

## Measure Twice, Cut Once: Appraising The Safety of ERCP in IBD

Asfari MM<sup>2\*</sup>, Perry I<sup>1</sup>, Sarmini MT<sup>2</sup>, Masood M<sup>3</sup>, Frazier H<sup>4</sup>, Hamid O<sup>5</sup>, Sridhar S<sup>1</sup> and Sifuentes H<sup>1</sup>

<sup>1</sup>Department of Gastroenterology & Hepatology, Medical College of Georgia/Augusta University, Augusta, Georgia, USA

<sup>2</sup>Department of Gastroenterology & Hepatology, Cleveland Clinic, Cleveland Ohio, USA

<sup>3</sup>Department of Internal Medicine, Medical College of Georgia, Augusta University, Augusta, Georgia, USA

<sup>4</sup>Medical College of Georgia, Augusta University, Augusta, Georgia, USA

<sup>5</sup>Department of Hospital Medicine, Cleveland Clinic, Cleveland Ohio, USA

### \*Corresponding author:

Mohammad Maysara Asfari,  
Department of Gastroenterology & Hepatology  
Medical College of Georgia, Augusta University,  
USA, Tel: 706-721-0207; Fax: 706-721-0331,  
E-mail: mma-86@hotmail.com

Received: 09 Feb 2022

Accepted: 21 Feb 2022

Published: 28 Feb 2022

J Short Name: JJGH

### Copyright:

©2022 Asfari MM, This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and build upon your work non-commercially.

### \*Authors Contribution:

Asfari MM, Perry I, Sarmini MT, Masood M, Frazier H, Hamid O, Sridhar S, Sifuentes H and these authors are contributed equally to this work.

### Citation:

Asfari MM, Measure Twice, Cut Once: Appraising The Safety of ERCP in IBD. Japanese J Gastro Hepato. 2022; V8(7): 1-6

## 1. Abstract

**1.1. Background:** Advanced endoscopy, namely endoscopic retrograde cholangiopancreatography (ERCP), has an integral role in the diagnosis and management of patients with Inflammatory Bowel Disease (IBD). ERCP is frequently performed in this population to diagnose Primary Sclerosing Cholangitis (PSC) or to manage strictures. This study aims to evaluate ERCP-related AEs in IBD patients using a large national database as there is limited published data available evaluating AEs in the IBD population.

**1.2. Methods:** This is a retrospective cohort study performed using the National Inpatient Sample (NIS) database 2011-2014. All adult patients ( $\geq 18$  years old) who underwent ERCP using the International Classification of Diseases ICD-9 codes were identified. These patients were then divided into two groups: patients with IBD (study group) and patients without IBD (control group). Primary outcomes included ERCP-related AEs including post-ERCP pancreatitis (PEP), bleeding, and perforation. Secondary outcomes included all-cause mortality (ACM) and length of hospital stay (LOS). Primary and secondary outcomes were compared between study and control group using multivariate logistic regression analysis.

**1.3 Results:** A total of 108,182 patients who underwent ERCP were identified, of which 1,230 (1.1%) had IBD. Patients with IBD were younger ( $54.36 \pm 18.45$  vs  $59.52 \pm 20.16$ ), less likely to be female (49.3% vs 59.8%), and more likely to be African American (9.2% vs 9.1%) compared to the control group ( $P < 0.05$  for all). Additionally, IBD patients had less alcohol abuse (3.4% vs 4.3%,  $P > 0.05$ ) com-

pared to the control group. Using multivariate logistic regression and after adjusting for potential confounding factors including age, race, gender, and Elixhauser comorbidities, patients with IBD had no statistically significant difference in PEP (OR 0.9, 95% CI: 0.67-1.62), bleeding (OR 0.61, 95% CI: 0.23-1.6), post-ERCP perforation (OR 2.06, 95% CI: 0.28-15.24) or ACM (OR 0.56, 95% CI: 0.25-1.27), ( $P > 0.05$  for all). However, the adjusted LOS was slightly longer in the IBD group compared to the control group ( $5.93 \pm 5.58$  days' vs  $5.49 \pm 5.03$  days,  $P < 0.05$ ).

