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PREVENTION OF POST-ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP) PANCREATITIS: A SYSTEMATIC REVIEW

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ABSTRACT

Background: Endoscopic retrograde cholangiopancreatography (ERCP) is a relatively complex procedure, with pancreatitis being this procedure's most commonly reported complication. Many randomized clinical trials (RCTs) have been conducted to assess the best prevention modality of post-ERCP pancreatitis (PEP). This systematic review aims to collate evidence from RCTs on the best modality for the prevention of PEP. **Methods:** A systematic search was conducted across the following databases: PubMed, Cochrane library, EBSCO, and Web of Science. Relevant articles were located between January 2012 through August 2022. The following keywords were used: ERCP, post-endoscopic retrograde cholangiopancreatography pancreatitis, prevention, and post-ERCP. Duplicates were manually removed. This systematic review was conducted adhering to PRISMA statement 2020 guidelines. The reference lists were additionally searched (umbrella methodology). **Results:** Of the 2482 studies that were identified, 2010 were reviewed for titles and abstracts. Finally, 28 articles were assessed for full-text eligibility, of which 13 RCTs met the inclusion criteria. The most commonly used prevention technique was Pancreatic Stent Placement (PSP) (n=977), which had a statistically significant reduced incidence of PEP. The second most commonly used methodology was Wire-Guided Biliary Cannulation (WGC) (n=1329), which showed overall protective findings. With Endoscopic Nasobiliary Drainage (ENBD) (n=153), there was an independent risk of patients acquiring PEP with the procedure. Lastly, Needle Knife Sphincterotomy (NKS) (n=73) showed no improvement in PEP. **conclusion:** There are multiple modalities of preventing PEP. Patients at high risk of post-ERCP complications must undergo both pharmacological and surgical prevention. In this systematic review, pancreatic stent placement was found to be the most effective technique to prevent PEP. It is, however, recommended that the administration of pharmacological agents, diagnostic procedures of PEP, and procedural techniques be optimized to reduce the patient burden of PEP.

BACKGROUND

Endoscopic retrograde cholangiopancreatography (ERCP) is a specialized endoscopic procedure that is intended to manage pancreaticobiliary disorders (i.e., relieving biliary obstruction, and removal of bile duct stones).[1,2] Current literature cites that the most common

post-ERCP complication is pancreatitis, which leads to many other complications.[3] These may include pancreatic necrosis and organ failure in some instances, a common basis for ERCP-related patient dissatisfaction.[4] At this juncture, it is pertinent to understand the procedural techniques and pharmacological agents that can prevent the risk of post-ERCP pancreatitis (PEP).[5]

The consensus among many medical societies worldwide is to define PEP as "new or worsening abdominal pain 24 hours post ERCP that is combined with three or more times the value of lipase or amylase, requiring hospital admission or extension of stay".[6] At present, the incidence across studies on average of post-ERCP has ranged between 3.5-9.7%.[7,9] While most of these cases are mild, the rates of severe pancreatitis have ranged between 0.3-0.8%, which may still lead to mortality among patients (0.1-0.7%).[7,9] When considering the risk factors of what may lead to post-ERCP pancreatitis, it is typically related to increased pressure in the main pancreatic duct that is generally caused by instrumentation used during ERCP.[10] Therefore, it is essential to be mindful of procedure-related factors, difficulty of bile duct cannulation, and repeated guidewire cannulation in the main pancreatic duct, among others.[11]

At present, literature guidance on the prevention of post-ERCP pancreatitis and associated risks such as organ failure includes primarily general measures, endoscopic techniques, and pharmacological prophylaxis.[12] In those patients that have higher risks, additional interventions such as pancreatic duct stunting may be utilized.[12] This systematic review will collate all current evidence pertaining to the prevention of post-ERCP pancreatitis prevention.

METHODS

A systematic search of the literature was conducted using the following databases: PubMed, Cochrane library, EBSCO, and Web of Science. Studies published in the past 10 years were included (2012-2022) to ensure that only recent developments in the area are covered. The key terms were applied using the BOOLEAN logic (and/or) and are as follows: ERCP, post-endoscopic retrograde cholangiopancreatography pancreatitis, prevention, post-ERCP. Only randomized controlled trials (RCTs) were included with an active interventional and control group employing any of the following prevention strategies for post-ERCP pancreatitis:

1. Endoscopic Nasobiliary Drainage (ENBD),
2. Wire-Guided Biliary Cannulation (WGC),
3. Pancreatic Stent Placement (PSP),
4. Needle Knife Sphincterotomy (NKS).

