

# World Journal of *Gastroenterology*

*World J Gastroenterol* 2021 May 28; 27(20): 2434-2663



**REVIEW**

- 2434 Role of modern radiotherapy in managing patients with hepatocellular carcinoma  
*Chen LC, Lin HY, Hung SK, Chiou WY, Lee MS*
- 2458 Open reading frame 3 protein of hepatitis E virus: Multi-function protein with endless potential  
*Yang YL, Nan YC*
- 2474 Breakthroughs and challenges in the management of pediatric viral hepatitis  
*Nicastro E, Norsa L, Di Giorgio A, Indolfi G, D'Antiga L*

**MINIREVIEWS**

- 2495 Pancreatitis after endoscopic retrograde cholangiopancreatography: A narrative review  
*Ribeiro IB, do Monte Junior ES, Miranda Neto AA, Proença IM, de Moura DTH, Minata MK, Ide E, dos Santos MEL, Luz GO, Matuguma SE, Cheng S, Baracat R, de Moura EGH*
- 2507 RON in hepatobiliary and pancreatic cancers: Pathogenesis and potential therapeutic targets  
*Chen SL, Wang GP, Shi DR, Yao SH, Chen KD, Yao HP*
- 2521 Evolving role of endoscopy in inflammatory bowel disease: Going beyond diagnosis  
*Núñez F P, Krugliak Cleveland N, Quera R, Rubin DT*
- 2531 Deep learning for diagnosis of precancerous lesions in upper gastrointestinal endoscopy: A review  
*Yan T, Wong PK, Qin YY*
- 2545 State of machine and deep learning in histopathological applications in digestive diseases  
*Kobayashi S, Saltz JH, Yang VW*
- 2576 COVID-19 in normal, diseased and transplanted liver  
*Signorello A, Lenci I, Milana M, Grassi G, Baiocchi L*

**ORIGINAL ARTICLE****Basic Study**

- 2586 Upregulation of long noncoding RNA W42 promotes tumor development by binding with DBN1 in hepatocellular carcinoma  
*Lei GL, Niu Y, Cheng SJ, Li YY, Bai ZF, Yu LX, Hong ZX, Liu H, Liu HH, Yan J, Gao Y, Zhang SG, Chen Z, Li RS, Yang PH*

**Retrospective Cohort Study**

- 2603 Understanding celiac disease monitoring patterns and outcomes after diagnosis: A multinational, retrospective chart review study  
*Lundin KEA, Kelly CP, Sanders DS, Chen K, Kayaniyl S, Wang S, Wani RJ, Barrett C, Yoosuf S, Petersen ES, Sambrook R, Leffler DA*

- 2615** Development and validation of a prognostic model for patients with hepatorenal syndrome: A retrospective cohort study

*Sheng XY, Lin FY, Wu J, Cao HC*

**Observational Study**

- 2630** Inflammatory bowel disease in Tuzla Canton, Bosnia-Herzegovina: A prospective 10-year follow-up

*Tulumović E, Salkić N, Tulumović D*

**META-ANALYSIS**

- 2643** Association between oral contraceptive use and pancreatic cancer risk: A systematic review and meta-analysis

*Ilic M, Milicic B, Ilic I*

**CASE REPORT**

- 2657** Cyclophosphamide-associated enteritis presenting with severe protein-losing enteropathy in granulomatosis with polyangiitis: A case report

*Sato H, Shirai T, Fujii H, Ishii T, Harigae H*

**ABOUT COVER**

Editorial Board Member of *World Journal of Gastroenterology*, Fernando J Castro, MD, AGAF, FACC, Gastroenterology Training Program Director, Cleveland Clinic Florida, 2950 Cleveland Clinic Blvd, Weston, FL 33331, United States. castrof@ccf.org

**AIMS AND SCOPE**

The primary aim of *World Journal of Gastroenterology* (WJG, *World J Gastroenterol*) is to provide scholars and readers from various fields of gastroenterology and hepatology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online. WJG mainly publishes articles reporting research results and findings obtained in the field of gastroenterology and hepatology and covering a wide range of topics including gastroenterology, hepatology, gastrointestinal endoscopy, gastrointestinal surgery, gastrointestinal oncology, and pediatric gastroenterology.

**INDEXING/ABSTRACTING**

The WJG is now indexed in Current Contents®/Clinical Medicine, Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports®, Index Medicus, MEDLINE, PubMed, PubMed Central, and Scopus. The 2020 edition of Journal Citation Report® cites the 2019 impact factor (IF) for WJG as 3.665; IF without journal self cites: 3.534; 5-year IF: 4.048; Ranking: 35 among 88 journals in gastroenterology and hepatology; and Quartile category: Q2. The WJG's CiteScore for 2019 is 7.1 and Scopus CiteScore rank 2019: Gastroenterology is 17/137.

**RESPONSIBLE EDITORS FOR THIS ISSUE**

Production Editor: Ji-Hong Lin, Production Department Director: Yun-Xiaojuan Wu, Editorial Office Director: Ze-Mao Gong.

**NAME OF JOURNAL**

*World Journal of Gastroenterology*

**ISSN**

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

**LAUNCH DATE**

October 1, 1995

**FREQUENCY**

Weekly

**EDITORS-IN-CHIEF**

Andrzej S Tarnawski, Subrata Ghosh

**EDITORIAL BOARD MEMBERS**

<http://www.wjgnet.com/1007-9327/editorialboard.htm>

**PUBLICATION DATE**

May 28, 2021

**COPYRIGHT**

© 2021 Baishideng Publishing Group Inc

**INSTRUCTIONS TO AUTHORS**

<https://www.wjgnet.com/bpg/gerinfo/204>

**GUIDELINES FOR ETHICS DOCUMENTS**

<https://www.wjgnet.com/bpg/GerInfo/287>

**GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH**

<https://www.wjgnet.com/bpg/gerinfo/240>

**PUBLICATION ETHICS**

<https://www.wjgnet.com/bpg/GerInfo/288>

**PUBLICATION MISCONDUCT**

<https://www.wjgnet.com/bpg/gerinfo/208>

**ARTICLE PROCESSING CHARGE**

<https://www.wjgnet.com/bpg/gerinfo/242>

**STEPS FOR SUBMITTING MANUSCRIPTS**

<https://www.wjgnet.com/bpg/GerInfo/239>

**ONLINE SUBMISSION**

<https://www.f6publishing.com>

## Pancreatitis after endoscopic retrograde cholangiopancreatography: A narrative review

Igor Braga Ribeiro, Epifanio Silvino do Monte Junior, Antonio Afonso Miranda Neto, Igor Mendonça Proença, Diogo Turiani Hourneaux de Moura, Mauricio Kazuyoshi Minata, Edson Ide, Marcos Eduardo Lera dos Santos, Gustavo de Oliveira Luz, Sergio Eiji Matuguma, Spencer Cheng, Renato Baracat, Eduardo Guimarães Hourneaux de Moura

**ORCID number:** Igor Braga Ribeiro 0000-0003-1844-8973; Epifanio Silvino do Monte Junior 0000-0001-7304-8222; Antonio Afonso Miranda Neto 0000-0002-9439-9088; Igor Mendonça Proença 0000-0003-0274-038X; Diogo Turiani Hourneaux de Moura 0000-0002-7446-0355; Mauricio Kazuyoshi Minata 0000-0002-9243-1371; Edson Ide 0000-0003-4533-6117; Marcos Eduardo Lera dos Santos 0000-0001-9759-3807; Gustavo de Oliveira Luz 0000-0001-7396-8440; Sergio Eiji Matuguma 0000-0002-9956-7183; Spencer Cheng 0000-0001-9584-203X; Renato Baracat 0000-0002-2701-9006; Eduardo Guimarães Hourneaux de Moura 0000-0003-1215-5731.

