PEP. Past history of pancreatitis in some studies showed that it increases the risk of PEP but there are conflicting results between studies regarding this item <sup>(13)</sup>. Moreover past history of previous PEP increased up to 8 fold the risk of recent PEP in another study. These data suggest that some persons have reactive pancreas put them in more risk <sup>(14)</sup>. Moreover it has been shown in the current results that previous cholecystectomy was present in about half of cases, also previous sphincterotomy for specific reason has been occurred in 12.5% of our patients. Regarding previous cholecystectomy a study showed that it is significant risk factor for PEP. Also previous sphincterotomy in another study showed that it is not significant risk factor for PEP. So, there is conflicting data regarding this issue <sup>(15)</sup>. Laboratory features of patients have great importance as a predictor of occurrence of PEP, so we noticed that serum bilirubin less than 2 mg/ml or normal level was more obvious in cases of PEP in the current study. Some studies demonstrated that normal serum bilirubin was associated with increased risk of PEP <sup>(16)</sup>. Another one showed that normal bilirubin level is not considered to be risk factor of PEP <sup>(17)</sup>.

ERCP has a lot of therapeutic indications, CBD stones are one of the most common indication followed by biliary leak, cancer pancreas and biliary strictures. It was noticed in these results that collectively benign causes have more incidence of PEP than malignant diseases. Meanwhile, benign nature of disease indicated for ERCP in some studies showed no difference from malignant causes, but it may show higher incidence of PEP in most of cases specially gallbladder stones. This might be connected to the pancreatic duct hypertension that can arise from either a stone lodged at the ampulla or damage to the ampulla caused by the stone's passage. It can also be related to the reflux of harmful bile into the pancreatic duct <sup>(18)</sup>, however malignant causes of obstruction have less incidence of PEP. This may be due to atrophy of pancreatic parenchyma with chronic obstruction <sup>(19)</sup>.

Our results showed that the smaller the duct size the higher the incidence of PEP. The majority of research has not discovered any independent relationship between duct size and PEP risk. However, a number of early researches proposed that a small CBD diameter could be a risk factor for pancreatitis <sup>(20)</sup>. The majority of patients at these centers had non-dilated bile ducts and sphincter dysfunction, which led to the initial reports of small CBD diameter as a risk factor.

The current study revealed that precut sphincterotomy was done in most of cases in comparison with standard biliary sphincterotomy so it is likely to be related to PEP. However, other study showed that a major risk factor for PEP was not conventional sphincterotomy. This result is consistent with previous research, which suggest that there is no discernible increase in the risk of pancreatitis after ERCP with biliary sphincterotomy <sup>(21)</sup>.

A marginally significant (OR: 1.2) risk factor for PEP was precut sphincterotomy. The association between precut sphincterotomy and the development of pancreatitis and other problems is a topic of debate in the literature <sup>(22)</sup>. It is questionable if the cannulation efforts or the precutting procedure itself is more likely to cause an increase in pancreatitis rates after precut sphincterotomy <sup>(23)</sup>. In a randomised controlled trial comparing precutting papillotomy and continuous cannulation, the incidence of pancreatitis was the same. However, a meta-analysis showed that precut sphincterotomy was a highly significant risk factor for pancreatitis after ERCP <sup>(24)</sup>.

In our study, difficulty of cannulation was graded where it was revealed that moderate to difficult cannulation was present in most of patients, so it might be matched with PEP occurrence. Furthermore, other study demonstrated that early precut had a much lower rate of complications compared to delayed precut and numerous cannulation tries (6.9% vs. 25.6% and 28.6% respectively). This supports the hypothesis that when performed by experienced individuals, precut may be superior to many cannulation attempts, particularly in patients at high risk for post-procedure pancreatitis. This finding aligns with the findings of two recent meta-

analyses. 2.5% of patients who had early needle-knife sphincterotomy suffered from post-endoscopic retrograde cholangiopancreatography pancreatitis (PEP), according to the initial analysis. On the other hand, 5.3% of patients who had early needle-knife sphincterotomy after several cannulation attempts experienced PEP. The second investigation showed that the incidence of PEP was considerably decreased from 5.4% to 2.5% with early needle-knife sphincterotomy<sup>(25)</sup>. On the other hand, the complication rate for precut sphincterotomy was found to be identical to that for standard sphincterotomy in several series from tertiary referral centers, indicating that precut sphincterotomy risk is remarkably operator-dependent<sup>(26)</sup>.