Using the PRISMA Statement 2020 guidelines, the titles and abstracts were reviewed.[13] This was followed by a full manuscript review by two authors, with a third present party for any disagreements. Additionally, an umbrella search of shortlisted studies was conducted, and the reference lists were scanned for any additional RCTs in this area. RCTs that analyzed the prevention of post-ERCP pancreatitis using ENBD, WGC, PSP, or NKS were included. There were no language restrictions.

Review articles, editorials, commentaries, case reports, cohorts, case controls, and any non-randomized trials were omitted. The PRISMA diagram is attached in Figure 1.

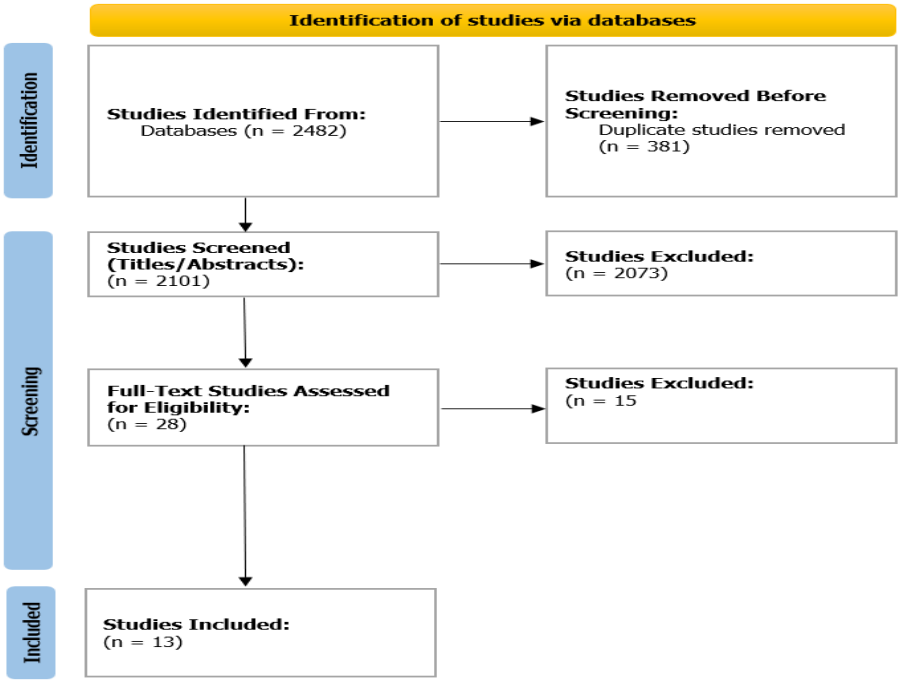

Figure 1: PRISMA flowchart.

RESULTS

Out of 2482 studies located, a total of 13 RCTs were included. The characteristics are tabulated in Table 1. The most commonly used prevention technique was Pancreatic Stent Placement (PSP), documented in 7 RCTs (Table 1). In total, there were 519 patients assigned to the interventional group, and 478 were assigned to the control group. All 997 patients were assessed for incidence of post-ERCP pancreatitis. The incidence ranged from 5.5% in Fujisawa et al.'s trial.[14] to 45% in Pan's trial. Notably, the countries included Japan (n=3), South Korea (n=1), China (n=1), South Korea (n=1), and Italy (n=1). Fujisawa et al. found that the pancreatitis rate was lower with a stent size of 3 cm compared to 5 cm (2% vs 8%, P=0.035).[14] Conigliaro et al. (2013) reported a post-ERCP pancreatitis incidence of 15%. PSP was conducted in 29% of patients with immediate stent removal. While PSP was not performed in patients that had the stent left in place (P=0.021).[15] However, the authors concluded that the findings were questionable for the prevention of pancreatitis (Table 1).[15] Lee et al. in 2012, reported a post-ERCP pancreatitis incidence of 20.8%. It was determined that prophylactic placement of PSP was the only preventive factor for PEP of beneficial relevance (OR=0.126, 95% CI=0.025-0.632, P=0.012).[16] Sofuni et al. reported an incidence of 11.5%, mentioning that pancreatitis had a different incidence based on risk factors including i) pancreatography, ii) nonplacement of a pancreatic duct stent after ERCP, iii) procedure time of 30 minutes or more, iv) sampling of pancreatic tissue by any method, v) intraductal ultrasonography, and vi) difficulty of cannulation (≥15 minutes). Patients with three or more risk factors had a higher PEP incidence. The trial's authors concluded that while PSP reduces the incidence of pancreatitis, several risk factors are associated with incidence.[17] Pan et al. in 2011 reported the highest incidence of 45%, wherein pancreatitis was significantly less in the PSP group as compared to the non-PSP group (P<0.01).[18] Ito et al. in 2010, reported an incidence of 12.9% for pancreatitis post-ERCP, mentioning that pancreatitis was higher in frequency in the PSP compared to the no-stent group (2.9% vs 23%, RR=0.13).[19] Ito et al. recommended stenting with a pancreatic guidewire (PGW) to achieve selective biliary cannulation and to reduce the incidence of pancreatitis.[19] Kawaguchi et al. reported an incidence of 7.5%, mentioning a lower frequency of post-ERCP pancreatitis with pancreatic duct stent placement (1.7%) as compared to the non-stenting group (P=0.032), with no other risk factors found to be significant for pancreatic outcomes.[20]