**Author contributions:** Ribeiro IB performed the acquisition of data, analysis, interpretation of data, drafting the article, revising the article, final approval; do Monte Junior ES, Miranda Neto AA, Proença IM, de Moura DTH, and Minata MK conducted data analysis and interpretation, revised the article, and final approval; Ide E, and de Moura EGH conducted data analysis and interpretation, drafted the article, and final approval; dos Santos MEL, Matuguma SE, Cheng S, and Baracat R revised, edited and

Igor Braga Ribeiro, Epifanio Silvino do Monte Junior, Antonio Afonso Miranda Neto, Igor Mendonça Proença, Diogo Turiani Hourneaux de Moura, Mauricio Kazuyoshi Minata, Edson Ide, Marcos Eduardo Lera dos Santos, Gustavo de Oliveira Luz, Sergio Eiji Matuguma, Spencer Cheng, Renato Baracat, Eduardo Guimarães Hourneaux de Moura, Department of Gastrointestinal Endoscopy Unit, University of São Paulo School of Medicine, São Paulo 05403-010, Brazil

**Corresponding author:** Igor Braga Ribeiro, MD, Research Scientist, Surgeon, Department of Gastrointestinal Endoscopy Unit, University of São Paulo School of Medicine, Av. Dr Enéas de Carvalho Aguiar, 225, 6o andar, bloco 3, Cerqueira Cesar, São Paulo 05403-010, Brazil. [igorbraga1@gmail.com](mailto:igorbraga1@gmail.com)

### Abstract

Acute post-endoscopic retrograde cholangiopancreatography pancreatitis (PEP) is a feared and potentially fatal complication that can be as high as up to 30% in high-risk patients. Pre-examination measures, during the examination and after the examination are the key to technical and clinical success with a decrease in adverse events. Several studies have debated on the subject, however, numerous topics remain controversial, such as the effectiveness of prophylactic medications and the amylase dosage time. This review was designed to provide an update on the current scientific evidence regarding PEP available in the literature.

**Key Words:** Endoscopic retrograde cholangiopancreatography; Pan-creatitis; Post-endoscopic retrograde cholangiopancreatography pancreatitis; Adverse events; Pancreatitis; Prevention

©The Author(s) 2021. Published by Baishideng Publishing Group Inc. All rights reserved.

**Core Tip:** Acute post-endoscopic retrograde cholangiopancreatography pancreatitis (PEP) is a feared and potentially fatal complication. Early diagnosis remains the key to the clinical success of these patients. Unfortunately, several topics remain controversial, especially early diagnosis with hyperamylasemia still being mistaken for PEP.

drafted the article, and final approval.

**Conflict-of-interest statement:** Dr. Moura reports personal fees from Boston Scientific, personal fees from Olympus, outside the submitted work.

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

**Manuscript source:** Invited manuscript

**Specialty type:** Gastroenterology and hepatology

**Country/Territory of origin:** Brazil

**Peer-review report's scientific quality classification**

Grade A (Excellent): A, A  
Grade B (Very good): 0  
Grade C (Good): C  
Grade D (Fair): 0  
Grade E (Poor): 0

**Received:** December 10, 2020

**Peer-review started:** December 10, 2020

**First decision:** January 27, 2021

**Revised:** January 30, 2021

**Accepted:** March 18, 2021

**Article in press:** March 18, 2021

**Published online:** May 28, 2021

**P-Reviewer:** Draganov P, Xiao B

**S-Editor:** Fan JR

**L-Editor:** Webster JR

**P-Editor:** Ma YJ



The purpose of this review is to demonstrate the evidence in the current literature on PEP.

**Citation:** Ribeiro IB, do Monte Junior ES, Miranda Neto AA, Proença IM, de Moura DTH, Minata MK, Ide E, dos Santos MEL, Luz GO, Matuguma SE, Cheng S, Baracat R, de Moura EGH. Pancreatitis after endoscopic retrograde cholangiopancreatography: A narrative review. *World J Gastroenterol* 2021; 27(20): 2495-2506

**URL:** <https://www.wjgnet.com/1007-9327/full/v27/i20/2495.htm>

**DOI:** <https://dx.doi.org/10.3748/wjg.v27.i20.2495>

## INTRODUCTION

Starting in 1968, endoscopic retrograde cholangiopancreatography (ERCP) was a watershed in the diagnosis and treatment of biliopancreatic diseases. Since then, an accurate indication for this examination is very important given the potential adverse effects associated with the procedure[1].

Early recognition and proper management of potential adverse events are essential to reduce associated morbidity and mortality.

As in other endoscopic procedures, there are safety determinants for ERCP, in addition to the precise indication, the clinical condition of the patient, age, sex, the type of sedation used, what type of therapeutic procedure performed, the appropriate use of accessories and the training of the endoscopist and assistants are taken into consideration[2].

Acute pancreatitis is the most common serious complication after ERCP[3,4], often confused with an increase in serum amylase concentration that occurs in up to 75% of patients[5,6].

Acute clinical pancreatitis itself, defined as a clinical syndrome of abdominal pain and hyperamylasemia which requires hospitalization, is much less common than it appears. There are still some controversies in the literature on the subject. The purpose of this review is to provide an update on post-ERCP pancreatitis and its prevention.

## PATHOGENESIS

The determinants of the inflammatory process in the pancreas are multifactorial. Several proposed factors can act independently or in combination to induce post-ERCP pancreatitis (PEP). The two most important are mechanical injury due to instrumentation in the pancreatic duct and hydrostatic injury due to contrast injection[7].

During ERCP and sphincterotomy, the pancreas is exposed to various forms of trauma: mechanical, chemical, hydrostatic, thermal, and even allergic[8].

It is also known that prolonged manipulation around the papillary orifice, inadvertent cannulation of the pancreatic duct and multiple injections into the pancreatic duct are common when selective cannulation of the bile duct is difficult[9,10]. This can result in mechanical damage to the duct or ampoule. Thermal injury to the electrocautery current can also produce edema of the pancreatic orifice, leading to obstruction of the duct, impairing the emptying of pancreatic secretions[11].

Hydrostatic injury due to excessive injection of contrast into the pancreatic duct is probably an important cause of PEP[12].

Either by allergy or chemical injury, contrast agents can lead to injuries. In a study by George *et al*[13], there was no statistically significant difference between the types of contrast in the analysis of randomized studies.

## EPIDEMIOLOGY AND RISK FACTORS

### Incidence

The incidence of pancreatitis post-ERCP can vary from 1% to 10%, reaching an alarming 30% in high-risk patients[14,15]. Stratification of the degree of post-examination pancreatitis shows incidence rates of 3.6% to 4% for mild acute pancre-

atitis, 1.8% to 2.8% for moderate acute pancreatitis, and 0.3% to 0.5% for severe acute pancreatitis[16,17] with a mortality rate of 0.2%[18]. Higher rates are observed in patients undergoing evaluation for possible sphincter of Oddi dysfunction[19].

### **Risk factors**

According to the guidelines of the European Society for Gastrointestinal Endoscopy (ESGE)[20] and the American Society for Gastrointestinal Endoscopy (ASGE)[2]: History of pancreatitis, suspected sphincter of Oddi dysfunction, female gender, and young age are definitely “patient-related risk factors” for PEP. On the other hand, difficult cannulation, pancreatic injection, and pre-cut sphincterotomy are “risk factors related to the procedure”[3,4].

### **Patient-related factors**

There are several factors related to the patient, the most common factors are female gender, normal levels of bilirubin, young adults, history of recurrent pancreatitis, and patients with suspected sphincter of Oddi dysfunction. Patients with a history of chronic pancreatitis have a protective effect against PEP[2].

Unfortunately, risk factors are additive[7,21,22]. For example, the combination of female gender, patients with suspected sphincter of Oddi dysfunction, young age, difficult cannulation, bilirubin within the acceptable standard, and absence of bile duct stones are associated with a risk of the pancreatitis of more than 40%.

