

Format for ANSWERING REVIEWERS

April 26, 2019



Dear Editor:

Please find enclosed the edited manuscript in Word format (file name: 47015 Revised Manuscript 2019.4.26).

Title: Pancreatic stents to prevent post-ERCP pancreatitis: a meta-analysis

Author: Mitsuru Sugimoto, Tadayuki Takagi, Rei Suzuki, Naoki Konno, Hiroyuki Asama, Yuki Sato, Hiroki Irie, Ko Watanabe, Jun Nakamura, Hitomi Kikuchi, Mika Takasumi, Minami Hashimoto, Takuto Hikichi, and Hiromasa Ohira

Name of Journal: *World Journal of Meta-Analysis*

ESPS Manuscript NO: 47015

The manuscript has been improved according to the reviewers' suggestions:

1 The format has been updated.

2 Revisions have been made according to the reviewers' suggestions.

Reviewer 1: I commend the authors for their work. They have tried to review the existing evidence for the use of the pancreatic duct stents to prevent PEP. I feel that there are several limitations to their work which they should try to better address:

1. Study definitions: the authors should define what they mean by PEP and severe PEP and if the trials they have included also have followed the same definition

Response: Thank you for the valuable comment. We added the definition of PEP (Lines 172-187)

2. Study characteristics: the authors have not specified if they took all patients or high risk patients- most of the trials that the authors have looked at have included high risk patients only. This also goes in line with the very high risk of PEP that the authors have found in the control group. Maybe they could do a subgroup to look at the two groups differently.

Response: Thank you for this comment. Originally, a prophylactic pancreatic stent was inserted into high-risk patients. Therefore, all patients involved in the RCTs were high-risk patients. We modified the description (Lines 101-106).

3. Why did the authors use intention to treat? I think a per-protocol method would be much better as that would allow us to include patients who failed prophylactic PEP stenting as well.

Response: Thank you for this comment. Because of attrition bias, the intention to treat

method should be used in meta-analysis.

4. Did any of the trials use rectal indomethacin or other concurrent PEP prophylaxis strategies?

Response: Thank you for this comment. Proteinase inhibitor or antibiotics were administered; however, rectal indomethacin was not used in any study (Lines 166-168).

5. Minor typographical errors

Response: Thank you for this comment. We have revised the errors.

Reviewer 2: ARTICLE: Pancreatic stents to prevent post-ERCP pancreatitis: a meta-analysis Less than four years ago a very nice article has been published on the same subject less than four years ago, and the conclusions were identical to those in the proposed manuscript (Fan et al. Updated meta-analysis of pancreatic stent placement in preventing post- endoscopic retrograde cholangiopancreatography pancreatitis. *WJG* 2015; 21(24): 7577-83). Although the article titled "Pancreatic stents to prevent post-ERCP pancreatitis: and meta-analysis" is well written, in the context of my opinion, the pancreatic stent problem in post-ERCP pancreatitis is "already overwhelmed" so that the manuscript should not be published in the *WJG*.

Response: This comment is mistaken. First, the recent previous meta-analyses involved a non-RCT by Cha et al. (*Gastrointestinal Endosc* 2013, Page 209-216). In the study by Cha et al., the no stent group was not randomized (*Gastrointestinal Endosc* 2013, Page 212, Figure 1). The stent group or stent-removed group was randomized. In this report, the intervention was different from other RCTs. The following meta-analyses included the non-RCT.

1 Mazaki T, Mado K, Masuda H, Shiono M. Prophylactic pancreatic stent placement and post-ERCP pancreatitis: an updated meta-analysis. *J Gastroenterol* 2014; **49**(2): 343-355 [PMID: 23612857 DOI: 10.1007/s00535-013-0806-1]

2 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* 2015; **21**(24): 7577-7583 [PMID: 26140006 PMCID: PMC4481455 DOI: 10.3748/wjg.v21.i24.7577]

Reviewer 2 said that the meta-analysis was already updated by Fan et al. However, the above two meta-analyses included not only a non-RCT but also articles consisting of only the abstract. Originally, meta-analysis should include RCTs with full-length articles.

Furthermore, our manuscript number 47015→48671 is the only meta-analysis that involves only RCTs with full-length article and the most recent RCT by Yin et al. We precisely confirmed the contents of each RCT, and therefore, we were able to remove the non-RCT by Cha et al.

We added the meta-analysis written by Fan et al. in the references and the abovementioned contents (Lines 111-113).

Reviewer 3: In this meta-analysis the authors confirm the efficacy of pancreatic stent to prevent post-ERCP pancreatitis. I think the manuscript is interesting and well-written.

Response: Thank you for the review of our manuscript.

Reviewer 4: This paper described the prevention of post-ERCP pancreatitis by stenting, but no further explore the cause of its occurrence, especially for the prevention of post-ERCP pancreatitis in high-risk groups, which should be supplemented.

Response: In addition to pancreatic stents, several methods exist for preventing PEP. However, that is different from the topic of this meta-analysis.

Thank you again for publishing our manuscript in the *World Journal of Meta-analysis*.

Sincerely,
Tadayuki TAKAGI, MD, Associate Professor
Department of Gastroenterology
Fukushima Medical University, School of Medicine
1 Hikarigaoka, Fukushima City, Fukushima Prefecture
960-1295, Japan
Tel.: +81-24-547-1202 Fax: +81-24-547-2055
E-mail: daccho@fmu.ac.jp