ORIGINAL ARTICLE

# Pancreatic Stent Placement for Prevention of Post-ERCP Pancreatitis in High-Risk Patients: A Systematic Review and Meta-Analysis

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## ABSTRACT

**Background and Aims** Acute pancreatitis is one common and severe complication after endoscopic retrograde cholangiopancreatography. Randomized controlled trials have reported that pancreatic stenting may efficiently prevent post-ERCP pancreatitis. **Methods** Systematic review was conducted on MEDLINE/PubMed and other databases randomized controlled trials comparing patients undergoing endoscopic retrograde cholangiopancreatography with pancreatic stent versus endoscopic retrograde cholangiopancreatography without stent. Two independent reviewers assessed the eligibility. Primary outcome is to assess the degree of severity of pancreatitis (mild, moderate, and severe) and secondary hyperamylasemia, cholangitis, abdominal pain, duration of endoscopic retrograde cholangiopancreatography and length of hospital stay. **Results** Twelve randomized controlled trials selected a total of 3.310 patients. Meta-analysis showed that pancreatic stenting reduced pancreatitis risk to PEP (mild PEP: RD 0.06, 95% CI-0.09 - 0.03; moderate PEP: RD 0.03, 95 % CI-0.06 -0.01; severe PEP: (RD 0.02, 95% CI-0.05-0.01); Hyperaylasemia (RD-0.62, 95% CI-0.65-0.59) showed statistically significant difference. Cholangitis (RD 0.03, 95% CI-0.03-0.09), abdominal pain (RD 0.10, 95% CI-0.21-0.01), length of hospital stay after ERCP (RD 1.55, 95% CI-4.39 -1.29), total duration of the procedure (RD 2.97, 95% CI-0.19-6.12), showed no statistical significance. **Conclusions** Pancreatic stent placement is effective in reducing post-endoscopic retrograde cholangiopancreatography acute pancreatitis incidence in high-risk patients.

## INTRODUCTION

The Endoscopic Retrograde Cholangiopancreatography (ERCP) is an advanced endoscopic procedure for diagnosis and treatment of several biliary and pancreatic disorders [1]. The ERCP is usually safe and carries expedited postoperative recovery. However, related complications such as post-ERCP pancreatitis (PEP), gastrointestinal bleeding/perforation, biliary infection (cholangitis), and even death may occur [2].

PEP is the most common complication following ERCP. The estimated related annual costs exceed 150 million dollars in the United States [1]. The incidence ranges from 2% to 10% and most patients present non-severe and self-limited forms of PEP. However, some patients may present severe pancreatitis and demand aggressive medical interventions, particularly those with associated risk factors [3]. Risk factors for PEP entail young age, female gender, previous history of cholangitis or pancreatitis, prior post-ERCP pancreatitis, recurrent pancreatitis, sphincter of Oddi dysfunction, repeated bile/pancreatic duct cannulations, iatrogenic procedural injury, presence of gallstones, periampullary diverticulum, and insufficient pancreatic drainage. In high-risk patients, the incidence of PEP ranges from 20% to 30% and increase length of stay and medical costs [4, 5].

Pancreatic stenting is a prophylactic intervention to avoid PEP, even though its mechanism of action is not clear [6, 7]. Previous meta-analyses [3] have shown that pancreatic stent placement benefits especially high-risk patients. However, some of those studies included both abstracts and full-text articles, and did not assess related complications, which may have led to inaccurate conclusions. Others, enrolled different populations in the same analysis (high and low risk patients) [3, 4]. Once again, there was no evaluation of complications.

Therefore, we performed this systematic review and meta-analysis to elucidate efficacy and safety of pancreatic stenting to prevent PEP in high-risk patients through a strict and clear methodology.

## MATERIALS AND METHODS

This systematic review was performed according to the recommendations of the Preferred Reporting Items

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**Keywords** Cholangiopancreatography, Endoscopic Retrograde; Pancreatitis
**Abbreviations** ERCP endoscopic retrograde cholangiopancreatography; RCT randomized controlled trials;
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for Systematic Reviews and Meta-Analysis (PRISMA) [8] and was registered in the PROSPERO database (CRD42017056261).

**Eligibility criteria**

Types of studies: Only RCTs were included. There was no language or publication dates restriction. Abstracts and studies enrolling low-risk patients were excluded [9, 10, 11].

Types of participants: Patients older than 18 years who underwent ERCP.

Types of intervention: Pancreatic stenting (intervention) versus no stent (control).

Types of outcomes: The main outcome was the incidence and severity of PEP; secondary outcomes were: hyperamylasemia rate, presence of abdominal pain, incidence of cholangitis, duration of ERCP and length of stay.

**Databases**

We searched MEDLINE/PubMed, LILACS, Embase, and Cochrane CENTRAL databases from inception to October 2016; then, a manual search was performed using references of the selected studies and previous systematic reviews regarding PEP in high-risk patients. The search strategy for MEDLINE was: (Endoscopic Retrograde Cholangiopancreatography OR ERCP OR Cholangiopancreatography, Endoscopic Retrograde OR Retrograde Cholangiopancreatography Endoscopic) AND (stent*) AND (pancreatitis OR pancreatic).