**1.4. Conclusion:** IBD patients undergoing ERCP may have a slight increase in LOS. However, carrying a diagnosis of IBD did not increase the risk of ERCP related complications or inpatient mortality.

## 2. Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is a commonly utilized procedure that is frequently performed in patients with inflammatory bowel disease (IBD) [1]. Due to advances in endoscopy, it has become a relatively safe and effective procedure [2]. However, as ERCP has become increasingly utilized, adverse events (AEs) have been noted; AEs commonly reported in the literature include post-ERCP pancreatitis (PEP), bleeding, perforation, or infection. Patients with certain comorbidities such as End-Stage Renal Disease (ESRD) and Chronic Kidney Disease (CKD) may have increased post-ERCP AEs [3].

The incidence of PEP has been estimated to be 3 to 5% in many large clinical studies [4-6]. Risk factors for PEP in the general population include prior PEP, female gender, and young age. Suspected

or known sphincter of Oddi dysfunction also poses a risk for PEP [7]. Recent studies have suggested that NSAIDs, notably rectal indomethacin, could by itself be effective in preventing PEP [8].

Post-ERCP bleeding occurs most often with sphincterotomy [9]. Most bleeding episodes tend to be mild to moderate in severity and self-limited. Patients with known bleeding disorders may suffer from life-threatening bleeding which may necessitate surgical or angiographic intervention [10]. The risk of bleeding can be mitigated by identifying patients with coagulation disorders, correcting clotting defects, and utilizing careful endoscopic technique. Furthermore, multiple attempts of common bile duct (CBD) cannulation and precut sphincterotomy may increase the risk of duodenal perforation which can be fatal in patients with known bleeding disorders [11].

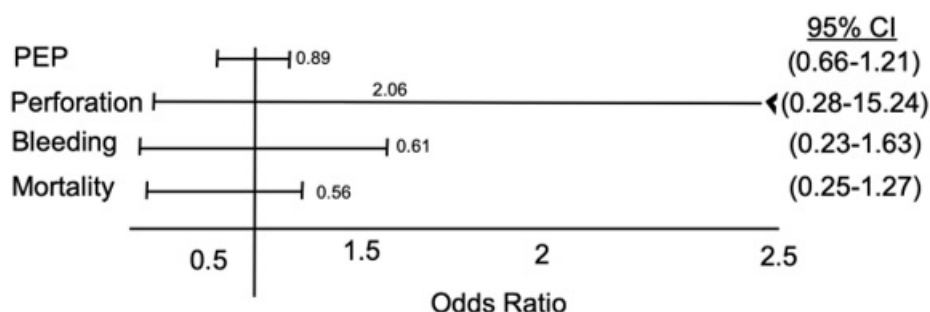
Emerging data suggests that CKD may be a significant risk factor for post-ERCP AEs in hospitalized patients, including both PEP and bleeding. One potential explanation for increased PEP in these patients may be due to papillary edema from fluid overload that makes cannulation difficult. Alternatively, increased bleeding in patients with ESRD and CKD may be related to platelet dysfunction and coagulopathy in the setting of uremia<sup>3</sup>. Physicians should cautiously select patients, ensure optimization of volume status, and perform close post-procedural monitoring to mitigate adverse outcomes in patients with CKD.

There is limited data published which evaluates post-ERCP adverse events in patients with IBD and no large clinical studies to date which explore ERCP-related adverse effects in this population. This is the largest study to date that aims to evaluate ERCP-related AEs in IBD patients using a large national data base.

**Supplementary Table 1:** International Classification of Diseases, ninth edition, clinical modification and clinical classifications software codes used to identify comorbidities, procedures and outcomes.