Our results showed that endoscopic balloon dilatation was present in about 36.7% of cases. Several studies demonstrated that balloon dilation of the CBD orifice for stone extraction was an insignificant factor for increasing occurrence of PEP<sup>(27)</sup>. However, further studies revealed that balloon dilatation has been linked to a noticeably higher incidence of PEP<sup>(28)</sup>.

The cannulation and whole procedure time were recorded it was noticed that long duration of cannulation or procedure could be correlated with risk of PEP as most of studied patients had long cannulation time. The length of the procedure and the cannulation time were significant variables that raised the risk of pancreatitis in univariate analysis, but not in multivariate analysis. This result is in agreement with two extensive researches<sup>(29)</sup>. These two factors time of procedure and difficulty of cannulation may lead to more PEP incidence. Adding to it the current study revealed that parapapillary diverticulum was present in 31.7% of cases that might cause more difficulty of cannulation. An approximate 10-fold increase in the incidence of pancreatitis was associated with more than 15 attempts to cannulate the Vater's papilla. PEP and cannulation difficulty demonstrated an inverse association indicating that there is a direct correlation between the level of difficulty in cannulation and the occurrence of pancreatitis. The significant risk of pancreatitis following many cannulation attempts, even in the absence of pancreatic duct contrast injection demonstrates that the degree of papilla manipulation and recurrent damage caused by the use of guide wires and cannulation devices results in impairment of pancreatic drainage related to sphincter hypertension and papillary edoema<sup>(30)</sup>.

One of the technical issues that may occur during endoscopy may be anatomical one. We revealed that pancreatic duct cannulation have been occurred in more than half of cases with pancreatic duct injection in some patients so it could be related to risk of PEP and should be considered. Moreover, according to a multicenter study, asymptomatic hyperamylasemia and pancreatitis are significantly increased by pancreatic deep wire pass. Frequent deep wire passes into the pancreatic duct cause damage to the tissue and raise the risk of post-ERCP pancreatitis and asymptomatic hyperamylasemia. The

reasons behind pancreatitis in certain individuals and asymptomatic hyperamylasemia in others are yet unknown. There are two potential explanations: One factor relates to the severity of damage to the pancreas, whereas the other factor relates to differences in the intensity of the inflammatory response following pancreatic injury<sup>(31)</sup>. Pancreatic duct injection ( $\geq 2$ ) with a three-fold increase in risk was an independent risk factor for PEP. This finding is consistent with the majority of other studies<sup>(32)</sup>. According to a different research, the multivariate analysis did not reveal the importance of pancreatic duct injection, only the univariate analysis did<sup>(33)</sup>.

Endoscopic metal biliary endoprosthesis is regarded as a highly successful treatment for biliary strictures, maintaining luminal patency of the obstructed bile duct. In our results it had been shown that 14% of patients with metal endoprosthesis developed PEP, so it may be related to the risk of pancreatitis. Another study showed that the rate of PEP was much greater in this group of patients, and the incidence of post-ERCP pancreatitis was 7.3%. Nevertheless, the occurrence rate of post-ERCP pancreatitis was comparable in patients with covered (6.9%) and uncovered (7.5%) metal biliary stents<sup>(34)</sup>.

Choledocholithiasis is one of most common causes of obstructed bile ducts needing ERCP, difficulty of stone extraction was graded. It was highly evident that the more difficult extraction of stones the more incidence of PEP occurrence in our cases. Also, stone basket catheter use was present in 21.7% of studied patients, all of these factors should be thoroughly investigated as risk factors for PEP. In one research, the challenging stone extraction process was also found to be a significant factor, according to both univariate and multivariate analyses (OR: 2.6). The PEP and the level of stone extraction difficulties are inversely correlated. This means that as the level of difficulty in extracting stones rises, so does the occurrence of pancreatitis<sup>(12)</sup>. This outcome can be attributed to the repetitive physical injury experienced during the extraction process, as well as the extended duration of cannulation and the procedure time.