**Selection of studies**

Two independent reviewers assessed the studies for eligibility. Discrepancies were resolved by consensus with the others authors.

**Risk of bias in studies**

We analyzed the risk of bias in the studies by means of a standardized table considering randomization, allocation, blinding, withdrawal, prognostic factors, outcomes, and intention-to-treat analysis. Also, all studies were classified according the JADAD scoring system [12].

**Data extraction**

The first author extracted data from eligible studies and organized spreadsheets divided in two groups (intervention and control). A second author checked the extracted data.

**Statistical Analysis**

The analyses were carried out with RevMan 5.3 software. Risk difference (RD) expressed differences between outcomes for dichotomous variables and means difference (MD) for continuous variables using the Cochrane–Mantel–Haenszel test (95% confidence interval). Also, we used inverse variance with fixed-effect (95% confidence interval).

The heterogeneity among studies was assessed with the Higgin`s test ($I^2$). Sensitivity analysis was performed when the heterogeneity was greater than 50%. A funnel plot analysis aimed at identifying the study most likely to carry publication bias (outlier). If an outlier was identified, we excluded it and ran another analysis. If an outlier study was not distinguishable, we considered true heterogeneity and ran analysis using random-effect model to reduce the impact of heterogeneity on outcomes. Forest plots expressed graphically the results from the meta-analysis.

## RESULTS

The initial search identified 2.805 articles screened through title and abstract assessment. Fifteen articles were selected. Among them, two studies presented only abstracts [9, 10] while another did not evaluate high-risk factors [11] and thus were excluded from this meta-analysis. Finally, 12 RCTs enrolling 3.310 patients were considered eligible **(Figure 1)**. All trials were published between 1990 and 2016 and randomly assigned 1673 high-risk patients to pancreatic stenting group and 1673 to the no stent group **(Table 1)**.

Pancreatitis Severity Subgroups

*A. Mild pancreatitis:* The incidence of mild pancreatitis was higher among no stent group patients: 11% (70/632) *vs.* 4.8% (30/617). The meta-analysis showed statistical difference in mild PEP incidence between groups ($p$<0.0001) with RD of -0.06 (95% CI-0.09 -0.03) and low heterogeneity ($I^2$=0%) **(Figure 2)**. The number needed to treat was 2.5.

*B. Moderate pancreatitis:* The incidence of moderate pancreatitis was also higher in the no stent group: 4.8% (28/572) versus 1.4% (8/557). The risk difference was -0.03 (95% CI-0.06 -0.01) favoring the pancreatic stenting group ($p$<0.0001) in a highly homogenous analysis ($I^2$=0%). The number needed to treat was 5.

*C. Severe pancreatitis:* Again, the incidence of severe pancreatitis was higher in the no stent group: 2.5% (12/469) versus 0.2% (1/463). The risk difference between groups was -0.02 (95% CI- 0.04 -0.00) with $p$<0.0001 and $I^2$=47% **(Figure 2)**. The number needed to treat was 9.1.

**Hyperamylasemia**

All articles assessed hyperamylasemia rate. In pancreatic stenting group, 167 out of 710 patients (23.5%) presented increased amylase in comparison with 619 among the 721 patients from the no-stent group. The pancreatic stenting group showed significant lower risk for hyperamylasemia ($p$<0.0001) (RD -0.62, 95% CI-0.65 -0.59). The number needed to treat was 0.2. However, we detected high heterogeneity in this analysis ($I^2$=100%) but there was no distinguishable outlier in the funnel plot. Therefore, we assumed heterogeneity to be real and ran a random-effect analysis **(Figure 3)**.

**Abdominal pain**

Our results showed that 47 of the 399 patients in pancreatic stenting group developed abdominal pain compared to 69 of the 338 patients in the no-stent group