### **Operator-related factors**

These are the most subjective factors. It is believed that the experience of the endoscopist, the presence of fellows and multiple operators is an independent risk factor for PEP[23,24].

### **Procedure-related factors**

The factors related to the procedure are the best studied and discussed in the literature. Pre-cut sphincterotomy, often used in difficult ERCP, time and number of cannulation times, trauma, and edema of the major duodenal papillae due to the number of attempts are independent factors for PEP[25].

In a systematic review with a meta-analysis that included 25 randomized controlled trials (RCTs) evaluating the incidence of PEP in patients undergoing sphincterotomy, ballooning dilation of the major duodenal papilla without sphincterotomy and patients undergoing both procedures, it was concluded that the incidence of PEP was similar between the groups[26].

The risk factors can be divided into three groups and are shown in [Table 1](#)[7,27-29].

---

## **CLINICAL MANIFESTATIONS**

The clinical manifestations of PEP are the same as those seen in patients with acute pancreatitis due to other causes.

These include epigastric or upper right quadrant pain, abdominal tenderness and high levels of amylase and lipase.

Post-ERCP acute pancreatitis can be classified as mild, moderate or severe based on the American Gastroenterology Association[30] and the American College of Gastroenterology[31]: (1) mild-amylase levels 24 h after the examination, remaining above up to three times the reference value with necessary hospitalization; (2) moderate-need for hospitalization of 4 to 10 d; and (3) severe-need for hospitalization over 10 d or need for invasive therapeutic intervention.

---

## **DIAGNOSIS**

Most patients with PEP have an acute onset of severe and persistent epigastric abdominal pain and in approximately 50% of patients, the pain radiates to the back. Approximately 90% of patients experience nausea and vomiting that can persist for several hours[32].

Patients with severe acute pancreatitis may have dyspnea due to diaphragmatic inflammation secondary to pancreatitis, pleural effusions, or acute respiratory distress syndrome, and 5% to 10% of patients with severe acute pancreatitis may have painless disease and unexplained hypotension[33].

**Table 1 Risk factors for post-endoscopic retrograde cholangiopancreatography pancreatitis related to the operator and the procedure**

Operator related	Factors related to the procedure
Inadequate training	Extended procedure time ( $\geq 30$ min)
Lack of experience	Difficult cannulation ( $\geq 15$ min)
<b>Patient-related risk factors</b>	Injection of contrast into the pancreatic duct
Young age	Sphincter of Oddi manometry
Women	Pancreatic sphincterotomy
Normal serum bilirubin	Small papillary sphincterotomy
Recurrent pancreatitis	Biliary balloon sphincteroplasty
Previous ERCP-induced pancreatitis	Endoscopic papillectomy with loop
Sphincter of Oddi dysfunction	Pancreatic intraductal ultrasound
	Precut sphincterotomy

ERCP: Endoscopic retrograde cholangiopancreatography.

For diagnostic confirmation, radiological evidence with computed tomography may be necessary[34] but biochemical tests are more commonly used, as they are inexpensive and sensitive[35].

Early diagnosis of PEP is crucial as late diagnosis can be fatal[36,37].

### **Pancreatic enzymes**

The diagnosis of PEP can be complicated, since elevations in pancreatic enzymes are common after the examination, but are generally not associated with clinical pancreatitis.

There is no consensus in the literature on the ideal time after examination to request serum amylase levels and their real meaning. Two prospective studies including 263 and 886 patients found that the 4-h post-ERCP amylase level proved useful in predicting PEP[38,39]. We suggest that the patient should fast for the next 12 h and amylase analysis should be requested for all patients.

In patients with suspected pancreatitis, the degree and speed of elevations in pancreatic enzymes may be a way of differentiating patients with PEP from those in pain due to other causes. Some studies state that patients with PEP often have serum amylase levels more than five times the upper limit of normal[40,41].

Patients undergoing a contrast study of the main pancreatic duct should be admitted if the 4-h amylase level is greater than 2.5 times the upper reference limit. Patients who have not undergone a contrast study should be admitted if the 4-h amylase level is greater than five times the upper limit of normal[38]. The 4-h post-ERCP amylase level was useful in predicting PEP in two prospective studies including 263 and 886 patients, respectively[38,39].

## **DIFFERENTIAL DIAGNOSIS**

Not all patients with pain after ERCP have pancreatitis. Other causes of abdominal pain after ERCP include discomfort due to air insufflation[42-44] and perforation.

In patients with discomfort due to air insufflation, the pain is generally not as severe as that seen with PEP, and pancreatic enzyme levels may be normal or elevated, as pancreatic enzymes are elevated in most patients after ERCP[5].

If serum lipase is less than three times the upper limit of normal, pancreatitis is unlikely (specificity of 85 to 98%). However, it should be borne in mind that amylase and lipase start to increase several hours after the onset of pancreatitis; thus, blood tests taken soon after ERCP can show false negative results.

If the clinical suspicion of pancreatitis is high, tests should be repeated at least 4-6 h after ERCP. Perforated patients may experience diffuse abdominal pain, bloating, tachycardia, fever, and leukocytosis.

Symptoms can be immediate after the examination or hours later[45]. Many of the perforation symptoms overlap with those of acute pancreatitis and, if perforation is



suspected, an abdominal tomography should be performed immediately for intraperitoneal and retroperitoneal evaluation[46].

---

## TREATMENT

---

Most of the patients who develop PEP requiring hospitalization are classified as mild. In severe cases, admission to an intensive care unit may be necessary[30-31]. Initial treatment should focus on the following:

### **Pain control**

This usually manifests as abdominal pain and must be one of the main pillars in the treatment, since its non-control can lead to hemodynamic instability. There is still a lot of controversy in the use of opioids such as morphine as it has been shown to increase pressure in the sphincter of Oddi, but without clinical data that this has resulted in worsening of pancreatitis. Indicated: Meperidine, fentanyl, and morphine[47].

Particular attention should be given to patients who are dehydrated or who have not received an adequate amount of fluids since hypovolemia and hemoconcentration can cause ischemic pain and increased lactic acidosis.

### **Fluid replacement**

Fluid replacement is one of the main items in the treatment of patients with PEP. The use of crystalloid solutions, mainly Ringer Lactate, from 5 to 10 mL/kg/h is recommended in patients without restrictions. In critically ill patients, with hemodynamic instability, 20 mL/kg is recommended in 30 min followed by 3 mL/kg/h in the next 8 to 12 h[48,49].

### **Monitoring**

As these patients' condition may worsen in the next 24 h, it is recommended that they be monitored for at least 48 h. This surveillance includes vital signs, urine volume, electrolytes, and blood glucose[48].

### **Antibiotics**

Prophylactic antibiotics are not recommended in patients with PEP regardless of the type or severity of the disease. Antibiotics should only be used in about 20% of patients who develop extrapancreatic infections[48,50].

### **Nutrition**

Fasting is recommended for all patients with PEP. The time for restarting oral feeding is dependent on the severity of pancreatitis[51].

---

## PREVENTION

---

Certain measures can reduce the incidence of PEP[7]: (1) adequate training and experience of endoscopists and assistants; (2) use of wire-guided techniques for biliary cannulation; (3) minimizing the number of cannulation attempts; (4) placement of a prophylactic pancreatic stent in patients at high risk of developing PEP; (5) placement of prophylactic pancreatic stents in patients who require the assistance of a pancreatic guidewire for biliary cannulation (double guidewire technique); (6) selective cannulation of the bile duct if an assessment of the pancreatic duct is not necessary; (7) minimizing the volume of contrast medium injected into the pancreatic duct, if necessary; (8) careful use of the electrocautery current during sphincterotomy; (9) high-risk patients should undergo ERCP in specialized centers; and (10) use of carbon dioxide for luminal insufflation to decrease post-procedure abdominal pain that can be mistaken for pancreatitis.

