

Dear editor:

Thank you very much for your letter and the comments from reviewers and editors about our manuscript. We have revised the manuscript according to the comments.

Detailed responses to comments and suggestions from reviewers and editors are as follows:

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: Standardization of stent size, 10Fr, was not enough to be a excellent paper.

Thanks to the reviewer's comment.

Plastic stents with an outer diameter of 10 Fr are commonly used in clinical practice, so we first made this type of anti-reflux plastic stents and carried out clinical trials. The use of different types of anti-reflux plastic stents is more conducive to personalized treatment of patients, so we also try to make an anti-reflux valve suitable for plastic stents with a smaller outer diameter (8.5 Fr or 7 Fr). However, due to the need to consider both the patency and anti-reflux function of the plastic stents, it is very difficult to make an anti-reflux valve suitable for plastic stents with a smaller outer diameter, and we are still trying to make it. After different types of anti-reflux plastic stents are successfully developed, we will also conduct clinical trials to evaluate their safety and efficacy.

Reviewer #2:

Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: As a sequel to their preliminaries study, the authors are trying to clarify the usefulness of the new anti-reflux plastic stent in a larger number of cases. I think this stent is very promising and interesting. However, I think that there are major problems with the definition and the method of case accumulation.

1. This study is reported to be included 172 cases, but it is actually a review of

172 ERCP procedures in 133 patients. This content is only listed in Table 1 and is very difficult to understand. I think the results of the first stent alone in 133 patients should be described, because the second stent may have a shorter time to recurrent biliary obstruction due to debris.

Thanks to the reviewer's suggestion.

There is indeed a risk of shorter stent patency after the second or third stent placement, and repeat inclusion of patients may increase selection bias and results bias. Therefore, in the revised manuscript, only patients who underwent first endoscopic biliary stenting were included in the final analysis. The results of the first stent alone in 133 patients were described in detail in the Results Section. The brief results are as follows: sixty-seven patients in the ARPS group and 66 patients in the TPS group were included. Fewer patients experienced stent-related cholangitis in the ARPS group than that in the TPS group (8 vs. 18 patients;  $P=0.030$ ). The median time till the onset of first stent-related cholangitis was later in the ARPS group than that in the TPS group (128.5 vs. 76 days;  $P=0.039$ ). The cumulative median stent patency in the ARPS group was 185 days, which was significantly longer than that in the TPS group (133 days;  $P=0.001$ ).

2. You should describe how many times each stent exchange was performed on how many patients. Did any patients be inserted a different stent for the first and second stent? Please state clearly.

Thanks to the reviewer's suggestion and question.

In the revised manuscript, only patients who underwent first endoscopic biliary stenting were included in the final analysis; thus, the results of 133 ERCPs in 133 patients were analyzed. The results of stent exchange were not included in the revised manuscript.

3. I think that the definition of "Stent-related cholangitis" and "Stent dysfunction" are not clearly distinguished. Please refer to the following paper to make a clear distinction. Isayama H, Hamada T, Yasuda I, et al. TOKYO criteria 2014 for transpapillary biliary stenting. Digestive Endoscopy 2015; 27: 259-264

Thanks to the reviewer's suggestion.

After referring to the above mentioned paper, we redefined the definition of

stent-related cholangitis. In the early stage of stent occlusion, bacteria from the duodenum refluxed into the biliary tract and colonized, thus causing non-stent dysfunction cholangitis. After stent occlusion, biliary obstruction and bacteria refluxed from duodenum into the biliary tract via stent work together to cause stent dysfunction cholangitis. Therefore, the new definition is as follow: Stent-related cholangitis, including non-stent dysfunction cholangitis and stent dysfunction cholangitis, was considered if patients developed symptoms of acute cholangitis during the follow-up period and post-ERCP cholangitis was excluded. Non dysfunction cholangitis was diagnosed when acute cholangitis observed and when there was no definite finding of stent occlusion or migration. Post-ERCP cholangitis was defined as cholangitis that developed within two weeks after ERCPs without definite findings of stent dysfunction, related to ERCP procedures,. The diagnostic criteria for acute cholangitis refer to Tokyo Guidelines 2018.

4. For "Stent patency", I think it is enough to state the cumulative median calculated by Kaplan-Meier method and its comparison. I think "There were no ~( $P=0.084$ ) between the two groups." in the "Stent patency" section is unnecessary. Delete them, leaving only the results you consider necessary.

Thanks to the reviewer's suggestion.

We have delete the unnecessary results from the "Stent patency" Section.

5. Figure 4; Please list the number of cases for the entire group, not the censored number. And all Kaplan-Meier curves should be marked with the number at risk (Figure 4 and Figure 5).

Thanks to the reviewer's suggestion.

We have showed the patients at risk on all Kaplan-Meier curves in the revised manuscript. The number of patients for the entire group was also listed.

Reviewer #3:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: This is a retrospective study of anti-reflux and conventional plastic stents for both malignant and benign biliary obstructions.

1.The authors previously published a RCT and demonstrated superiority of this anti-reflux stent. This RCT cohort was also included in this retrospective study. However, the evidence level of the previous RCT is higher than this retrospective study. The authors may want to focus on benign biliary strictures, or add additional analysis to explore subgroups who would benefit best from anti-reflux plastic stents.

Thanks to the reviewer's comments.

In the previous RCT study, we focused on the patency of the new anti-reflux plastic stent and included patients with distal malignant biliary strictures for analyses. In the present study, we not only focused on stent patency, but also focused on stent-related cholangitis. Patients with benign or malignant biliary strictures were all included for analyses.

2.I am somewhat confused by stent patency and stent-related cholangitis. In general, patients with cholangitis have stent occlusion or vice versa when plastic stents are placed. Why those Kaplan-Meier curves are so different between stent patency and stent-related cholangitis?