Variable	Source	Code(s)
ERCP	ICD-9-CM	51.10, 51.11, 51.64, 51.82, 51.84, 51.85, 51.87, 51.88, 52.13, 52.14, 52.93, 52.98
Post procedural bleeding	ICD-9-CM	998.1, 998.11, 998.12, 998.13
Perforation	ICD-9-CM	576.3
IBD	CCS	154

Abbreviations: CCS = Clinical Classification Software; ICD-9-CM = International Classification of Diseases, Ninth Edition, Clinical Modification, IBD: inflammatory bowel disease



P > 0.05 for all.

Abbreviations: PEP: post-ERCP Pancreatitis; OR: odds ratio, CI: confidence interval

**Figure 1:** Odds Ratio for the Adverse Events Post ERCP Comparison Between Inflammatory Bowel Disease and Non- Inflammatory Bowel Disease Patients

**Supplementary Table 2:** List of Elixhauser Comorbidities included in our analysis

1	Acquired immune deficiency
2	Alcohol abuse
3	Deficiency anemia
4	Rheumatoid arthritis/collagen vascular disease
5	Chronic blood loss anemia
6	Congestive heart failure
7	Coagulopathy
8	Depression
9	Diabetes mellitus, uncomplicated
10	Diabetes mellitus, complicated
11	Drug abuse
12	Hypertension
13	Hypothyroidism
14	Liver disease
15	Lymphoma
16	Fluid and electrolyte abnormality
17	Metastatic cancer
18	Neurodegenerative disorder
19	Obesity
20	Paralysis
21	Peripheral vascular disease
22	Psychosis
23	Pulmonary circulation disorders
24	Renal Failure
25	Solid tumor without metastasis
26	Peptic ulcer disease
27	Valvular disease
28	Weight loss

### 3.3. Outcome Assessment

Primary outcomes included post-ERCP AEs: PEP, bleeding, and perforation. Secondary outcomes included LOS and in-hospital mortality. All patients who underwent ERCP were divided into two groups: IBD group (study group) and non-IBD group (control group). ERCP AEs were isolated from admission diagnosis by considering the primary and secondary diagnosis as indications for admission (DX 1 and 2) and the subsequent diagnoses (DX 3-25) as AEs. Patients with primary or secondary diagnosis of acute pancreatitis (DX1 and DX2) were classified as acute pancreatitis not related to ERCP. Patients with acute pancreatitis codes from DX3-25 who did not have acute pancreatitis code in DX1 and 2 were considered PEP. This method was used and validated in prior studies [12,13].

### 3.4. Statistical Analysis

The data are expressed as mean values  $\pm$  standard deviation and frequencies were reported in percentages. Independent t-tests were used for the comparison of continuous variables measurements, while chi-square test was used for categorical variables. Multivariate logistic regression analysis was used to assess AEs. The regression model was adjusted for the following: patient's age, race, gender, hospital location, patient medical insurance and socioeconomic status, and Elixhauser comorbidities. P-value  $\leq 0.05$  were considered statistically significant. SPSS version 25 software (IBM Corp, Armonk, NY) was used for all statistical analyses.

### 3.5. Results

A total of 108,182 patients underwent ERCP were identified, of which 1,230 (1.13%) had IBD. IBD patients were younger ( $54.36 \pm 18.45$  vs  $59.52 \pm 20.16$ ), less likely to be female (49.3% vs 59.8%), and more likely to be African American (9.2% vs 9%) compared to the control group ( $P < 0.05$  for all). In addition, IBD patients had less alcohol abuse compared to the non-IBD group (3.3% vs 4.3%,  $P < 0.05$ ). Using multivariate logistic regression and after adjusting for potential confounding factors, the IBD group had no statistically significant difference in the odds of PEP (OR 0.89, 95% CI: 0.66–1.21,  $P > 0.05$ ), bleeding rate (OR 0.61, 95% CI: 0.23 – 1.63), perforation (OR 2.06, 95% CI: 0.28- 15.24) or inpatient mortality (OR 0.56, 95% CI: 0.25- 1.27), ( $P > 0.05$  for all). Of note, the adjusted LOS was slightly longer in the IBD group compared to the control group ( $5.49 \pm 5.03$  vs  $5.93 \pm 5$ ), ( $P < 0.05$ ).