### **Effectiveness of preventive measures**

**Endoscopic techniques:** The endoscopic technique is an important factor in the development of PEP. Cannulation guided by a hydrophilic-coated wire, careful use of electrocautery during sphincterotomy, and placement of a prophylactic pancreatic stent should be undertaken in patients at high risk of developing PEP.

**Cannulation techniques:** Various instruments such as guidewires are available and can decrease the risk of PEP as suggested by the ASGE and ESGE[52-55].

A systematic review that included only randomized trials, evaluating a total of 3450 patients, demonstrated that cannulation guided by a guidewire was superior to contrast-assisted cannulation technique[56]. Cannulation rates were higher for the wire-guided technique, and the risk of PEP was halved.

In a multicenter RCT, including 274 patients with naïve papilla undergoing ERCP using wire-guided cannulation in whom the guidewire was inadvertently inserted into the main pancreatic duct, the patients were randomized to undergo the double guidewire technique or a new cannulation attempt with a single wire. Conversion to the double guidewire technique did not facilitate selective bile duct cannulation and did not decrease the incidence of PEP compared to the new single guidewire cannulation attempt. However, double guidewire cannulation was more effective in patients with malignant biliary stenosis[57].

**Electrocautery:** In a recent systematic review evaluating 11 randomized studies involving 1791 patients, it was found that the performance of sphincterotomy with electrocautery in pure cut mode leads to a higher incidence of mild bleeding compared to endocut and blend. However, this modality may have a lower incidence of pancreatitis. Monopolar mode causes higher rates of pancreatitis compared to bipolar mode[11].

**Pancreatic stent:** Pancreatic stent placement can be performed as prophylaxis for PEP mainly in high-risk patients. We suggest the use in patients undergoing pancreatic sphincterotomy, a contrasting study of the main pancreatic duct when it is necessary to use the double guidewire technique, in patients with suspected sphincter of Oddi dysfunction, and in patients undergoing pre-cut sphincterotomy[7].

The possible benefit is believed to be related to a reduction in pancreatic intraductal pressure of papillary edema.

Studies have shown that in special situations, the passage of a pancreatic stent in the DPP may be necessary to prevent the evolution of pancreatitis after ERCP. This procedure must be performed 8 to 20 h after the start of PEP[58-60].

Pancreatic stents should be short (less than 5 cm and small in diameter (5 French), plastic, and not have flanges distally[7]. Non-flanged stents can lead to spontaneous migration to the gastrointestinal tract, which occurs in 95% of cases within 10 d[55]. If radiographs show evidence of persistent stent within 1 wk, a high endoscopy should be performed to remove the stent[55].

**Intravenous hydration:** ASGE guidelines suggest the use of periprocedural intravenous hydration with lactated Ringer to decrease the risk of PEP[2].

In a RCT of 150 patients, the PEP rate was lower in patients who received aggressive intravenous hydration compared to standard therapy[61].

In patients with contraindications to rectal non-steroidal anti-inflammatory drugs (NSAIDs), who are not at risk of fluid overload and a pancreatic stent has not been placed, the suggested alternative is aggressive hydration with lactated Ringer's solution (3 mL/kg/h during ERCP, 20 mL/kg bolus after ERCP and 3 mL/kg/h for 8 h after the examination)[25].

### **Chemoprevention**

Since 1977, more than 35 different drugs have been evaluated for the prevention of PEP with variable results[62,63]. The available options are discussed below:

#### **NSAIDs**

**Rectal NSAIDs:** The ASGE and the ESGE recommend the administration of NSAIDs to reduce the incidence and severity of PEP (for example, 100 mg of indomethacin or diclofenac rectally immediately before or after ERCP)[2,20].

A systematic review with meta-analysis evaluating 21 RCTs with a total of 6854 patients, found that the rectal administration of NSAIDs in all patients adequately reduced the incidence of PEP and that mild pancreatitis was the only preventable result. In this context, both diclofenac and indomethacin are considered effective[64].

Rectal NSAIDs were also compared indirectly with stenting of the pancreatic duct. A meta-analysis showed that rectal NSAIDs were superior to pancreatic duct stenting for the prevention of PEP (OR 0.48, 95%CI: 0.26-0.87)[65].

**Non-rectal NSAIDs:** There are no data in the current literature to support the prophylactic use of any NSAIDs administered by any non-rectal route or in combination with

other agents.

In a multicenter study with 430 patients, oral diclofenac (50 mg) before and after ERCP showed no benefit compared to placebo[66].

**Other agents in the prevention of PEP:** There are several drugs potentially useful for the prevention of PEP although some drugs are difficult to access and few are used for this purpose.

#### **Topical adrenaline**

A systematic review with meta-analysis evaluating 6 randomized and 2 observational studies including 4123 patients found that topical adrenaline does not provide any additional advantage in combination with rectal indomethacin in the prevention of PEP in patients who underwent ERCP. However, topical adrenaline alone is associated with a lower risk of PEP compared to placebo and can be considered if rectal indomethacin is not available or if the patient has any contraindications to its use[67].

#### **Nitrates**

In a systematic review with 2000 patients, the use of nitroglycerin was compared to placebo and it was found that the intervention group demonstrated a 10% reduction in the development of PEP[68].

These data suggest that nitrates combined with rectal NSAIDs may provide more benefits than NSAIDs alone[69,70]. In a randomized trial including 886 patients undergoing ERCP, the risk of PEP was lower in patients treated with diclofenac suppositories and sublingual isosorbide dinitrate compared to patients receiving diclofenac suppositories alone (RR: 0.59, 95%CI: 0.37-0.95)[70].

---

## **PANCREATIC SECRETION INHIBITORS**

---

#### **Somatostatin**

Somatostatin leads to a reduction in pancreatic exocrine secretion of basal origin and also when stimulated. A meta-analysis that included 9 studies concluded that somatostatin was ineffective in preventing PEP when administered in the short-term (< 6 h) or long-term ( $\geq 12$  h)[71]. Another meta-analysis, which included 11 RCTs with a total of 2869 patients, found no benefit when somatostatin was administered as a short-term infusion, but showed a benefit when administered as a single bolus or as a long-term infusion[72].

#### **Octreotide**

Two systematic reviews with meta-analyses found no benefit of octreotide use in PEP prophylaxis[73,74].

---

## **INHIBITORS OF PROTEASE ACTIVATION**

---

The most studied protease inhibitors include gabexate mesylate, nafamostat mesylate, and ulinastatin. As the activation of proteolytic enzymes can contribute to PEP, protease inhibitors have been investigated in the prevention of PEP. In a meta-analysis of 18 studies involving 4966 patients, there was a small benefit with the use of protease inhibitors[75].

#### **Gabexate mesylate**

Although controversial results have been observed, a meta-analysis of five studies concluded that gabexate mesylate was ineffective in reducing pancreatitis and post-ERCP pain[71].

#### **Nafamostat mesylate**

Although controversial results have been observed, a meta-analysis that included 7 RCTs with 2956 patients found that the incidence of PEP was reduced by 53% compared to patients in the control groups (RR: 0.47, 95%CI: 0.34-0.63)[76].

Another meta-analysis which included 26 studies, found that unlike gabexate mesylate and ulinastatin, nafamostat mesylate and NSAIDs were associated with decreased risk of PEP[77].

### Ulinastatin

A systematic review with a meta-analysis that included 7 RCTs comparing ulinastatin with placebo or gabexate demonstrated a decreased risk of PEP in patients receiving ulinastatin[77].

---

## MONITORING CARE AFTER ERCP

---

Many complications of ERCP are apparent during the first 6 h after the procedure, and others may take days to manifest. We suggest the following recommendations: (1) Serum amylase: Studies have shown that the 4-h serum amylase level is a useful measure in predicting PEP; (2) Clinical monitoring: The immediate post-examination period is critical and the patient must be monitored for signs and symptoms of adverse events; and (3) Diet: We recommend fasting the patient for 6 to 12 h after the examination and discharge only after the serum amylase results and clinical reassessment (patient without complaints of abdominal pain, for example).