Three RCTs utilized Wire-Guided Biliary Cannulation (WGC) for post-ERCP pancreatitis. The three trials were each conducted in Japan, South Korea, and the Asia Pacific, enrolling a total of 1329 patients. Kobayashi et al. in 2013 reported an incidence of 6.2%, with the incidence being the same between the two groups (6.1% vs 6.3%).[21] However, accidental guidewire insertions or unintended infections caused by contrast into the main pancreatic duct were ascertained to be independent risk factors for post-ERCP pancreatitis (RR=8.7, 95% CI 2.46-30.81, P=0.001).[21] The incidence of PEP was reported to be 6.7% by Lee et al. in 2009 and notably, WGC has been deemed a protective factor (OR=0.1, 95% CI=0.024-0.49, P=0.004). Additionally, female gender and sphincter of Oddi dysfunction were found to be the associated risk factors for developing pancreatitis post-procedure.[22] Lastly, Bassan et al. reported an incidence of 8.6%. However, the pancreatitis rates between the WGC groups of 0.025 inch and the 0.035-inch one did not display significance (7.8% vs. 9.3%, P=0.51).[23]

In total, two RCTs applied Endoscopic Nasobiliary Drainage (ENBD). Both of these trials were conducted in China. Huang et al. in 2018, reported an incidence of 5.8%, mentioning that not undergoing ENBD was an independent risk factor for post-ERCP pancreatitis (OR=0.087, 95% CI=0.011-0.734, P=0.025).[24] Xu et al, 2015 reported a higher incidence of 8.3%, mentioning that post-ERCP pancreatitis occurred more frequently in the endoscopic papillary balloon dilation (EPBD) as compared to the ENBD group (7.4% vs 4.3%, P=0.05).[25]

Finally, one RCT by Swan et al. assessed the outcomes of Needle Knife Sphincterotomy (NKS) and determined that there was no significant difference in the incidence of PEP among patients in the early NKS group (20.5%) compared to standard cannulation (17.6%) (P>0.05).[26]

Table 1: Characteristics of all included RCTs.

Author, Year	Country	N (Interventional vs Other)	Study Type	Incidence of Post-ERCP Pancreatitis (PEP)	Procedure Performed	Findings	Comment
Huang et al., 2018 [24]	China	160 vs 155	Randomized Controlled Trial	9 (5.8%)	Endoscopic Nasobiliary Drainage (ENBD)	Not undergoing ENBD was an independent risk factor for PEP (OR=0.087, 95% CI=0.011-0.734; P=0.025)	ENBD was effective and safe in preventing PEP in patients undergoing endoscopic papillary large