**Table 1:** Baseline Characteristics Comparison of Inflammatory Bowel Disease and Non- Inflammatory Bowel Disease Patients

Variable	IBD	Non-IBD	P-Value
Age (mean $\pm$ SD)	54.36 $\pm$ 18.45	59.52 $\pm$ 20.16	<0.05
Females %	49.3	59.8	<0.05
Race %			<0.05
White	80.8	66.2	
Black	9.2	9	
Hispanic	5.4	16	
Asian or Pacific Islander	1.1	3.6	
Native American	0.4	0.6	
Other	3.0	3.4	
Hospital Region %			<0.05
Northeast	23.2	20	
Midwest	25.2	22.2	
South	30.8	33.5	
West	20.8	24.3	
Bed Size %			<0.05
Small	8.9	10.5	
Medium	219.7	25.1	
Large	71.4	64.4	
Location/Teaching Status %			<0.05
Rural	3.6	4.6	
Urban Nonteaching	25	35.5	
Urban Teaching	71.4	59.9	
Primary expected payer %			<0.05
Medicare	40	46.6	
Medicaid	9	13.5	
Private Insurance	44.5	29.9	
Self-Pay	2.7	6.3	
No Charge	0.5	0.7	
Other	3.3	3	
Median Household Income %			<0.05
0 to 25 percentiles	20.9	26.5	
26 to 50 percentiles	21.5	25.8	
51 to 75 percentiles	28.1	25.2	
76 to 100 percentiles	29.4	22.5	
Alcohol abuse %	3.3	4.3	<0.001

#### 4. Discussion

Advanced endoscopy, particularly ERCP, has an integral role in the diagnosis and management of patients with IBD; However, prior to this study, the safety of the IBD population undergoing ERCP had not yet been extensively evaluated. Given the limited availability of published data, our study is the largest to date to evaluate ERCP-related AEs in IBD patients using a large national database. We demonstrate that IBD patients undergoing ERCP may have a slight increase in their LOS, but no increased risk of ERCP-related complications (PEP, bleeding, perforation) or inpatient mortality. As the use of ERCP continues to rise, it becomes increasingly important to risk stratify patients to prevent complications [23].

Hepatobiliary disorders occur frequently in patients with IBD and commonly exist as an extra intestinal manifestation, though concurrent autoimmune hepatobiliary disease can occur separately [14]. Hepatobiliary disorders are equally common in patients with ulcerative colitis (UC) and Crohn's disease (CD) [15]. Hepatobiliary symptoms do not generally parallel the activity of bowel inflammation [16]. ERCP is frequently used in IBD patients with primary sclerosing cholangitis (PSC), dominant strictures, and cholangiocarcinoma [17].

PSC is characterized by progressive inflammation, obliterative fibrosis, and destruction of the intra - hepatic and/or extra - hepatic bile ducts which can lead to biliary cirrhosis [18, 19]. Most patients

with PSC have underlying IBD, usually UC, with a prevalence around 90% [20]. It is reported that 1.4–7.5% of patients with IBD will go on to develop PSC during the course of their disease [21]. Patients with symptomatic (pruritis, cholangitis) dominant strictures should undergo dilation and/or stent placement. Dominant strictures may harbor malignancy, mainly cholangiocarcinoma [22, 23]; Therefore, brushings for cytology, or preferably cholangioscopic-guided biopsies, should be considered. Forty percent of patients who do not have a dominant stricture initially will develop one in 5 years [24]. An annual incidence of cholangiocarcinoma was reported in 0.6–1% of PSC patients [25]. It may arise at any stage of PSC and may present as a liver mass or intraductal tumor [26].