**The limitation** of this study was in the small number of patients and more comparison is needed with patients who did not develop PEP. Also, the study was done in single center (multicenter study is advised) and some clinical characteristics were not documented.

## CONCLUSION

The physician can utilize the data from this research to determine whether or not to advise ERCP for a specific patient. Intraoperative laparoscopic cholangiography, magnetic resonance cholangiopancreatography (MRCP), and endoscopic ultrasound (EUS) all exhibit comparable levels of accuracy to ERCP in diagnosis and are becoming available. These procedures may be more favorable than

ERCP for patients who have uncertain indications of biliary blockage, particularly those who are at a high risk for post-ERCP pancreatitis (PEP). If a pathological obstruction, such as a stone, is clearly discovered utilizing one of these methods, so standard ERCP is advisable. If no pathological blockage is detected, it is advisable not to perform ERCP or consider referring the patient directly to a specialized center with significant expertise in manometric and pancreatic therapeutic ERCP. In the absence of a cost-effective preventive agent for post-ERCP pancreatitis, the main strategy for reducing the morbidity associated with ERCP is to rely on knowledge of the risk factors. This knowledge should guide decisions regarding the necessity of ERCP and the optimal approach for performing the procedure.

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## REFERENCES

1. **Mutneja H, Vohra I, Go A *et al.* (2021):** Temporal trends and mortality of post-ERCP pancreatitis in the United States: a nationwide analysis *Endoscopy*, 53: 357-366
2. **Kochar B *et al.* (2015):** Incidence, severity, and mortality of post-ERCP pancreatitis: a systematic review by using randomized, controlled trials. *Gastrointest Endosc.*, 81 (1): 143-149.
3. **Wang P, Li S, Liu F *et al.* (2009):** risk factors for ERCP-related complications: a prospective multicenter study. *Am J Gastroenterol.*, 104: 31–40.
4. **Ahmed M, Kanotra R, Savani T *et al.* (2017):** Utilization trends in inpatient endoscopic retrograde cholangiopancreatography (ERCP): a cross-sectional US experience. *Endosc Int Open*, 5: E261-271
5. **Balthazar J (2002):** Acute pancreatitis: assessment of severity with clinical and CT evaluation. *radiology*, 223 (3): 603-13
6. **Wang P, Li S, Liu F *et al.* (2009):** risk factors for ERCP-related complications: a prospective multicenter study. *Am J Gastroenterol.*, 104: 31–40.
7. **Vandervoort J, Tham K, Wong K *et al.* (1996):** Prospective analysis of risk factors for pancreatitis after diagnostic and therapeutic ERCP *Gastrointest Endosc.*, 43: 400-409
8. **Cheng CL, Sherman S, Watkins L *et al.* (2001):** Risk factors for post-ERCP pancreatitis: a prospective multicenter study. *Am J Gastroenterol.*, 101: 139–147.
9. **Cotton PB, Lehman G, Vennes J *et al.* (1991):** Endoscopic sphincterotomy complications and their management: An attempt at consensus. *Gastrointest Endosc.*, 37: 383–93
10. **Cheng C, Sherman S, Watkins J *et al.* (2006):** Risk factors for Post-ERCP pancreatitis: A prospective multicenter study. *Am J Gastroenterol.*, 101: 139–47
11. **Nishino T, Toki F, Oyama H *et al.* (2008):** More accurate prediction of post-ERCP pancreatitis by 4-H serum lipase levels than amylase levels. *Dig Endosc.*, 9: 169–177.
12. **Testoni A, Mariani A, Giussani A *et al.* (2010):** Risk factors for post-ERCP pancreatitis in high- and low-volume centers and among expert and non-expert operators: a prospective multicenter study. *Am J Gastroenterol.*, 105: 1753–1761