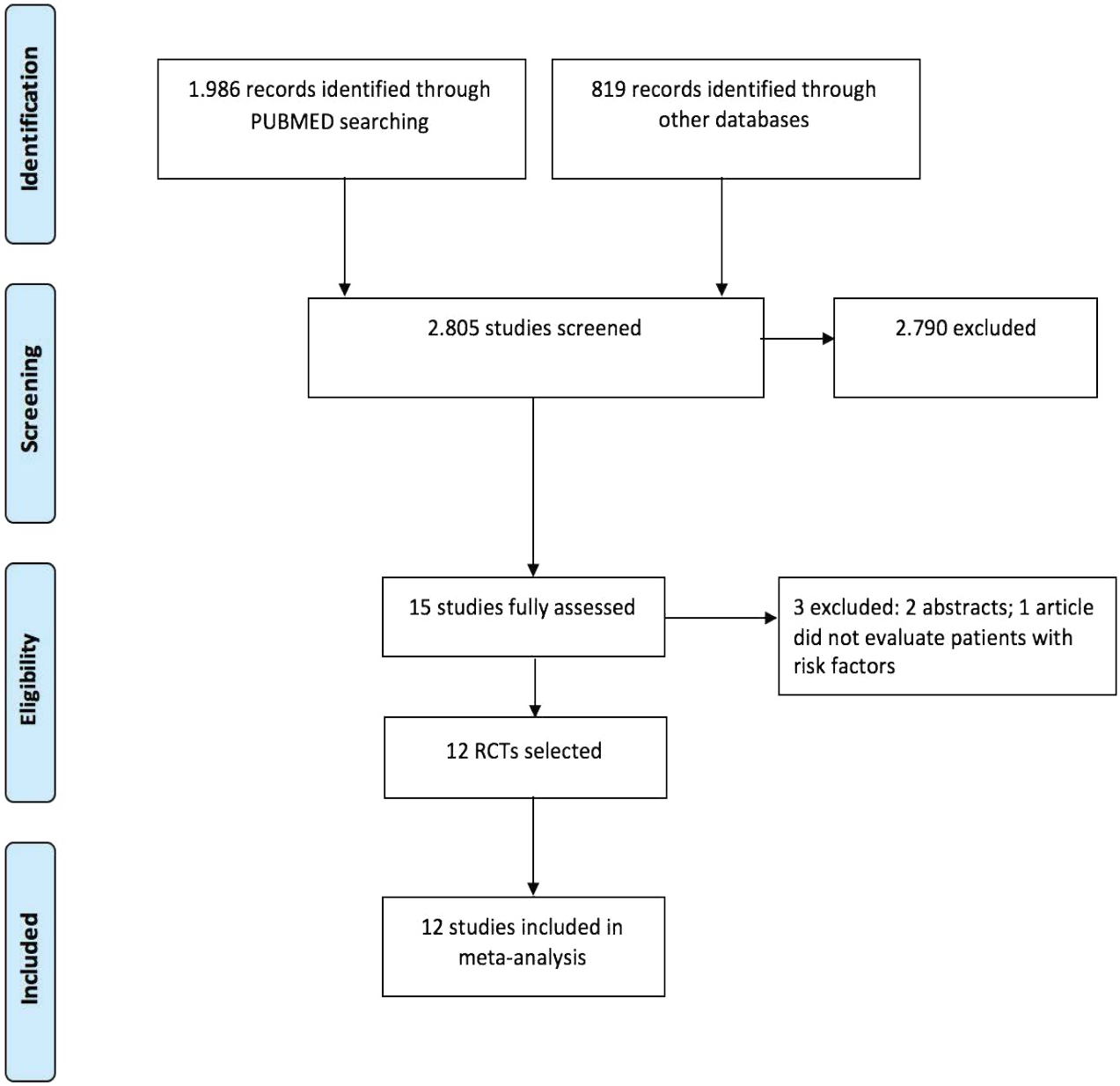


**Figure 1. PRISMA flowchart:** flow of information through the systematic review.

**Table 1.** Characteristics of the included studies.

| Characteristics of the included studies | | | | | | |
|---|---|---|---|---|---|---|
| **Ref.** | **Stent Group** | **No Stent** | **Total (n)** | **Risk Factors/Procedures** | **Types of Stent** | **Jadad** |
| Yin et al.[6] | 104 | 102 | 206 | Difficult cannulation, and endoscopic sphincterotomy | 5F (5, 7, 9 cm) | 5 |
| Kawaguchi et al.[24] | 60 | 60 | 120 | Previous history of PEP, difficult cannulation, and SOD, Endoscopic sphincterotomy | 5F (3 cm) | 4 |
| Lee et al.[25] | 50 | 51 | 101 | Difficult cannulation and endoscopic sphincterotomy | 3F (4, 6, 8 cm) | 5 |
| Sofuni et al.[26] | 94 | 103 | 197 | High-risk patients regardless of the type of risk factor | 5F (3 cm) | 5 |
| Ito et al.[27] | 26 | 35 | 61 | Difficult cannulation and endoscopic sphincterotomy | 5F (4 cm) | 4 |
| Sofuni et al.[14] | 213 | 203 | 416 | High-risk patients regardless of the type of risk factor | 5F (3 cm) | 5 |
| Tsuchiya et al.[28] | 32 | 32 | 64 | Previous history of PEP, difficult cannulation, and biliary duct | 5F (3, 4 cm) | 3 |
| Harewood et al.[29] | 9 | 10 | 19 | Ampullary adenoma and endoscopic ampullectomy | 5F (3, 5 cm) | 4 |
| Fazel et al.[22] | 38 | 36 | 74 | Difficult cannulation and endoscopic sphincterotomy | 5F (2 cm) | 2 |
| Tarnasky et al.[21] | 41 | 39 | 80 | SOD and endoscopic sphincterotomy | 5F and 7F (2, 2.5 cm) | 2 |
| Smithiline et al.[30] | 43 | 50 | 93 | SOD and biliary duct sphincterotomy | 5-7F, 2-2.5 cm | 4 |
| Cha et al.[31] | 46 | 58 | 104 | Difficult cannulation and endoscopic sphincterotomy | 5-7F, (2-2.5 cm) | 4 |

PEP post-cholangiopancreatography endoscopic retrograde pancreatitis; SOD sphyncter of oddi dysfunction