The overall incidence of PEP, derived from a systematic review of randomized control trials using stents and placebo/no-stent arms to prevent PEP, was found to be 9.7% [27, 28]. In a systematic survey of prospective studies evaluating the incidence rates of ERCP complications, PEP occurred in 3.47% of patients [10]. A retrospective analysis of ERCPs, which evaluated 294 patients with PSC who underwent 657 ERCPs, found that PEP was diagnosed in 1.2% of procedures [17]. Most studies demonstrate ranges of PEP between 3 and 5% [28]. Risk factors are additive and include females, younger age [29], sphincter of Oddi dysfunction [30], normal bilirubin, absence of bile duct stones, and difficult and prolonged cannulation. Procedural factors placing patients at high risk consist of multiple cannulation attempts, pancreatic sphincterotomy, precut sphincterotomy, pneumatic dilation or ampullectomy, multiple contrast injections into the pancreatic duct, or excessive injections of contrast into the pancreatic duct [31, 32]. Patients with IBD are frequently on pancreatotoxic medications such as azathioprine and prednisone, which may increase their risk of developing PEP. In a retrospective study evaluating 173 patients, pancreatotoxic drugs significantly increased the risk of PEP (OR 3.7, 95% CI 1.1–12.4) [33]. In our study the risk of PEP was not significantly increased when comparing the IBD to non IBD population (OR 0.9, 95% CI: 0.67–1.62).

Patients with PSC have an increased risk of cholangitis due to difficulty in achieving complete drainage [34]. Elevated biliary pressures lead to biliary-venous reflux causing sepsis [35]. If biliary stents become occluded, cholangitis is a frequent complication [36]. In a retrospective analysis, cholangitis was diagnosed in 2.4% of procedures despite intraoperative antibiotics [17]. A systematic survey of prospective studies recorded a post-ERCP infection rate of 1.4% of patients [10]. Efforts should be made to utilize as little contrast as possible, aspirate bile before injection, decompress obstruction (ERCP or surgically), and administer prophylactic antibiotics, especially in patients with PSC [37].

With regards to bleeding, a retrospective analysis states post-ERCP bleeding occurred in 0.7% of procedures [17]. A systematic survey of prospective studies recorded a post-ERCP bleeding rate in 1.3% of patients [10]. Bleeding typically occurs after sphincterotomy. In a systematic survey of 21 prospective studies of over 16,000 patients

undergoing ERCP, there were a total of 226 bleeding episodes (1.3 percent), with eight deaths (0.05 percent), with severe bleeding in 66 of the 226 episodes (29%) [10]. Our study suggests that IBD itself is not a patient-related factor which would increase the risk of post-ERCP bleeding.

Many studies have reported on the incidence of post-ERCP perforation, occurring overall in approximately 0.4% of patients. The historical incidence was as high as 2.1% but has since decreased due to increasing skill of endoscopists [38]. Type I perforations (free bowel wall) account for 25% of perforations, type II (periampullary injury) for 46%, type III (pancreatic or bile duct) for 22%, and type IV (retroperitoneal air) for 3% [39]. Our study focused on the presence of IBD as a risk factor for perforation incidence – there was no evidence to suggest a correlation of IBD and increased risk of perforation.

To the best of the authors' knowledge, this the largest cross-sectional study that evaluated the risk of post-ERCP AEs in IBD population. Naturally, our study comprises some limitations. NIS relies on the accuracy of clinical data and the validity of medical diagnoses, which might differ among individuals and facilities. Furthermore, NIS cannot specify the severity of the IBD disease or the medications being used for the treatment. NIS is based on inpatient data this inclusion could lead to a larger number of sick individuals in the data, which might have affected the generalizability of the results. The exclusion of academic hospitals by the database could potentially exclude patients with more complex diseases.