13. **Friedland S, Soetikno M, Vandervoort J *et al.* (2002):** Bedside scoring system to predict the risk of developing pancreatitis following ERCP. *Endoscopy*, 34: 483–488
14. **Freeman L, Guda N (2004):** Prevention of post-ERCP pancreatitis: a comprehensive review. *Gastrointest Endosc.*, 7: 854–864.
15. **Cheng L, Sherman S, Watkins L *et al.* (2006):** Risk factors for post-ERCP pancreatitis: a prospective multicenter study. *Am J Gastroenterol.*, 101: 139–147.
16. **Masci E, Toti G, Mariani A *et al.* (2001):** Complications of diagnostic and therapeutic ERCP: a prospective multicenter study. *Am J Gastroenterol.*, 96: 417–423
17. **Cha W, Leung D, Lehman A *et al.* (2013):** Does leaving a main pancreatic duct stent in place reduce the incidence of precut biliary sphincterotomy-associated pancreatitis? A randomized, prospective study. *Gastrointest Endosc.*, 77: 209–216.
18. **Cappell MS (2008):** Acute pancreatitis: etiology, clinical presentation, diagnosis, and therapy. *Med Clin North Am.*, 92: 889–923.
19. **Banerjee N, Hilden K, Baron H *et al.* (2011):** Endoscopic biliary sphincterotomy is not required for transpapillary SEMS placement for biliary obstruction. *Dig Dis Sci.*, 56: 591–595
20. **Vandervoort J, Soetikno M, Tham C *et al.* (2002):** Risk factors for complications after performance of ERCP. *Gastrointest Endosc.*, 56: 652–656
21. **Freeman L, DiSario A, Nelson B *et al.* (2001):** Risk factors for post-ERCP pancreatitis: a prospective, multicenter study. *Gastrointest Endosc.*, 54: 425–434
22. **Freeman L, Guda M (2005):** ERCP cannulation: a review of reported techniques. *Gastrointest Endosc.*, 61: 112-125
23. **Eminler A, Parlak E, Koksall S *et al.* (2016):** Endoscopic treatment of biliary stones in patients with liver transplantation. *Surg Endosc.*, 31: 1327–35
24. **Tang SJ, Haber GB, Kortan P *et al.* (2005):** Precut papillotomy vs. persistence in difficult biliary cannulation: A prospective randomized trial. *Endoscopy*, 37: 58–65
25. **Gong B, Hao L, Bie L *et al.* (2010):** Does precut technique improve selective bile duct cannulation or increase post-ERCP pancreatitis rate? A meta-analysis of randomized controlled trials. *Surg Endosc.*, 24: 2670–2680.
26. **Tang J, Haber GB, Kortan P *et al.* (2005):** Precut papillotomy vs. persistence in difficult biliary cannulation: a prospective randomized trial. *Endoscopy*, 37: 58–65
27. **Watanabe H, Yoneda M, Tominaga K *et al.* (2007):** Comparison between endoscopic papillary balloon dilatation and endoscopic sphincterotomy for the treatment of common bile duct stones. *J Gastroenterol.*, 42: 56–62
28. **Disario A, Freeman L, Bjorkman J *et al.* (2004):** Endoscopic balloon dilation compared with sphincterotomy for extraction of bile duct stones. *Gastroenterology*, 127: 1291–1299
29. **Friedland S, Soetikno M, Vandervoort J *et al.* (2002):** Bedside scoring system to predict the risk of developing pancreatitis following ERCP. *Endoscopy*, 34: 483–488.
30. **Cheng L, Sherman S, Watkins L *et al.* (2006):** Risk factors for post-ERCP pancreatitis: a prospective multicenter study. *Am J Gastroenterol.*, 101: 139–147
31. **Cooper T, Slivka A (2007):** Incidence, risk factors, and prevention of post-ERCP pancreatitis. *Gastroenterol Clin N Am.*, 36: 259–76
32. **Aronson N, Flamm R, Bohn L *et al.* (2002):** Evidence-based assessment: patient, procedure, or operator factors associated with ERCP complications. *Gastrointest Endosc.*, 56: S294–S302
33. **Wang P, Li ZS, Liu F *et al.* (2009):** risk factors for ERCP-related complications: a prospective multicenter study. *Am J Gastroenterol.*, 104: 31–40
34. **Cote GA, Kumar N, Ansstas M *et al.* (2010):** Risk of post-ERCP pancreatitis with placement of self-expandable metallic stents. *Gastrointest Endosc.*, 72: 748–54.