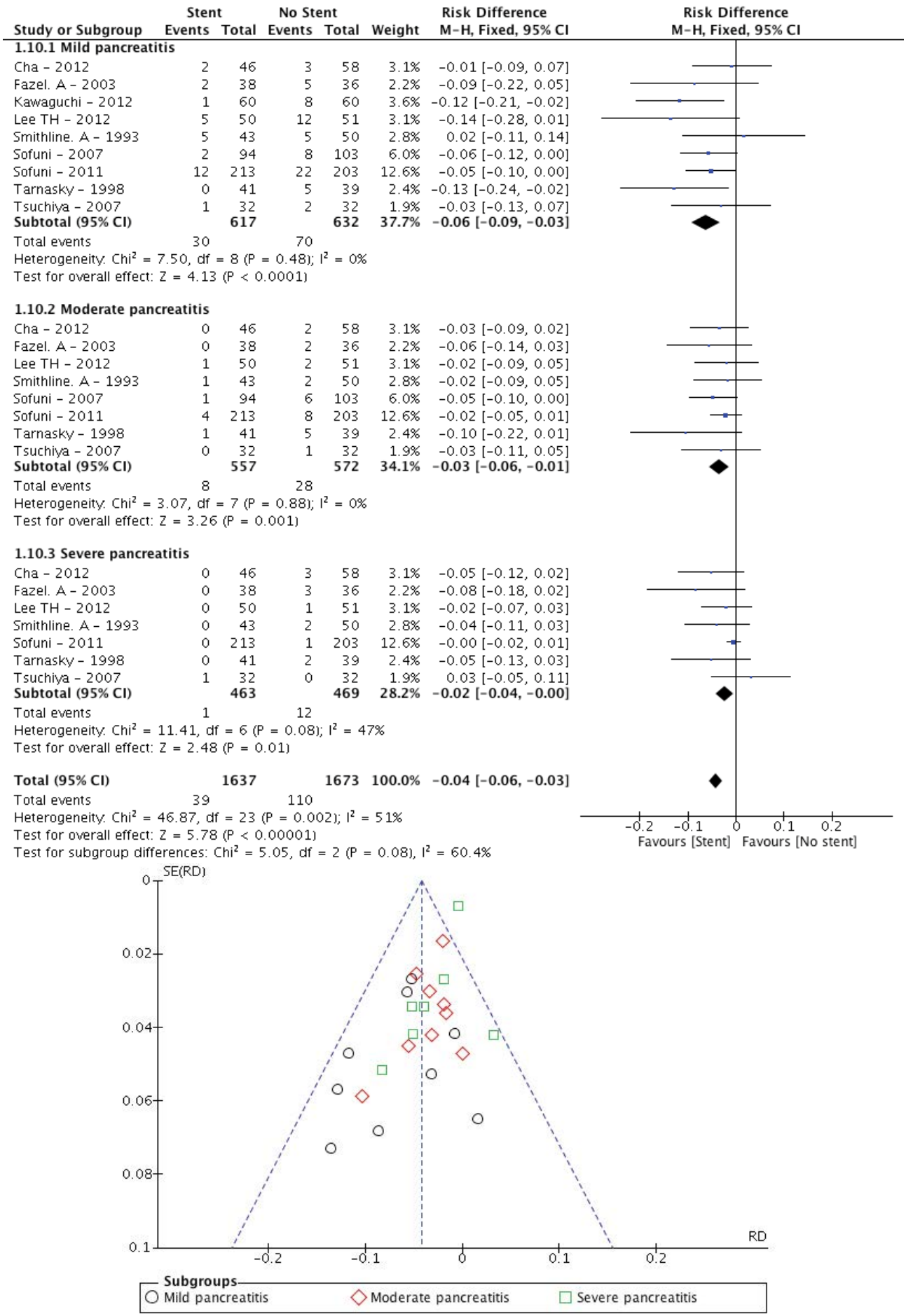


**Figure 2.** Forest plots and funnel plot. Forest plot depicting the incidence of post-endoscopic retrograde cholangiopancreatography pancreatitis (PEP) in the analyzed studies according to pancreatitis severity. **(a).** Mild pancreatitis; **(b).** Moderate pancreatitis; **(c).** Severe pancreatitis.