## 5. Conclusion

In conclusion, our study, the largest study to date investigating the risk of post-ERCP adverse events in IBD patients, reveals no evidence of increased risk of perforation, bleeding, pancreatitis, or inpatient mortality post-ERCP. This study promises the safety of ERCP in this high-risk patient population, however, thoughtful selection for this invasive procedure is always advised.

## References

1. KDJ, AP, B. T, et al. Endoscopic Retrograde Cholangiopancreatography-Related Complications and Their Management Strategies: A “Scoping” Literature Review. *Dig Dis Sci*. 2020. doi:10.1007/s10620-019-05970-3 LK.
2. Alfieri S, Rosa F, Cina C. Management of duodeno-pancreato-biliary perforations after ERCP: Outcomes from an Italian tertiary referral center. *Surg Endosc*. 2013.
3. Sawas T, Asfari MM, Cho WK. Endoscopic Retrograde Cholangiopancreatography Is Safe in Inflammatory Bowel Disease: 864. *Am J Gastroenterol*. 2017; 112.
4. Wang P, Li ZS, Liu F. Risk factors for ERCP-related complications: A prospective multicenter study. *Am J Gastroenterol*. 2009.
5. Cheon YK, Cho KB, Watkins JL. Frequency and severity of post-ERCP pancreatitis correlated with extent of pancreatic ductal opacification. *Gastrointest Endosc*. 2007.