							balloon dilation together with ENBD
Xu et al., 2015 [25]	China	113 vs 115	Randomized Controlled Trial	18 (8.3%)	Endoscopic Nasobiliary Drainage (ENBD)	PEP occurred more frequently in the EPBD group (7.4% vs 4.3%, P=0.05)	If the CBD stone is successfully cleared, ENBD is only beneficial if an Endoscopic papillary balloon dilatation (EPBD) procedure has been performed
Kobayashi et al., 2013 [20]	Japan	163 vs 159	Randomized Controlled Trial	20 (6.2%)	Wire-Guided Biliary Cannulation (WGC)	PEP incidence was the same between the groups (6.1% vs 6.3%, P=0.95); accidental guidewire insertions/unintended injections of contrast into the main pancreatic duct (PD) were independent risk factors for PEP (RR=8.7, 95% CI= 2.46-30.81, P=0.001)	The WGC technique did not reduce the risk of PEP and did not improve the success rate of selective bile duct cannulation
Lee et al., 2009 [22]	South Korea	150 vs 150	Prospective Randomized Trial	20 (6.7%)	Wire-Guided Biliary Cannulation (WGC)	WGC was a protective factor (OR=0.1; 95% CI=0.024-0.490, P = 0.004). Female sex and sphincter of Oddi dysfunction were risk factors for PEP.	WGC was associated with a lower rate of PEP, but WGC may not prevent PEP in individuals with suspected SOD and unintentional pancreatic duct guidewire cannulation
Bassan et al., 2018 [23]	Asia Pacific	707	Prospective, Single Blinded Randomized Controlled Trial	61 (8.6%)	Wire-Guided Biliary Cannulation (WGC)	PEP rates between the 0.025-inch and the 0.035-inch wire groups did not differ significantly (7.8% vs 9.3%; P = 0.51)	Similar rates of successful cannulation and PEP were demonstrated with the use of 0.025-inch and 0.035-inch guidewires
Fujisawa et al., 2016 [14]	Japan	120 vs 120	Prospective Randomized Trial	11 (5.5%)	Pancreatic Stent Placement (PSP)	PEP rate was lower with the short stent than with the long stent (2% vs. 8.8%, P=0.035)	When assessing prophylactic pancreatic stents, the 3 cm size was superior to the 5-cm one
Conigliaro et al., 2013	Italy	21 vs 19	Prospective Randomized	6 (15%)	Pancreatic Stent	PEP occurred in 29 % of patients with	Pancreatic duct stent placement

[15]			Trial		Placement (PSP)	immediate stent removal and in 0% of patients who left the stent in place (P = 0.021). Stents dislodged spontaneously in 74 % of patients within 24-96 hours, whereas uneventful endoscopic removal was carried out after 96 hours in 5 patients	only for the duration of ERCP does not prevent PEP
Lee et al., 2012 [16]	South Korea	50 vs 51	Prospective Randomized Trial	21 (20.8%)	Pancreatic Stent Placement (PSP)	Prophylactic placement of PS was the only prophylactic factor for PEP (OR=0.126, 95% CI=0.025-0.632, P = 0.012)	Prophylactic temporary 3F PS placement for patients with difficult biliary cannulation during ERCP is a safe and effective strategy to reduce PEP, has a high rate of spontaneous passage of stents without complications
Sofuni et al., 2011 [17]	Japan	213 vs 213	Randomized Controlled Trial	47 (11.5%)	Pancreatic Stent Placement (PSP)	PEP incidence was different among groups with the following risk factors: i) pancreatography, ii) nonplacement of a pancreatic duct stent after ERCP, iii) procedure time of 30 minutes or more, iv) sampling of pancreatic tissue by any method, v) intraductal ultrasonography, and vi) difficulty of cannulation (≥15 min). Patients with three or more risk factors had higher PEP incidence.	PSP reduces the incidence of PEP. Several risk factors were associated with PEP
Pan et al., 2011 [18]	China	20 vs 20	Randomized Controlled Trial	18 (45%)	Pancreatic Stent Placement (PSP)	PEP was significantly less in the PSP group than in the non-PSP group (4 vs. 14 cases; P < 0.01)	PSP was effective in reducing the incidence of PEP and shortening the duration of

							hospitalization
Ito et al., 2010 [19]	Japan	35 vs 35	Prospective Randomized Controlled Trial	9 (12.9%)	Pancreatic Stent Placement (PSP)	PEP had a higher frequency in the PSP group than in the no-stent group (2.9 vs. 23%, RR=0.13, CI=0.016-0.95)	Pancreatic duct stenting after PGW for achieving selective biliary cannulation was recommended to reduce the incidence of PEP
Kawaguchi et al., 2012 [21]	Japan	60 vs 20	Randomized Controlled Trial	9 (7.5%)	Pancreatic Stent Placement (PSP)	The frequency of PEP was lower in PD stents (1.7%) compared to non-stent groups (13.3%) (P = 0.032); there were no significant differences in high-risk factors between the two groups	Pancreatic stent placement was a safe and effective technique to prevent PEP and should be used in high-risk patients
Swan et al., 2013	Australia	34 vs 39	Randomized Controlled Trial	14 (19.2%)	Needle Knife Sphincterotomy (NKS)	No significant difference in the development of PEP among patients in the early NKS group (20.5%) vs standard cannulation (17.6%) (P>0.05)	Early NKS application during difficult cannulation does not increase the risk of PEP. However, the risk of PEP increases greatly after 7-8 attempts or failure of cannulation