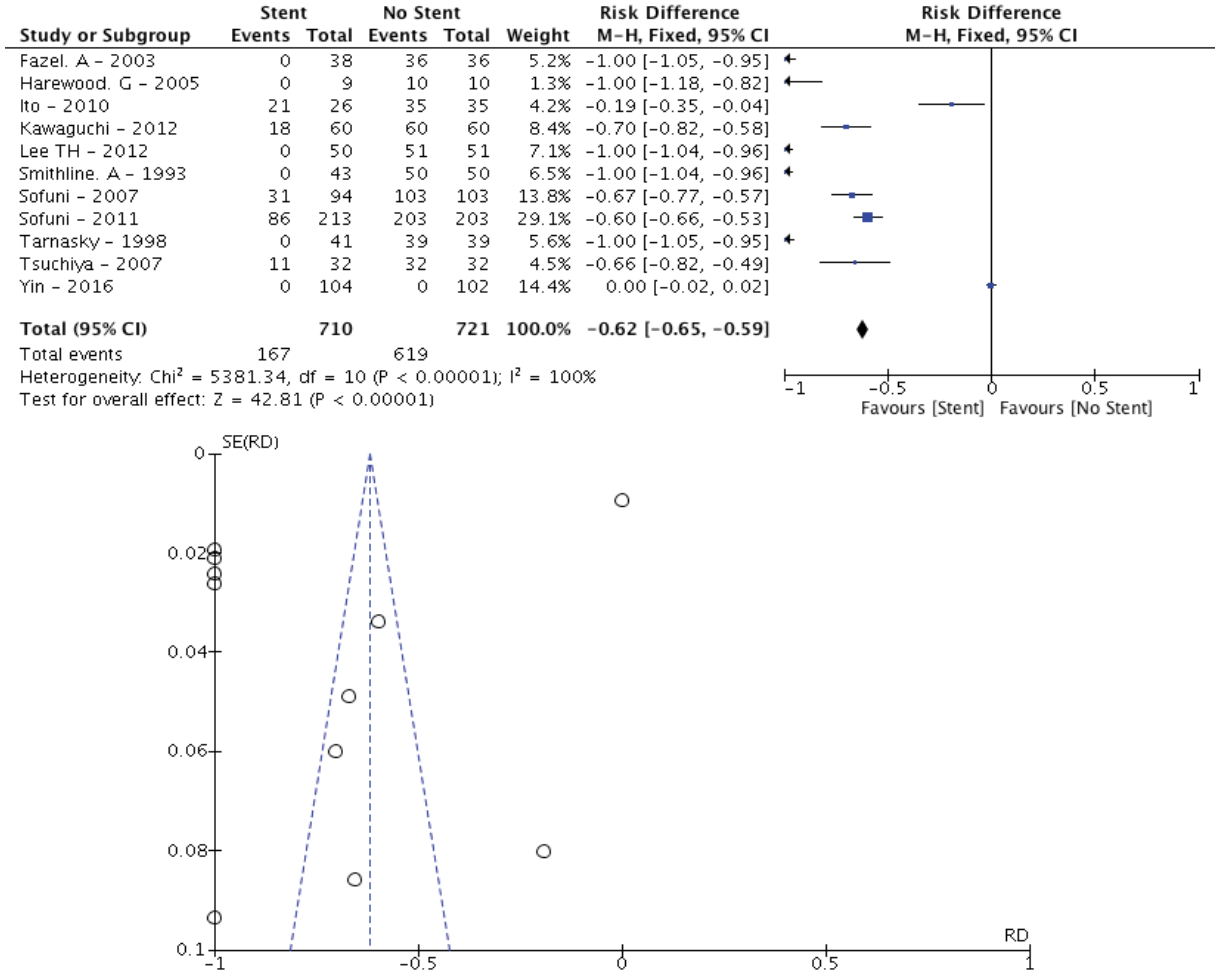


**Figure 3.** Forest plots and funnel plot. Meta-analysis showing the effects of pancreatic stent placement for hyperamylasemia.

(11.7% *vs.* 20.4%). The meta-analysis showed no statistical difference ($p$<0.08) between groups (RD-0.10, 95% CI-0.21 0.01). Again, we identified high heterogeneity ($I^2$=67%) but no study was distinguishable as an outlier after funnel plot analysis. Therefore, we assumed true heterogeneity and performed a random-effect analysis **(Figure 4)**.

### Cholangitis

Only 2 of the 67 patients (2.9%) in the pancreatic stenting group presented post-ERCP cholangitis versus none among the 74 patients in the no-stent group. The meta-analysis showed no difference ($p$<0.29) between groups (RD -0.03, 95% CI-0.03 0.09) and low heterogeneity ($I^2$=0%) **(Figure 5)**.

### Duration of ERCP

The comparison regarding the total duration of ERCP was highly homogenous ($I^2$=0%) and showed no difference between pancreatic stenting and no-stent group ($p$<0.07) (RD 2.97, 95% CI−0.19 6.12) **(Figure 6)**.

### Length of stay

The length of stay was similar between groups ($p$>0.05) with mean difference of -1.55 (95% CI-4.39 1.29). The meta-analysis showed high heterogeneity ($I^2$=99%) but since only two trial assessed length of stay, a single exclusion would impair the pooled analysis **(Figure 7)**. Therefore, we assumed it as true heterogeneity and performed a random-effect analysis.

## DISCUSSION

ERCP is central for the treatment of several biliary and pancreatic diseases. However, the endoscopic manipulation may impair the normal flow of the pancreatic duct and activate intracellular proteolytic enzymes. Also, it may cause bacterial contamination which results in chemical pancreatic injury. All those factors trigger pancreatitis [3, 4].

Pancreatitis is the most common adverse event of ERCP. PEP increases morbidity and mortality significantly, especially in severe cases. Likewise, it carries increased length of stay, which raises associated costs. The reported incidence of PEP ranges from 2% to 30% [4, 12, 13, 14, 15, 16]. This wide variation is due to differences in patient selection and procedure-related risk factors. Risk factors for PEP include female gender, age <60 years, previous history of PEP, pancreatic sphincterotomy, sphincter of Oddi dysfunction, difficult cannulation, long duration of procedure, pancreatic duct biopsy and less experienced endoscopist [17, 18].