---

## CONCLUSION

---

Pancreatitis after ERCP is a feared, potentially fatal, and not entirely preventable complication. The correct and early diagnosis is a turning point in the outcome of the disease. Pre-examination measures such as a correct indication for the procedure, use of rectal NSAIDs, and well-trained staff are necessary. During the examination: Hyperhydration, examination with precision and speed with the correct technique and appropriate material, and prophylactic use of a pancreatic stent. After the examination, maintaining fasting and the appropriate amylase dosage are essential for the clinical and technical success of the procedure.

---

## REFERENCES

---

- 1 **Thiruvengadam NR**, Kochman ML. Emerging Therapies to Prevent Post-ERCP Pancreatitis. *Curr Gastroenterol Rep* 2020; **22**: 59 [PMID: 33188441 DOI: 10.1007/s11894-020-00796-w]
- 2 **ASGE Standards of Practice Committee**, Chandrasekhara V, Khashab MA, Muthusamy VR, Acosta RD, Agrawal D, Bruining DH, Eloubeidi MA, Fanelli RD, Faulx AL, Gurudu SR, Kothari S, Lightdale JR, Qumseya BJ, Shaikat A, Wang A, Wani SB, Yang J, DeWitt JM. Adverse events associated with ERCP. *Gastrointest Endosc* 2017; **85**: 32-47 [PMID: 27546389 DOI: 10.1016/j.gie.2016.06.051]
- 3 **Feurer ME**, Adler DG. Post-ERCP pancreatitis: review of current preventive strategies. *Curr Opin Gastroenterol* 2012; **28**: 280-286 [PMID: 22450899 DOI: 10.1097/MOG.0b013e3283528e68]
- 4 **ASGE Standards of Practice Committee**, Anderson MA, Fisher L, Jain R, Evans JA, Appalaneni V, Ben-Menachem T, Cash BD, Decker GA, Early DS, Fanelli RD, Fisher DA, Fukami N, Hwang JH, Ikenberry SO, Jue TL, Khan KM, Krinsky ML, Malpas PM, Maple JT, Sharaf RN, Shergill AK, Dominitz JA. Complications of ERCP. *Gastrointest Endosc* 2012; **75**: 467-473 [PMID: 22341094 DOI: 10.1016/j.gie.2011.07.010]
- 5 **Pieper-Bigelow C**, Strocchi A, Levitt MD. Where does serum amylase come from and where does it go? *Gastroenterol Clin North Am* 1990; **19**: 793-810 [PMID: 1702756]
- 6 **Hormati A**, Alemi F, Mohammadbeigi A, Sarkeshikian SS, Saeidi M. Prevalence of Endoscopic Retrograde Cholangiopancreatography Complications and Amylase Sensitivity for Predicting Pancreatitis in ERCP Patients. *Gastroenterol Nurs* 2020; **43**: 350-354 [PMID: 32889967 DOI: 10.1097/SGA.0000000000000473]
- 7 **Boškoski I**, Costamagna G. How to Prevent Post-Endoscopic Retrograde Cholangiopancreatography Pancreatitis. *Gastroenterology* 2020; **158**: 2037-2040 [PMID: 32197979 DOI: 10.1053/j.gastro.2020.03.019]
- 8 **Funatsu E**, Masuda A, Takenaka M, Nakagawa T, Shiomi H, Yoshinaka H, Kobayashi T, Sakai A, Yagi Y, Yoshida M, Arisaka Y, Okabe Y, Kutsumi H, Azuma T. History of Post-Endoscopic Retrograde Cholangiopancreatography Pancreatitis and Acute Pancreatitis as Risk Factors for Post-ERCP Pancreatitis. *Kobe J Med Sci* 2017; **63**: E1-E8 [PMID: 29434167]
- 9 **Johnson GK**, Geenen JE, Johanson JF, Sherman S, Hogan WJ, Cass O. Evaluation of post-ERCP pancreatitis: potential causes noted during controlled study of differing contrast media. Midwest Pancreaticobiliary Study Group. *Gastrointest Endosc* 1997; **46**: 217-222 [PMID: 9378207 DOI: 10.1016/S0016-5107(97)70089-0]
- 10 **Proença IM**, dos Santos MEL, de Moura DTH, Ribeiro IB, Matuguma SE, Cheng S, McCarty TR, do Monte Junior ES, Sakai P, de Moura EGH. Role of pancreatography in the endoscopic management of encapsulated pancreatic collections – review and new proposed classification. *World J*