DISCUSSION

Post-ERCP pancreatitis is a serious complication that can lead to hospitalization, sepsis, and death.[27] In this systematic review, there were mixed results obtained from 13 RCTs for preventing post-ERCP pancreatitis, applying ENBD, WGC, PSP, and NKS. In general, the clinical symptomatology of post-ERCP pancreatitis is the same as seen in any other case, which may include epigastric pain, left upper quadrant pain, abdominal tenderness, and altered amylase/lipase levels[28] While abdominal imaging is not required to diagnose the condition, radiographic imaging tests are usually done. Reports indicate that patients may also have elevated amylase levels without abdominal pain (29). Therefore, the routine checking of enzymes is pertinent following ERCP.[5] The goal of prevention is to reduce the risk of PEP and any other associated risk factor[27] Currently, a combination of endoscopic and pharmacologic techniques is being used to prevent PEP. Endoscopic strategies are limited to minimizing the trauma directly to the biliary orifice. This may include reducing the number of cannulation attempts, for instance. In high-risk patients, it is recommended to use measures such as pancreatic duct stenting, which aligns with the results of our systematic review as it has demonstrated significant benefit compared to no stenting.[30]

Pharmacologic prophylaxis, which is beyond the scope of this systematic review, is also a key modality for prevention[5] It is currently suggested that pharmacological prophylaxis with rectal administration of nonsteroidal-inflammatory drugs (NSAIDs) compared to no drug administration is beneficial as it has shown efficacy in reducing the risk of PEP[5] Typically, diclofenac suppository 100 mg or indomethacin suppository 100 mg is given immediately before ERCP as a means of prevention[31]

Medications such as ibuprofen and naproxen have been shown to be effective in preventing post-ERCP pancreatitis but only have short-term effects[32] Acetaminophen has also been associated with reduced risks of post-ERCP pancreatitis. Pancreatic enzymes are another possible means of prevention for post-ERCP pancreatitis. Medications such as ursodiol and pancrelipase have additionally been linked to reducing

the risk of post-ERCP pancreatitis[33] Other common pharmacological interventions include prophylactic erythromycin, which is usually given for 14 days following the procedure. Other choices include bile-salt binders like cholestyramine, colestipol, and colesevelam, and pancreatic enzyme supplements like pancrelipase or amylase[32,34]

Intravenous hydration with ringer's lactate solution is also considered to be a better alternative to normal saline given that it decreases the risk of systemic inflammatory responses. A systematic review also evaluated the role of hydration in PEP prophylaxis. While the evidence reported was inconclusive, another randomized controlled trial found that hydration with Ringer's lactate prevented the occurrence of PEP among high-risk patients[35,36] Therefore, intravenous hydration must be considered an alternative for those who otherwise have contraindications to NSAIDs. The combination of rectal NSAIDs and intravenous hydration has been notably reported in the literature as well. Current literature also reports that somatostatin inhibits secretions from the pancreas. For instance, Bai and colleagues write that somatostatin reduces the levels of amylase while preventing PEP in patient populations[37] A systematic review reports moderate benefits in PEP prophylaxis, whereas two other studies report no benefit of somatostatin use in PEP prevention,[38,39] Somatostatin, thus, is not currently recommended, given low evidence of reducing PEP risks.

Antioxidants, including allopurinol, and beta-carotene do not have conclusive evidence in favor of PEP prevention[40] However, N-acetylcysteine (NAC) an antioxidant helps protect the pancreas from free radical damage and reduces inflammation[34] The medication has been shown to reduce the severity of pain and inflammation but does not affect the mortality rate. Protease inhibitors are considered viable treatment options in cases of acute pancreatitis. These medications block the inflammatory cascade and different enzymes in the pancreas. Inhibitors such as ulinastatin and nafamostat have been investigated in preventing PEP[41] Nitroglycerin works by affecting the pressure of the sphincter of Oddi, smooth muscle relaxation, and increased blood flow to the pancreas. Katsinelos and colleagues report that a combination of glucagon and nitroglycerin is more likely to reduce the incidence of PEP[42]