Several drugs and techniques have been investigated to avoid PEP [18, 19, 20] and the pancreatic stenting is one of the most robust in terms of available evidence. The stent may assure the pancreatic flow in case of papillary edema

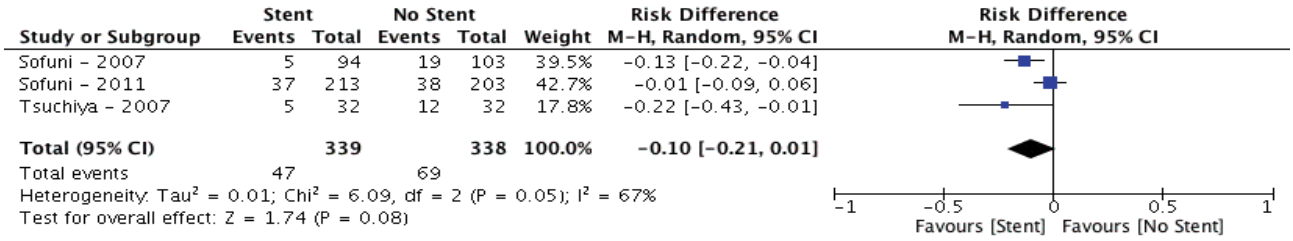


**Figure 4.** Meta-analysis showing the effects of pancreatic stent placement for abdominal pain.

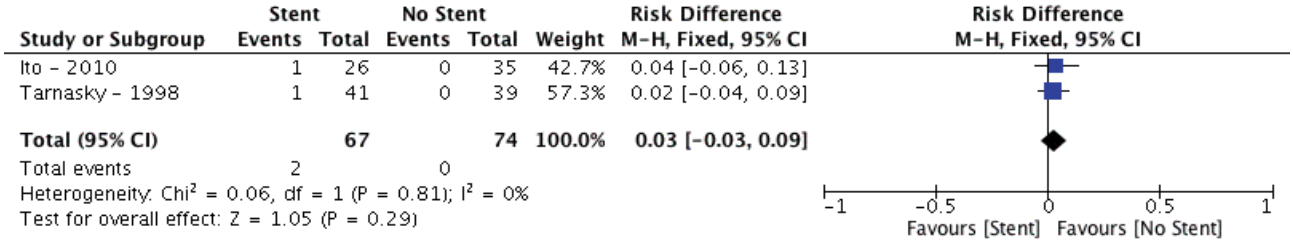


**Figure 5.** Meta-analysis showing the effects of pancreatic stent placement for cholangitis.

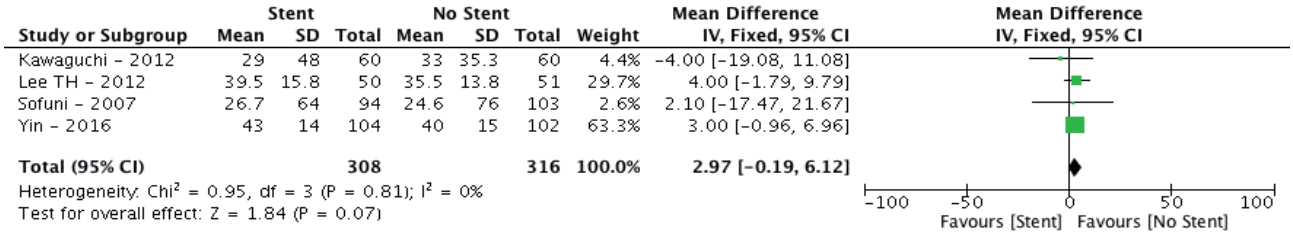


**Figure 6.** Meta-analysis showing the effects of pancreatic stent placement for duration of ERCP.

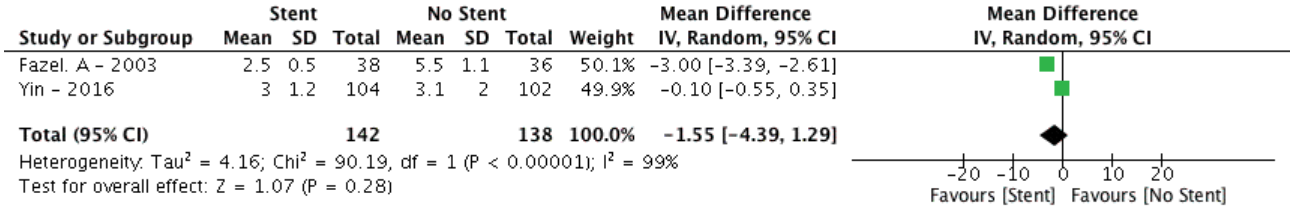


**Figure 7.** Meta-analysis showing the effects of pancreatic stent placement for length of hospital stay.

or sphincter spasms caused by the endoscopic manipulation. Possibly, this is the mechanism of action through which the pancreatic stent effectively prevent PEP [3, 16].