- Gastroenterol* 2020; 26: 7104-7117 [PMID: 33362371 DOI: 10.3748/wjg.v26.i45.7104]
- 11 **Funari MP**, Ribeiro IB, de Moura DTH, Bernardo WM, Brunaldi VO, Rezende DT, Resende RH, de Marco MO, Franzini TAP, de Moura EGH. Adverse events after biliary sphincterotomy: Does the electric current mode make a difference? *Clin Res Hepatol Gastroenterol* 2020; 44: 739-752 [PMID: 32088149 DOI: 10.1016/j.clinre.2019.12.009]
  - 12 **Sherman S**, Hawes RH, Troiano FP, Lehman GA. Pancreatitis following bile duct sphincter of Oddi manometry: utility of the aspirating catheter. *Gastrointest Endosc* 1992; 38: 347-350 [PMID: 1376705 DOI: 10.1016/S0016-5107(92)70430-1]
  - 13 **George S**, Kulkarni AA, Stevens G, Forsmark CE, Draganov P. Role of osmolality of contrast media in the development of post-ERCP pancreatitis: a meta-analysis. *Dig Dis Sci* 2004; 49: 503-508 [PMID: 15139506 DOI: 10.1023/B:DDAS.0000020511.98230.20]
  - 14 **Zhao ZH**, Hu LH, Ren HB, Zhao AJ, Qian YY, Sun XT, Su S, Zhu SG, Yu J, Zou WB, Guo XR, Wang L, Li ZS, Liao Z. Incidence and risk factors for post-ERCP pancreatitis in chronic pancreatitis. *Gastrointest Endosc* 2017; 86: 519-524. e1 [PMID: 28062312 DOI: 10.1016/j.gie.2016.12.020]
  - 15 **Sun HL**, Han B, Zhai HP, Cheng XH, Ma K. Rectal NSAIDs for the prevention of post-ERCP pancreatitis: a meta-analysis of randomized controlled trials. *Surgeon* 2014; 12: 141-147 [PMID: 24332479 DOI: 10.1016/j.surge.2013.10.010]
  - 16 **Vandervoort J**, Soetikno RM, Tham TC, Wong RC, Ferrari AP Jr, Montes H, Roston AD, Slivka A, Lichtenstein DR, Ruyman FW, Van Dam J, Hughes M, Carr-Locke DL. Risk factors for complications after performance of ERCP. *Gastrointest Endosc* 2002; 56: 652-656 [PMID: 12397271 DOI: 10.1067/mge.2002.129086]
  - 17 **Ferreira Ade F**, Bartelega JA, Urbano HC, de Souza IK. Acute pancreatitis gravity predictive factors: which and when to use them? *Arq Bras Cir Dig* 2015; 28: 207-211 [PMID: 26537149 DOI: 10.1590/S0102-67202015000300016]
  - 18 **Kochar B**, Akshintala VS, Afghani E, Elmunzer BJ, Kim KJ, Lennon AM, Khashab MA, Kalloo AN, Singh VK. Incidence, severity, and mortality of post-ERCP pancreatitis: a systematic review by using randomized, controlled trials. *Gastrointest Endosc* 2015; 81: 143-149. e9 [PMID: 25088919 DOI: 10.1016/j.gie.2014.06.045]
  - 19 **Yaghoobi M**, Pauls Q, Durkalski V, Romagnuolo J, Fogel EL, Tarnasky PR, Aliperti G, Freeman ML, Kozarek RA, Jamidar PA, Wilcox CM, Elta GH, Hawes RH, Wood-Williams A, Cotton PB. Incidence and predictors of post-ERCP pancreatitis in patients with suspected sphincter of Oddi dysfunction undergoing biliary or dual sphincterotomy: results from the EPISOD prospective multicenter randomized sham-controlled study. *Endoscopy* 2015; 47: 884-890 [PMID: 26165739 DOI: 10.1055/s-0034-1392418]
  - 20 **Dumonceau JM**, Andriulli A, Elmunzer BJ, Mariani A, Meister T, Deviere J, Marek T, Baron TH, Hassan C, Testoni PA, Kapral C; European Society of Gastrointestinal Endoscopy. Prophylaxis of post-ERCP pancreatitis: European Society of Gastrointestinal Endoscopy (ESGE) Guideline - updated June 2014. *Endoscopy* 2014; 46: 799-815 [PMID: 25148137 DOI: 10.1055/s-0034-1377875]
  - 21 **Freeman ML**, Nelson DB, Sherman S, Haber GB, Herman ME, Dorsher PJ, Moore JP, Fennerty MB, Ryan ME, Shaw MJ, Lande JD, Pheley AM. Complications of endoscopic biliary sphincterotomy. *N Engl J Med* 1996; 335: 909-918 [PMID: 8782497 DOI: 10.1056/NEJM199609263351301]
  - 22 **Freeman ML**, DiSario JA, Nelson DB, Fennerty MB, Lee JG, Bjorkman DJ, Overby CS, Aas J, Ryan ME, Bochna GS, Shaw MJ, Snady HW, Erickson RV, Moore JP, Roel JP. Risk factors for post-ERCP pancreatitis: a prospective, multicenter study. *Gastrointest Endosc* 2001; 54: 425-434 [PMID: 11577302 DOI: 10.1067/mge.2001.117550]
  - 23 **Pan Y**, Zhao L, Leung J, Zhang R, Luo H, Wang X, Liu Z, Wan B, Tao Q, Yao S, Hui N, Fan D, Wu K, Guo X. Appropriate time for selective biliary cannulation by trainees during ERCP--a randomized trial. *Endoscopy* 2015; 47: 688-695 [PMID: 25750038 DOI: 10.1055/s-0034-1391564]
  - 24 **Morales SJ**, Sampath K, Gardner TB. A Review of Prevention of Post-ERCP Pancreatitis. *Gastroenterol Hepatol (N Y)* 2018; 14: 286-292 [PMID: 29991936]
  - 25 **Dumonceau JM**, Kapral C, Aabakken L, Papanikolaou IS, Tringali A, Vanbiervliet G, Beyna T, Dinis-Ribeiro M, Hritz I, Mariani A, Paspatis G, Radaelli F, Lakhtakia S, Veitch AM, van Hooft JE. ERCP-related adverse events: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy* 2020; 52: 127-149 [PMID: 31863440 DOI: 10.1055/a-1075-4080]
  - 26 **Matsubayashi CO**, Ribeiro IB, de Moura DTH, Brunaldi VO, Bernardo WM, Hathorn KE, de Moura EGH. Is Endoscopic Balloon Dilation Still Associated With Higher Rates of Pancreatitis? *Pancreas* 2020; 49: 158-174 [PMID: 32049951 DOI: 10.1097/MPA.0000000000001489]
  - 27 **Badalov N**, Tenner S, Baillie J. The Prevention, recognition and treatment of post-ERCP pancreatitis. *JOP* 2009; 10: 88-97 [PMID: 19287099]
  - 28 **Testoni PA**, Mariani A, Giussani A, Vailati C, Masci E, Macarri G, Ghezzi L, Familiari L, Giardullo N, Mutignani M, Lombardi G, Talamini G, Spadaccini A, Briglia R, Piazzini L; SEIFRED Group. 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* 2010; 105: 1753-1761 [PMID: 20372116 DOI: 10.1038/ajg.2010.136]
  - 29 **Mariani A**, Giussani A, Di Leo M, Testoni S, Testoni PA. Guidewire biliary cannulation does not reduce post-ERCP pancreatitis compared with the contrast injection technique in low-risk and high-risk patients. *Gastrointest Endosc* 2012; 75: 339-346 [PMID: 22075192 DOI: 10.1016/j.gie.2011.09.002]
  - 30 **Crockett SD**, Wani S, Gardner TB, Falck-Ytter Y, Barkun AN; American Gastroenterological