Overall, numerous pharmacological interventions may be used to prevent this. The following is a key list of the pharmacological interventions subsequently discussed:

1. NSAIDs: Readily available, cheap, and highly effective in preventing PRP.
2. Intravenous hydration: Maintains perfusion to the pancreas and suppresses the inflammatory cascade.
3. Rectal NSAIDs and intravenous hydration: The combination reportedly prevents patients at high risk of PEP.
4. Somatostatin: Inhibits secretions from the pancreas and prevents PEP.
5. Antioxidants: Their role is considered less beneficial overall.
6. Protease inhibitors: These are possible treatment options in acute pancreatitis.
7. Nitrates: Work by reducing the sphincter of Oddi pressure, thereby enhancing blood flow to the pancreas.

A key finding of this systematic review is pancreatic duct stenting[43] Ultimately the decision to place a prophylactic pancreatic stent is based on the patient. Still, risk factors or technical errors may be encountered for which endoscopist expertise and preference ought to be considered.

CONCLUSION

The well-known complication of acute pancreatitis can occur post-ERCP. There are certain risk factors, such as the female gender, that may lead to even higher requirements of well-curated prevention strategies. While the causation and effect of Endoscopic Nasobiliary Drainage (ENBD), Wire-Guided Biliary Cannulation (WGC), Pancreatic Stent Placement (PSP), and Needle Knife Sphincterotomy (NKS) have been tested in RCTs, it is still important to account for ongoing trials in this area for more favorable data. Key aspects of the prevention of post-ERCP pancreatitis may be achieved by pharmacological interventions as well. In general, NSAIDs emerge as safe and reliable option among high-risk patients with no precluding conditions. Bile-salt binders, prophylactic erythromycin, and pancreatic enzyme supplements such as amylase or pancrelipase are also currently in use; however, evidence of NAC is current inconclusive in the prevention of post-ERCP pancreatitis. Without a doubt, a multimodal approach is required to overcome incidence of post-ERCP pancreatitis. Given the multifactorial nature of the disease, the prevention of post-ERCP pancreatitis ought to be assessed with various aspects based on patient-related risk factors, procedural techniques, and the consideration of prophylactic pharmacological agents.

REFERENCES

1. Parekh PJ, Majithia R, Sikka SK, Baron TH. The “Scope” of post-ERCP pancreatitis. In: Mayo Clinic Proceedings. Elsevier, 2017; 434–48.
2. Freeman ML, Guda NM. Prevention of post-ERCP pancreatitis: a comprehensive review. Gastrointest Endosc, 2004; 59(7): 845–64.
3. Lee TH, Park DH. Endoscopic prevention of post-endoscopic retrograde cholangiopancreatography pancreatitis. World J Gastroenterol WJG, 2014; 20(44): 16582.
4. Trap R, Adamsen S, Hart-Hansen O, Henriksen M. Severe and fatal complications after diagnostic and therapeutic ERCP: a prospective series of claims to insurance covering public hospitals. Endoscopy, 1999; 31(02): 125–30.