The trials included in our meta-analysis showed that pancreatic stenting reduced the risk of mild and moderate pancreatitis. This data is in accordance with previous meta-analyses [3, 13, 19, 20, 21, 22, 23]. However, our study demonstrated that such intervention does not affect the incidence of severe PEP, even though there was a subtle trend toward risk decrease. Possibly, the tiny severe PEP incidence might explain the lack of statistical difference between groups. Therefore, further and larger studies might change this statement.

In addition, pancreatic stenting reduced the incidence of post-ERCP hiperamylasemia. This result goes according to with from previous meta- analyses [13, 23, 24, 25, 26]. these results support the claim that post-ERCP pancreatic stent prevents pancreatitis.

Regarding abdominal pain, we showed that pancreatic stenting group was similar to no-stent group, and the difference was not statistically significant. It should be noted that abdominal pain is one of the criteria to define acute pancreatitis and, once diagnosed, patients have a longer hospital stay and costs increase proportionally. This result goes according to with from previous meta- analyses [27, 28, 29]. Moreover, the analysis of cholangitis as a post-ERCP, showed no difference between groups. The heterogeneity between the trials was low. This data is in accordance with previous meta-analyses [6, 26, 30, 31].

The mean duration of ERCP was longer in the pancreatic stent group than in the no-stent group; however, there was no statistical significance. Although the insertion of a pancreatic stent reduces PEP incidence, it is important to note that it is a challenging procedure. Difficulties may arise in the identification and cannulation of the pancreatic duct ostium, and the progression of the guidewire and the pancreatic stent itself in the duct lumen may be complex, with increasing local manipulation and duration of the procedure.

The mean length of hospital stay was shorter in the pancreatic stent group than in the no-stent group; however, there was no statistical significance. Because there was no

stratification in the length of hospital stay, it was not possible to evaluate or predict costs; therefore, prospective studies focusing on this topic should ideally be performed.

Our study has some limitations. The first we could not evaluate the risk of post-ERCP pancreatitis in patients who failed PD stent placement. Finally various lengths of stents were used, which may result in evaluation bias.

ERCP is an essential procedure for the treatment of several pancreatobiliary disorders. In our study, we demonstrated that the placement of pancreatic stents is important because it prevents post-ERCP pancreatitis (mild and moderate). In addition, no serious complications were reported in individuals in the stent group. Thus, it is assumed that post-ERCP pancreatic stent placement leads to a reduction in morbidity, mortality, and possibly costs to the health system.

## CONCLUSION

Pancreatic stenting is effective in reducing the incidence of mild and moderate post-ERCP acute pancreatitis in high-risk patients.

## Conflict of Interest

The authors have no conflicts of interests to declare.

## References


1. ASGE Standards of Practice Committee, Chandrasekhara V, Khashab MA, Muthusamy VR, Acosta RD, Agrawal D, et al. Adverses event associated with ERCP. Gastrointest Endosc 2017; 8:32-47. [PMID: 27546389]

2. Freeman ML, DiSario JA, Nelson DB, Fennerty MB, Lee JG, Bjorkman DJ, et al. Risk factors for post-ERCP pancreatitis: a prospective, multicenter study. Gastrointest Endosc 2001; 54: 425–434. [PMID: 11577302]

3. Fan JH, Qian JB, Wang YM, Shi RH, Zhao CJ. Updated meta-analysis of pancreatic stent placement in preventing post-endoscopic retrograde cholangiopancreatography pancreatitis. World J Gastroenterol 2012; 21:7577–7583. [PMID: 26140006]

4. Shi QQ, Ning XY, Zhan LL, Tang GD, Lv XP. Placement of prophylactic pancreatic stents to prevent post-endoscopic retrograde cholangiopancreatography pancreatitis in high-risk patients: A meta-analysis. World J Gastroenterol 2014; 20:7040–7048. [PMID: 24944500]

5. Freeman ML, Nelson DB, Sherman S, Haber GB, Herman ME, Dorsher PJ, et al. Complications of endoscopic biliary sphincterotomy. N Engl J Med 1996; 335: 909–918. [PMID: 8782497]

6. Yin HK, Wu HE, Li QX, Wang W, Ou WL, Xia HH. Pancreatic stenting reduces post-ERCP pancreatitis and biliary sepsis in high-risk patients: a randomized, controlled study. Gastroenterol Res Pract 2016; 13:2655–2668. [PMID: 27057161]

7. Chahal P, Tarnasky PR, Petersen BT, Topazian MD, Levy MJ, Gostout CJ, et al. Short 5Fr vs long 3Fr pancreatic stents in patients at risk for post-endoscopic retrograde cholangiopancreatography pancreatitis. Clin Gastroenterol Hepatol 2009; 7:834–839. [PMID: 19447196]

8. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA statement for reporting systematic reviews and meta-analyzes of studies that evaluate health care interventions: explanation and elaboration. J Clin Epidemiol 2009; 62: 1–34.

9. Sherman S, Earle D, Bucksot L, Weber C, Gottlieb K, Lehman G. Does leaving a main pancreatic duct stent in place reduce the incidence of precut biliary sphincterotomy-induced pancreatitis? Randomized prospective study. Am J Gastroenterol 1995; 90: 241.