- Association Institute Clinical Guidelines Committee. American Gastroenterological Association Institute Guideline on Initial Management of Acute Pancreatitis. *Gastroenterology* 2018; **154**: 1096-1101 [PMID: 29409760 DOI: 10.1053/j.gastro.2018.01.032]
- 31 **Tenner S**, Baillie J, DeWitt J, Vege SS; American College of Gastroenterology. American College of Gastroenterology guideline: management of acute pancreatitis. *Am J Gastroenterol* 2013; **108**: 1400-15; 1416 [PMID: 23896955 DOI: 10.1038/ajg.2013.218]
- 32 **Swaroop VS**, Chari ST, Clain JE. Severe acute pancreatitis. *JAMA* 2004; **291**: 2865-2868 [PMID: 15199038 DOI: 10.1001/jama.291.23.2865]
- 33 **Lee PJ**, Papachristou GI. Management of Severe Acute Pancreatitis. *Curr Treat Options Gastroenterol* 2020; 1-12 [PMID: 33230385 DOI: 10.1007/s11938-020-00322-x]
- 34 **Manoharan D**, Srivastava DN, Gupta AK, Madhusudhan KS. Complications of endoscopic retrograde cholangiopancreatography: an imaging review. *Abdom Radiol (NY)* 2019; **44**: 2205-2216 [PMID: 30809695 DOI: 10.1007/s00261-019-01953-0]
- 35 **Boxhoorn L**, Voermans RP, Bouwense SA, Bruno MJ, Verdonk RC, Boermeester MA, van Santvoort HC, Besselink MG. Acute pancreatitis. *Lancet* 2020; **396**: 726-734 [PMID: 32891214 DOI: 10.1016/S0140-6736(20)31310-6]
- 36 **Freeman ML**, Nelson DB, Sherman S, Haber GB, Fennerty MB, DiSario JA, Ryan ME, Kortan PP, Dorsher PJ, Shaw MJ, Herman ME, Cunningham JT, Moore JP, Silverman WB, Imperial JC, Mackie RD, Jamidar PA, Yaksh PN, Logan GM, Pheley AM. Same-day discharge after endoscopic biliary sphincterotomy: observations from a prospective multicenter complication study. The Multicenter Endoscopic Sphincterotomy (MESH) Study Group. *Gastrointest Endosc* 1999; **49**: 580-586 [PMID: 10228255 DOI: 10.1016/S0016-5107(99)70385-8]
- 37 **Ho KY**, Montes H, Sossenheimer MJ, Tham TC, Ruymann F, Van Dam J, Carr-Locke DL. Features that may predict hospital admission following outpatient therapeutic ERCP. *Gastrointest Endosc* 1999; **49**: 587-592 [PMID: 10228256 DOI: 10.1016/S0016-5107(99)70386-X]
- 38 **Sutton VR**, Hong MK, Thomas PR. Using the 4-hour Post-ERCP amylase level to predict post-ERCP pancreatitis. *JOP* 2011; **12**: 372-376 [PMID: 21737899]
- 39 **Thomas PR**, Sengupta S. Prediction of pancreatitis following endoscopic retrograde cholangiopancreatography by the 4-h post procedure amylase level. *J Gastroenterol Hepatol* 2001; **16**: 923-926 [PMID: 11555108 DOI: 10.1046/j.1440-1746.2001.02547.x]
- 40 **Testoni PA**, Bagnolo F, Caporuscio S, Lella F. Serum amylase measured four hours after endoscopic sphincterotomy is a reliable predictor of postprocedure pancreatitis. *Am J Gastroenterol* 1999; **94**: 1235-1241 [PMID: 10235200 DOI: 10.1111/j.1572-0241.1999.01072.x]
- 41 **Testoni PA**, Bagnolo F. Pain at 24 hours associated with amylase levels greater than 5 times the upper normal limit as the most reliable indicator of post-ERCP pancreatitis. *Gastrointest Endosc* 2001; **53**: 33-39 [PMID: 11154486 DOI: 10.1067/mge.2001.111390]
- 42 **Shi H**, Chen S, Swar G, Wang Y, Ying M. Carbon dioxide insufflation during endoscopic retrograde cholangiopancreatography: a review and meta-analysis. *Pancreas* 2013; **42**: 1093-1100 [PMID: 23867366 DOI: 10.1097/MPA.0b013e3182909da5]
- 43 **Brethauer M**, Seip B, Aasen S, Kordal M, Hoff G, Aabakken L. Carbon dioxide insufflation for more comfortable endoscopic retrograde cholangiopancreatography: a randomized, controlled, double-blind trial. *Endoscopy* 2007; **39**: 58-64 [PMID: 17252462 DOI: 10.1055/s-2006-945036]
- 44 **Passos ML**, Ribeiro IB, de Moura DTH, Korkischko N, Silva GLR, Franzini TP, Bernardo WM, de Moura EGH. Efficacy and safety of carbon dioxide insufflation versus air insufflation during endoscopic retrograde cholangiopancreatography in randomized controlled trials: a systematic review and meta-analysis. *Endosc Int Open* 2019; **7**: E487-E497 [PMID: 31041365 DOI: 10.1055/a-0854-3739]
- 45 **Olaiya B**, Adler DG. Intestinal perforations after endoscopic retrograde cholangiopancreatography in the United States: a 16-year study using the national inpatient sample. *Minerva Gastroenterol Dietol* 2020 [PMID: 32492997 DOI: 10.23736/S1121-421X.20.02718-X]
- 46 **Borazan E**, Konduk BT. Comparison of early and delayed diagnosis of mortality in ERCP perforations: A high-volume patient experience. *Ulus Travma Acil Cerrahi Derg* 2020; **26**: 746-753 [PMID: 32946098 DOI: 10.14744/tjtes.2020.61289]
- 47 **Basurto Ona X**, Rigau Comas D, Urrútiá G. Opioids for acute pancreatitis pain. *Cochrane Database Syst Rev* 2013; CD009179 [PMID: 23888429 DOI: 10.1002/14651858.CD009179.pub2]
- 48 **Mederos MA**, Reber HA, Girgis MD. Acute Pancreatitis: A Review. *JAMA* 2021; **325**: 382-390 [PMID: 33496779 DOI: 10.1001/jama.2020.20317]
- 49 **Messallam AA**, Body CB, Berger S, Sakaria SS, Chawla S. Impact of early aggressive fluid resuscitation in acute pancreatitis. *Pancreatology* 2021; **21**: 69-73 [PMID: 33257225 DOI: 10.1016/j.pan.2020.11.006]
- 50 **Zhang J**, Zhu S, Tan D, Ma A, Yang Y, Xu J. A meta-analysis of early oral refeeding and quickly increased diet for patients with mild acute pancreatitis. *Saudi J Gastroenterol* 2019; **25**: 14-19 [PMID: 30226482 DOI: 10.4103/sjg.SJG\_240\_18]
- 51 **Lella F**, Bagnolo F, Colombo E, Bonassi U. A simple way of avoiding post-ERCP pancreatitis. *Gastrointest Endosc* 2004; **59**: 830-834 [PMID: 15173796 DOI: 10.1016/S0016-5107(04)00363-3]
- 52 **Artifon EL**, Sakai P, Cunha JE, Halwan B, Ishioka S, Kumar A. Guidewire cannulation reduces risk of post-ERCP pancreatitis and facilitates bile duct cannulation. *Am J Gastroenterol* 2007; **102**: 2147-2153 [PMID: 17581267 DOI: 10.1111/j.1572-0241.2007.01378.x]
- 53 **Bailey AA**, Bourke MJ, Williams SJ, Walsh PR, Murray MA, Lee EY, Kwan V, Lynch PM. A