5. Dumonceau J-M, Kapral C, Aabakken L, Papanikolaou IS, Tringali A, Vanbiervliet G, et al. ERCP-related adverse events: European Society of Gastrointestinal Endoscopy (ESGE) guideline. Endoscopy. 2020; 52(02): 127–49.
6. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. Gut. 2013;62(1):102–11.
7. Andriulli A, Loperfido S, Napolitano G, Niro G, Valvano MR, Spirito F, et al. Incidence rates of post-ERCP complications: a systematic survey of prospective studies. Off J Am Coll Gastroenterol ACG, 2007; 102(8): 1781–8.
8. Kochar B, Akshintala VS, Afghani E, Elmunzer BJ, Kim KJ, Lennon AM, et al. Incidence, severity, and mortality of post-ERCP pancreatitis: a systematic review by using randomized, controlled trials. Gastrointest Endosc, 2015; 81(1): 143–9.
9. Williams EJ, Taylor S, Fairclough P, Hamlyn A, Logan RF, Martin D, et al. Risk factors for complication following ERCP; results of a large-scale, prospective multicenter study. Endoscopy, 2007; 39(09): 793–801.
10. Chen J-J, Wang X-M, Liu X-Q, Li W, Dong M, Suo Z-W, et al. Risk factors for post-ERCP pancreatitis: a systematic review of clinical trials with a large sample size in the past 10 years. Eur J Med Res, 2014; 19(1): 1–7.
11. 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(2): 339–46.
12. Chandrasekhara V, Khashab MA, Muthusamy VR, Acosta RD, Agrawal D, Bruining DH, et al. Adverse events associated with ERCP. Gastrointest Endosc, 2017; 85(1): 32–47.
13. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ, 2021 Mar 29; 372.
14. Fujisawa T, Kagawa K, Ochiai K, Hisatomi K, Kubota K, Sato H, et al. Prophylactic Efficacy of 3- or 5-cm Pancreatic Stents for Preventing Post-ERCP Pancreatitis. J Clin Gastroenterol, 2016; 50(3): e30–4.
15. Conigliaro R, Manta R, Bertani H, Manno M, Barbera C, Caruso A, et al. Pancreatic duct stenting for the duration of ERCP only does not prevent pancreatitis after accidental pancreatic duct cannulation: a prospective randomized trial. Surg Endosc, 2013; 27(2): 569–74.
16. Lee TH, Moon JH, Choi HJ, Han SH, Cheon YK, Cho YD, et al. Prophylactic temporary 3F pancreatic duct stent to prevent post-ERCP pancreatitis in patients with a difficult biliary cannulation: a multicenter, prospective, randomized study. Gastrointest Endosc, 2012; 76(3): 578–85.
17. Sofuni A, Maguchi H, Mukai T, Kawakami H, Irisawa A, Kubota K, et al. Endoscopic pancreatic duct stents reduce the incidence of post–endoscopic retrograde cholangiopancreatography pancreatitis in high-risk patients. Clin Gastroenterol Hepatol, 2011; 9(10): 851–8.
18. Pan X-P, Dang T, Meng X-M, Xue K-C, Chang Z-H, Zhang Y-P. Clinical study on the prevention of post-ERCP pancreatitis by pancreatic duct stenting. Cell Biochem Biophys, 2011; 61(3): 473–9.
19. Ito K, Fujita N, Noda Y, Kobayashi G, Obana T, Horaguchi J, et al. Can pancreatic duct stenting prevent post-ERCP pancreatitis in patients who undergo pancreatic duct guidewire placement for achieving selective biliary cannulation? A prospective randomized controlled trial. J Gastroenterol. 2010; 45(11): 1183–91.
20. Kobayashi G, Fujita N, Imaizumi K, Irisawa A, Suzuki M, Murakami A, et al. Wire-guided biliary cannulation technique does not reduce the risk of post-ERCP pancreatitis: Multicenter randomized controlled trial. Dig Endosc, 2013; 25(3): 295–302.
21. Kawaguchi Y, Ogawa M, Omata F, Ito H, Shimosegawa T, Mine T. Randomized controlled trial of pancreatic stenting to prevent pancreatitis after endoscopic retrograde cholangiopancreatography. World J Gastroenterol WJG, 2012; 18(14): 1635.
22. Lee TH, Park DH, Park J-Y, Kim EO, Lee YS, Park JH, et al. Can wire-guided cannulation prevent post-ERCP pancreatitis? A prospective randomized trial. Gastrointest Endosc, 2009; 69(3): 444–9.
23. Bassan MS, Sundaralingam P, Fanning SB, Lau J, Menon J, Ong E, et al. The impact of wire caliber on ERCP outcomes: a multicenter randomized controlled trial of 0.025-inch and 0.035-inch guidewires. Gastrointest Endosc, 2018; 87(6): 1454–60.
24. Huang Q, Shao F, Wang C, Qi W, Qiu LJ, Liu Z. Nasobiliary drainage can reduce the incidence of post-ERCP pancreatitis after papillary large balloon dilation plus endoscopic biliary sphincterotomy: a randomized controlled trial. Scand J Gastroenterol, 2018; 53(1): 114–9.
25. Xu X-D, Dai J-J, Qian J-Q, Wang W-J. Nasobiliary drainage after endoscopic papillary balloon dilatation may prevent postoperative pancreatitis. World J Gastroenterol WJG, 2015; 21(8): 2443.
26. Swan MP, Alexander S, Moss A, Williams SJ, Ruppin D, Hope R, et al. Needle knife sphincterotomy does not increase the risk of pancreatitis in patients with difficult biliary cannulation. Clin Gastroenterol Hepatol. 2013; 11(4): 430–6.
27. Morales SJ, Sampath K, Gardner TB. A review of prevention of post-ERCP pancreatitis. Gastroenterol Hepatol (N Y), 2018; 14(5): 286.
28. Cotton PB, Lehman G, Vennes J, Geenen JE, Russell RCG, Meyers WC, et al. Endoscopic sphincterotomy complications and their