10. Patel R, Tarnasky PR, Hennessy WS. Does stenting after pancreatic sphincterotomy reduce post-ERCP pancreatitis in patients with prior biliary sphincterotomy' preliminary results of a prospective randomized study. Gastrointest Endosc 1999; 49. AB80.

11. Pan XP, Dang T, Meng XM, Xue KC, Chang ZH, Zhang YP. Clinical study on the prevention of post-ERCP pancreatitis by pancreatic duct stenting. Cell Biochem Biophys 2011; 61:473–479. [PMID: 21739262]

12. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials 1996; 17:1–12. [PMID: 8721797]

13. Choudhary A, Bechtold ML, Arif M, Szary NM, Puli SR, Othman MO, et al. Pancreatic stents for prophylaxis against post-ERCP pancreatitis: a meta-analysis and systematic review. Gastrointest Endosc 2011; 73: 275–282. [PMID: 21295641]

14. 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: 851–888. [PMID: 21749851]

15. 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. Am J Gastroenterol 2007; 102: 1781–1788. [PMID: 17509029]

16. Bourke MJ, Costamagna G, Freeman ML. Biliary cannulation during endoscopic retrograde cholangiopancreatography: core technique and recent innovations. Endoscopy 2009; 41: 612–617. [PMID: 19588290]

17. Cheng CL, Sherman S, Watkins JL, Barnett J, Freeman M, Geenen J, et al. Risk factors for post-ERCP pancreatitis: a prospective multicenter study. Am J Gastroenterol 2006; 101:139–147. [PMID: 16405547]

18. Shah TU, Liddle R, Branch MS, Jowell P, Obando J, Poleski M. Pilot study of aprepitant for prevention of post-ERCP pancreatitis in high risk patients: a phase II randomized, double-blind placebo controlled trial. JOP 2012; 13:514–518. [PMID: 22964958]

19. Otsuka T, Kawazoe S, Nakashita S, Kamachi S, Oeda S, Sumida C, et al. Low-dose rectal diclofenac for prevention of post-endoscopic retrograde cholangiopancreatography pancreatitis: a randomized controlled trial. J Gastroenterol 2012. [PMID: 22350703]

20. Abdel Aziz AM, Lehman GA. Pancreatitis after endoscopic retrograde cholangiopancreatography. World J Gastroenterol 2007; 13:2655–2668. [PMID: 17569133]

21. Tarnasky PR, Palesch YY, Cunningham JT, Mauldin PD, Cotton PB, Hawes RH. Pancreatic stenting prevents pancreatitis after biliary sphincterotomy in patients with sphincter of Oddi dysfunction. Gastroenterol 1998; 115:1518–1524. [PMID: 9834280]

22. Fazel A, Quadri A, Catalano MF, Meyerson SM, Geenen JE. Does a pancreatic duct stent prevent post-ERCP pancreatitis? A prospective randomized study. Gastrointest Endosc 2003; 57:291–294. [PMID: 12612504]

23. He LX, Gong P, Bie LK. The pancreatic stents to prevent the high risk patient s from post-ERCP pancreatitis: a metaanalysis. Zhonghua Xiaohua Neijing Zazhi 2010; 27: 94-98.

24. 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 2012; 18:1635–1641. [PMID: 22529693]

25. 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: 578–585. [PMID: 22771100]

26. Sofuni A, Maguchi H, Itoi T, Katanuma A, Hisai H, Niido T, et al. Prophylaxis of post-endoscopic retrograde cholangiopancreatography pancreatitis by an endoscopic pancreatic spontaneous dislodgement stent. Clin Gastroenterol Hepatol 2007; 5:1339–1346. [PMID: 17981247]

27. 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; 45:1183–1191. [PMID: 20607310]

28. Tsuchiya T, Itoi T, Sofuni A, Itokawa F, Kurihara T, Ishii K, et al. Temporary pancreatic stent to prevent post-endoscopic retrograde cholangiopancreatography pancreatitis: a preliminary, single-center, randomized controlled trial. J Hepatobiliary Pancreat Surg 2007; 14:302–307. [PMID: 17520207]

29. Harewood GC, Pochron NL, Gostout CJ. Prospective, randomized, controlled trial of prophylactic pancreatic stent placement for endoscopic snare excision of the duodenal ampulla. Gastrointest Endosc 2005; 62:367– 370. [PMID: 16111953]

30. Smithline A, Silverman W, Rogers D, Nisi R, Wiersema M, Jamidar P, et al. Effect of prophylactic main pancreatic duct stenting on the incidence of biliary endoscopic sphincterotomy-induced pancreatitis in high-risk patients. Gastrointest Endosc 1993; 39:652–657. [PMID: 8224687]

31. Cha SW, Leung WD, Lehman GA, Watkins JL, McHenry L, Fogel EL, et al. Does leaving a main pancreatic duct stent in place reduce the incidence of precut biliary sphincterotomy-associated pancreatitis? A randomized, prospective study. Gastrointest Endosc 2013; 77: 209–216. [PMID: 23084272]