- prospective randomized trial of cannulation technique in ERCP: effects on technical success and post-ERCP pancreatitis. *Endoscopy* 2008; **40**: 296-301 [PMID: 18389448 DOI: 10.1055/s-2007-995566]
- 54 **Testoni PA**, Mariani A, Aabakken L, Arvanitakis M, Bories E, Costamagna G, Devière J, Dinis-Ribeiro M, Dumonceau JM, Giovannini M, Gyokeres T, Hafner M, Halttunen J, Hassan C, Lopes L, Papanikolaou IS, Tham TC, Tringali A, van Hooff J, Williams EJ. Papillary cannulation and sphincterotomy techniques at ERCP: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. *Endoscopy* 2016; **48**: 657-683 [PMID: 27299638 DOI: 10.1055/s-0042-108641]
- 55 **Tse F**, Yuan Y, Moayyedi P, Leontiadis GI. Guide wire-assisted cannulation for the prevention of post-ERCP pancreatitis: a systematic review and meta-analysis. *Endoscopy* 2013; **45**: 605-618 [PMID: 23807804 DOI: 10.1055/s-0032-1326640]
- 56 **Sasahira N**, Kawakami H, Isayama H, Uchino R, Nakai Y, Ito Y, Matsubara S, Ishiwatari H, Uebayashi M, Yagioka H, Togawa O, Toda N, Sakamoto N, Kato J, Koike K. Early use of double-guidewire technique to facilitate selective bile duct cannulation: the multicenter randomized controlled EDUCATION trial. *Endoscopy* 2015; **47**: 421-429 [PMID: 25590186 DOI: 10.1055/s-0034-1391228]
- 57 **Madácsy L**, Kurucsai G, Joó I, Gódi S, Fejes R, Székely A. Rescue ERCP and insertion of a small-caliber pancreatic stent to prevent the evolution of severe post-ERCP pancreatitis: a case-controlled series. *Surg Endosc* 2009; **23**: 1887-1893 [PMID: 19057957 DOI: 10.1007/s00464-008-0199-z]
- 58 **Kerdsirichairat T**, Attam R, Arain M, Bakman Y, Radosevich D, Freeman M. Urgent ERCP with pancreatic stent placement or replacement for salvage of post-ERCP pancreatitis. *Endoscopy* 2014; **46**: 1085-1094 [PMID: 25216326 DOI: 10.1055/s-0034-1377750]
- 59 **Karjula H**, Nordblad Schmidt P, Mäkelä J, Liisanantti JH, Ohtonen P, Saarela A. Prophylactic pancreatic duct stenting in severe acute necrotizing pancreatitis: a prospective randomized study. *Endoscopy* 2019; **51**: 1027-1034 [PMID: 30895583 DOI: 10.1055/a-0865-1960]
- 60 **Shaygan-Nejad A**, Masjedizadeh AR, Ghavidel A, Ghojzadeh M, Khoshbaten M. Aggressive hydration with Lactated Ringer's solution as the prophylactic intervention for postendoscopic retrograde cholangiopancreatography pancreatitis: A randomized controlled double-blind clinical trial. *J Res Med Sci* 2015; **20**: 838-843 [PMID: 26759569 DOI: 10.4103/1735-1995.170597]
- 61 **Vadalà di Prampero SF**, Faleschini G, Panic N, Bulajic M. Endoscopic and pharmacological treatment for prophylaxis against postendoscopic retrograde cholangiopancreatography pancreatitis: a meta-analysis and systematic review. *Eur J Gastroenterol Hepatol* 2016; **28**: 1415-1424 [PMID: 27580214 DOI: 10.1097/MEG.0000000000000734]
- 62 **Kubiliun NM**, Adams MA, Akshintala VS, Conte ML, Cote GA, Cotton PB, Dumonceau JM, Elta GH, Fogel EL, Freeman ML, Lehman GA, Naveed M, Romagnuolo J, Scheiman JM, Sherman S, Singh VK, Elmunzer BJ; United States Cooperative for Outcomes Research in Endoscopy (USCORE). Evaluation of Pharmacologic Prevention of Pancreatitis After Endoscopic Retrograde Cholangiopancreatography: A Systematic Review. *Clin Gastroenterol Hepatol* 2015; **13**: 1231-9; quiz e70 [PMID: 25579870 DOI: 10.1016/j.cgh.2014.11.038]
- 63 **Serrano JPR**, de Moura DTH, Bernardo WM, Ribeiro IB, Franzini TP, de Moura ETH, Brunaldi VO, Salesse MT, Sakai P, De Moura EGH. Nonsteroidal anti-inflammatory drugs vs placebo for post-endoscopic retrograde cholangiopancreatography pancreatitis: a systematic review and meta-analysis. *Endosc Int Open* 2019; **07**: E477-E486 [PMID: 30957004 DOI: 10.1055/a-0862-0215]
- 64 **Akbar A**, Abu Dayyeh BK, Baron TH, Wang Z, Altayar O, Murad MH. Rectal nonsteroidal anti-inflammatory drugs are superior to pancreatic duct stents in preventing pancreatitis after endoscopic retrograde cholangiopancreatography: a network meta-analysis. *Clin Gastroenterol Hepatol* 2013; **11**: 778-783 [PMID: 23376320 DOI: 10.1016/j.cgh.2012.12.043]
- 65 **Ishiwatari H**, Urata T, Yasuda I, Matsusaki S, Hisai H, Kawakami H, Ono M, Iwashita T, Doi S, Kawakubo K, Hayashi T, Sonoda T, Sakamoto N, Kato J. No Benefit of Oral Diclofenac on Post-Endoscopic Retrograde Cholangiopancreatography Pancreatitis. *Dig Dis Sci* 2016; **61**: 3292-3301 [PMID: 27447477 DOI: 10.1007/s10620-016-4251-x]
- 66 **Iqbal U**, Siddique O, Khara HS, Khan MA, Haq KF, Siddiqui MA, Solanki S, Zuchelli TE, Shellenberger MJ, Birk JW. Post-endoscopic retrograde cholangiopancreatography pancreatitis prevention using topical epinephrine: systematic review and meta-analysis. *Endosc Int Open* 2020; **8**: E1061-E1067 [PMID: 32743060 DOI: 10.1055/a-1190-3777]
- 67 **Chen B**, Fan T, Wang CH. A meta-analysis for the effect of prophylactic GTN on the incidence of post-ERCP pancreatitis and on the successful rate of cannulation of bile ducts. *BMC Gastroenterol* 2010; **10**: 85 [PMID: 20673365 DOI: 10.1186/1471-230X-10-85]
- 68 **Sotoudehmanesh R**, Eloubeidi MA, Asgari AA, Farsinejad M, Khatibian M. A randomized trial of rectal indomethacin and sublingual nitrates to prevent post-ERCP pancreatitis. *Am J Gastroenterol* 2014; **109**: 903-909 [PMID: 24513806 DOI: 10.1038/ajg.2014.9]
- 69 **Tomoda T**, Kato H, Ueki T, Akimoto Y, Hata H, Fujii M, Harada R, Ogawa T, Wato M, Takatani M, Matsubara M, Kawai Y, Okada H. Combination of Diclofenac and Sublingual Nitrates Is Superior to Diclofenac Alone in Preventing Pancreatitis After Endoscopic Retrograde Cholangiopancreatography. *Gastroenterology* 2019; **156**: 1753-1760. e1 [PMID: 30772342 DOI: 10.1053/j.gastro.2019.01.267]
- 70 **Andriulli A**, Leandro G, Federici T, Ippolito A, Forlano R, Iacobellis A, Annesse V. Prophylactic administration of somatostatin or gabexate does not prevent pancreatitis after ERCP: an updated meta-analysis. *Gastrointest Endosc* 2007; **65**: 624-632 [PMID: 17383459 DOI: 10.1016/j.gie.2006.10.030]
- 71 **Qin X**, Lei WS, Xing ZX, Shi F. Prophylactic effect of somatostatin in preventing Post-ERCP pancreatitis: an updated meta-analysis. *Saudi J Gastroenterol* 2015; **21**: 372-378 [PMID: 26655132]

- DOI: [10.4103/1319-3767.167187](https://doi.org/10.4103/1319-3767.167187)]
- 72 **Bai Y**, Gao J, Zou DW, Li ZS. Prophylactic octreotide administration does not prevent post-endoscopic retrograde cholangiopancreatography pancreatitis: a meta-analysis of randomized controlled trials. *Pancreas* 2008; **37**: 241-246 [PMID: [18815543](https://pubmed.ncbi.nlm.nih.gov/18815543/) DOI: [10.1097/MPA.0b013e31816c90a1](https://doi.org/10.1097/MPA.0b013e31816c90a1)]
- 73 **Omata F**, Deshpande G, Tokuda Y, Takahashi O, Ohde S, Carr-Locke DL, Jacobs JL, Mine T, Fukui T. Meta-analysis: somatostatin or its long-acting analogue, octreotide, for prophylaxis against post-ERCP pancreatitis. *J Gastroenterol* 2010; **45**: 885-895 [PMID: [20373114](https://pubmed.ncbi.nlm.nih.gov/20373114/) DOI: [10.1007/s00535-010-0234-4](https://doi.org/10.1007/s00535-010-0234-4)]
- 74 **Seta T**, Noguchi Y. Protease inhibitors for preventing complications associated with ERCP: an updated meta-analysis. *Gastrointest Endosc* 2011; **73**: 700-706. e1-2 [PMID: [21145053](https://pubmed.ncbi.nlm.nih.gov/21145053/) DOI: [10.1016/j.gie.2010.09.022](https://doi.org/10.1016/j.gie.2010.09.022)]
- 75 **Yu G**, Li S, Wan R, Wang X, Hu G. Nafamostat mesilate for prevention of post-ERCP pancreatitis: a meta-analysis of prospective, randomized, controlled trials. *Pancreas* 2015; **44**: 561-569 [PMID: [25822153](https://pubmed.ncbi.nlm.nih.gov/25822153/) DOI: [10.1097/MPA.0000000000000310](https://doi.org/10.1097/MPA.0000000000000310)]
- 76 **Yuhara H**, Ogawa M, Kawaguchi Y, Igarashi M, Shimosegawa T, Mine T. Pharmacologic prophylaxis of post-endoscopic retrograde cholangiopancreatography pancreatitis: protease inhibitors and NSAIDs in a meta-analysis. *J Gastroenterol* 2014; **49**: 388-399 [PMID: [23720090](https://pubmed.ncbi.nlm.nih.gov/23720090/) DOI: [10.1007/s00535-013-0834-x](https://doi.org/10.1007/s00535-013-0834-x)]
- 77 **Chen S**, Shi H, Zou X, Luo H. Role of ulinastatin in preventing post-endoscopic retrograde cholangiopancreatography pancreatitis: the Emperor's New Clothes or Aladdin's Magic Lamp? *Pancreas* 2010; **39**: 1231-1237 [PMID: [20531245](https://pubmed.ncbi.nlm.nih.gov/20531245/) DOI: [10.1097/MPA.0b013e3181dc67e7](https://doi.org/10.1097/MPA.0b013e3181dc67e7)]





Published by **Baishideng Publishing Group Inc**  
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

**Telephone:** +1-925-3991568

**E-mail:** [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)

**Help Desk:** <https://www.f6publishing.com/helpdesk>

<https://www.wjgnet.com>