management: an attempt at consensus. Gastrointest Endosc. 1991;37(3):383–93.
29. Frank B, Gottlieb K. Amylase normal, lipase elevated: is it pancreatitis?: a case series and review of the literature. Am J Gastroenterol, 1999; 94(2): 463–9.
30. Kubiliun NM, Adams MA, Akshintala VS, Conte ML, Cote GA, Cotton PB, et al. Evaluation of pharmacologic prevention of pancreatitis after endoscopic retrograde cholangiopancreatography: a systematic review. Clin Gastroenterol Hepatol, 2015; 13(7): 1231–9.
31. Fakoya AOJ, Omenyi P, Anthony P, Anthony F, Etti P, Otohinoyi DA, et al. Stevens-Johnson syndrome and toxic epidermal necrolysis; extensive review of reports of drug-induced etiologies, and possible therapeutic modalities. Open access Maced J Med Sci., 2018; 6(4): 730.
32. Mariani A. Pharmacological prevention of post-ERCP pancreatitis: which therapy is best. JOP, 2003; 4(1): 68–74.
33. Sotoudehmanesh R, Ali-Asgari A, Khatibian M, Mohamadnejad M, Merat S, Sadeghi A, et al. Pharmacological prophylaxis versus pancreatic duct stenting plus pharmacological prophylaxis for prevention of post-ERCP pancreatitis in high risk patients: a randomized trial. Endoscopy. 2019; 51(10): 915–21.
34. Testoni PA. Pharmacological prevention of post-ERCP pancreatitis: the facts and the fiction. JOP, 2004; 5(4): 171–8.
35. Park C-H, Paik WH, Park ET, Shim CS, Lee TY, Kang C, et al. Aggressive intravenous hydration with lactated Ringer's solution for prevention of post-ERCP pancreatitis: a prospective randomized multicenter clinical trial. Endoscopy, 2018; 50(04): 378–85.
36. Smeets XJNM, Da Costa DW, Besselink MG, Bruno MJ, Fockens P, Mulder CJJ, et al. Systematic review: periprocedural hydration in the prevention of post-ERCP pancreatitis. Aliment Pharmacol Ther, 2016; 44(6): 541–53.
37. Bai Y, Ren X, Zhang X-F, Lv N-H, Guo X-G, Wan X-J, et al. Prophylactic somatostatin can reduce incidence of post-ERCP pancreatitis: multicenter randomized controlled trial. Endoscopy, 2015; 47(05): 415–20.
38. Concepción-Martín M, Gómez-Oliva C, Juanes A, Díez X, Prieto-Alhambra D, Torras X, et al. Somatostatin for prevention of post-ERCP pancreatitis: a randomized, double-blind trial. Endoscopy. 2014;46(10):851–6.
39. Wang Z, Yang Y, Cai F, Wang Y, Shi X, Ding C, et al. Is prophylactic somatostatin effective to prevent post-endoscopic retrograde cholangiopancreatography pancreatitis or hyperamylasemia? A randomized, placebo-controlled pilot trial. Chin Med J (Engl), 2013; 126(13): 2403–8.
40. Fuentes-Orozco C, Dávalos-Cobián C, García-Correa J, Ambriz-González G, Macías-Amezcua MD, García-Rentería J, et al. Antioxidant drugs to prevent post-endoscopic retrograde cholangiopancreatography pancreatitis: What does evidence suggest? World J Gastroenterol WJG, 2015; 21(21): 6745.
41. Yoo K-S, Huh KR, Kim YJ, Kim KO, Park CH, Hahn T, et al. Nafamostat mesilate for prevention of post-endoscopic retrograde cholangiopancreatography pancreatitis: a prospective, randomized, double-blind, controlled trial. Pancreas, 2011; 40(2): 181–6.
42. Katsinelos P, Lazaraki G, Chatzimavroudis G, Katsinelos T, Georgakis N, Anastasiadou K, et al. Impact of nitroglycerin and glucagon administration on selective common bile duct cannulation and prevention of post-ERCP pancreatitis. Scand J Gastroenterol, 2017; 52(1): 50–5.
43. Freeman ML. Pancreatic stents for prevention of post–endoscopic retrograde cholangiopancreatography pancreatitis. Clin Gastroenterol Hepatol, 2007; 5(11): 1354–65.