6. Christensen M, Matzen P, Schulze S, Rosenberg J. Complications of ERCP: A prospective study. *Gastrointest Endosc.* 2004.
7. Shih HY, Hsu WH, Kuo CH. Postendoscopic retrograde cholangiopancreatography pancreatitis. *Kaohsiung J Med Sci.* 2019.
8. Talukdar R. Complications of ERCP. *Best Pract Res Clin Gastroenterol.* 2016.
9. L.E.V.V.C. F, J. F, T.H. B. Clinically significant delayed postsphincterotomy bleeding: A twelve-year single center experience. *Minerva Gastroenterol Dietol.* 2007.
10. Andriulli A, Loperfido S, Napolitano G. Incidence rates of post-ERCP complications: A systematic survey of prospective studies. *Am J Gastroenterol.* 2007.
11. Mousa HM, Hefny AF, Abu-Zidan FM. Life-threatening duodenal perforation complicating endoscopic retrograde cholangiopancreatography: A case series. *Int J Surg Case Rep.* 2020.
12. Inamdar S, Berzin TM, Sejpal D V. Pregnancy Is a Risk Factor for Pancreatitis After Endoscopic Retrograde Cholangiopancreatography in a National Cohort Study. *Clin Gastroenterol Hepatol.* 2016.
13. Yadav D, O'Connell M, Papachristou G. Natural history after first-attack of acute pancreatitis (AP). *Pancreas.* 2011.
14. Huang C, Lichtenstein DR. Pancreatic and biliary tract disorders in inflammatory bowel disease. *Gastrointest Endosc Clin N Am.* 2002.
15. Heikius B, Niemelä S, Lehtola J, Karttunen T, Lahde S. Hepatobiliary and coexisting pancreatic duct abnormalities in patients with inflammatory bowel disease. *Scand J Gastroenterol.* 1997.
16. Venkatesh PGK, Navaneethan U, Shen B. Hepatobiliary disorders and complications of inflammatory bowel disease. *J Dig Dis.* 2011.
17. Navaneethan U, Jegadeesan R, Nayak S. ERCP-related adverse events in patients with primary sclerosing cholangitis. *Gastrointest Endosc.* 2015.
18. Chapman RWG, Arborgh BAM, Rhodes JM. Primary sclerosing cholangitis: A review of its clinical features, cholangiography, and hepatic histology. *Gut.* 1980. doi:10.1136/gut.21.10.870.
19. Lee YM, Kaplan MM. Primary sclerosing cholangitis. *N Engl J Med.* 1995.
20. Fausa O, Schrumpf E, Elgjo K. Relationship of inflammatory bowel disease and primary sclerosing cholangitis. *Semin Liver Dis.* 1991.
21. Broomé U, Bergquist A. Primary sclerosing cholangitis, inflammatory bowel disease, and colon cancer. *Semin Liver Dis.* 2006.
22. Spiceland CM, Lodhia N. Endoscopy in inflammatory bowel disease: Role in diagnosis, management, and treatment. *World J Gastroenterol.* 2018.
23. Coelho-Prabhu N, Shah ND, Van Houten H, Kamath PS, Baron TH. Endoscopic retrograde cholangiopancreatography: utilisation and outcomes in a 10-year population-based cohort. *BMJ Open.* 2013.
24. Stiehl A, Rudolph G, Kloters-Plachky P, Sauer P, Walker S. Development of dominant bile duct stenoses in patients with primary sclerosing cholangitis treated with ursodeoxycholic acid: Outcome after endoscopic treatment. *J Hepatol.* 2002.
25. Bergquist A, Ekblom A, Olsson R. Hepatic and extrahepatic malignancies in primary sclerosing cholangitis. *J Hepatol.* 2002.
26. Fevery J, Verslype C, Lai G, Aerts R, Van Steenberghe W. Incidence, diagnosis, and therapy of cholangiocarcinoma in patients with primary sclerosing cholangitis. *Dig Dis Sci.* 2007.
27. Kochar B, Akshintala VS, Afghani E, et al. Incidence, severity, and mortality of post-ERCP pancreatitis: A systematic review by using randomized, controlled trials. *Gastrointest Endosc.* 2015.
28. Freeman ML, Nelson DB, Sherman S, et al. Complications of endoscopic biliary sphincterotomy. *N Engl J Med.* 1996.
29. Maitin-Casalis N, Neeman T, Thomson A. Protective effect of advanced age on post-ERCP pancreatitis and unplanned hospitalisation. *Intern Med J.* 2015.
30. Cotton PB, Pauls Q, Keith J. The EPISOD study: long-term outcomes. *Gastrointest Endosc.* 2018.
31. Elmunzer BJ, Scheiman JM, Lehman GA. A randomized trial of rectal indomethacin to prevent post-ERCP pancreatitis. *N Engl J Med.* 2012.
32. Freeman ML, DiSario JA, Nelson DB. Risk factors for post-ercp pancreatitis: A prospective, multicenter study. *Gastrointest Endosc.* 2001.
33. Perney P, Berthier E, Pageaux GP. Are drugs a risk factor of post-ERCP pancreatitis? *Gastrointest Endosc.* 2003.
34. Motte S, Deviere J, Dumonceau JM, Serruys E, Thys JP, Cremer M et al. Risk factors for septicemia following endoscopic biliary stenting. *Gastroenterology.* 1991.
35. Subhani JM, Kibbler C, Dooley JS. Review article: Antibiotic prophylaxis for endoscopic retrograde cholangiopancreatography (ERCP). *Aliment Pharmacol Ther.* 1999.
36. Rerknimitr R, Fogel EL, Kalayci C, Esber E, Lehman GA, Sherman S. Microbiology of bile in patients with cholangitis or cholestasis with and without plastic biliary endoprosthesis. *Gastrointest Endosc.* 2002.
37. Thosani N, Zubarik RS, Kochar R. Prospective evaluation of bacteremia rates and infectious complications among patients undergoing single-operator choledochoscopy during ERCP. *Endoscopy.* 2016.
38. Rabenstein T, Schneider HT, Hahn EG, Ell C. 25 years of endoscopic sphincterotomy in Erlangen: assessment of the experience in 3498 patients. *Endoscopy.* 1998.
39. Vezakis A, Fragulidis G, Polydorou A. Endoscopic retrograde cholangiopancreatography-related perforations: Diagnosis and management. *World J Gastrointest Endosc.* 2015.