Thanks to the reviewer's question.

Stent-related cholangitis not only included non-stent dysfunction cholangitis (Isayama H, Hamada T, Yasuda I, et al. TOKYO criteria 2014 for transpapillary biliary stenting. Digestive Endoscopy 2015; 27: 259-264 ), but also included stent dysfunction cholangitis. In the early stage of stent occlusion, bacteria from the duodenum refluxed into the biliary tract and colonized, thus causing non-stent dysfunction cholangitis. After stent occlusion, biliary obstruction and bacteria refluxed from duodenum into the biliary tract via stent work together to cause stent dysfunction cholangitis. In the revised manuscript, 2 patients had non-stent dysfunction cholangitis and 6 patients had stent dysfunction cholangitis in the anti-reflux plastic stent group. Six patients had non-stent dysfunction cholangitis and 12 patients had stent dysfunction cholangitis in the traditional plastic stent group. According to the definition of stent-related cholangitis and stent patency, the difference of Kaplan-Meier curves between stent patency and stent-related cholangitis is understandable.

3. How was the durability of anti-reflux valve? Was the valve still intact at the time of reinterventions?

Thanks to the reviewer's question.

In the present study, the stent patency was used to indirectly reflect the durability of anti-reflux valve. The results showed that the anti-reflux plastic stent had longer stent patency than the traditional plastic stent without anti-reflux valve. It should be noted that when placing an anti-reflux plastic stent, the valve should be fully extended to prevent uncomplete expanded from obstructing bile drainage. According to our experience, some of the valves are still intact at the time of reinterventions, while others will be folded due to the attachment of large plant fibers and other intestinal contents.

4. More than half of patients were excluded from the analysis, especially because of plastic stents other than 10Fr. This should inevitably cause selection bias. Although the authors claimed there were no significant statistical differences between two groups, the authors may want to perform propensity score match analysis.

Thanks to the reviewer's comments.

Plastic stents with an outer diameter of 10 Fr are commonly used in clinical practice, so we first made this type of anti-reflux plastic stents and carried out clinical trials. We also tried to make an anti-reflux valve suitable for plastic stents with a smaller outer diameter (8.5 Fr or 7 Fr). However, due to the need to consider both the patency and anti-reflux function of the plastic stents, it is very difficult ,and we are still trying to make it.

Only anti-reflux plastic stents with 10 Fr are available, so the traditional plastic stents other than 10 Fr were excluded. There was no significant difference in baseline between the two groups; thus, the two groups were comparable. Propensity score analysis will be performed when there was significant difference between the two groups in baseline.

Science editor: 1 Scientific quality: The manuscript describes a retrospective study of the new anti-reflux plastic stent to reduce the risk of stent-related cholangitis in the treatment of benign or malignant biliary strictures. The topic is within the scope of the WJG. (1) Classification: Grade C, Grade B and Grade D; (2) Summary of the Peer-Review Report: The authors are trying to clarify the usefulness of the new anti-reflux plastic stent in a larger number of cases. It is very promising and interesting. However, the questions raised by

the reviewers should be answered; and (3) Format: There are 3 tables and 5 figures. (4) References: A total of 35 references are cited, including 3 references published in the last 3 years; (5) Self-cited references: There are 6 self-cited references. The self-referencing rates should be less than 10%. Please keep the reasonable self-citations that are closely related to the topic of the manuscript, and remove other improper self-citations. If the authors fail to address the critical issue of self-citation, the editing process of this manuscript will be terminated; and (6) References recommend: The authors have the right to refuse to cite improper references recommended by peer reviewer(s), especially the references published by the peer reviewer(s) themselves. If the authors found the peer reviewer(s) request the authors to cite improper references published by themselves, please send the peer reviewer's ID number to the editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately. 2 Language evaluation: Classification: Grade B, Grade B and Grade B. A language editing certificate issued by MedSci was provided. 3 Academic norms and rules: The authors provided the Biostatistics Review Certificate, the Institutional Review Board Approval Form, and the written informed consent. No academic misconduct was found in the Bing search. 4 Supplementary comments: This is an unsolicited manuscript. The study was supported by 1 grant. The topic has not previously been published in the WJG. 5 Issues raised: (1) The title is too long, and it should be no more than 18 words; (2) The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s); (3) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor; (4) The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text; and (5) The scientific quality can't meet the requirement of WJG. 6 Recommendation: Transferring to the WJCC.

Thanks to the science editor's comments.

There was one self-cited reference in the revised manuscript. We think the 36 references are all reasonable.

We have shortened the title of the manuscript. "New anti-reflux plastic stent to reduce the risk of stent-related cholangitis in the treatment of biliary strictures".

We have deleted the funding from the manuscript.

We have provided original pictures that can be reprocessed. The file name was "67958-Figures.pptx".

We have added the "Article Highlights" section at the end of the main text.

We believe that this paper will be of interest to the readership of WJG because we believe our study aligns with the philosophies of the Journal, and that our results will be valuable to patients and endoscopists alike. We hope the editor could reconsider the publication of the revised manuscript in WJG.

Company editor-in-chief: I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Gastroenterology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. The title of the manuscript is too long and must be shortened to meet the requirement of the journal (Title: The title should be no more than 18 words).

Thanks to the company editor-in-chief's comments.

We have shortened the title of the manuscript ("New anti-reflux plastic stent to reduce the risk of stent-related cholangitis in the treatment of biliary strictures"), which was no more than 18 words.

We believe that this paper will be of interest to the readership of WJG because we believe our study aligns with the philosophies of the Journal, and that our results will be valuable to patients and endoscopists alike. We hope the editor could reconsider the publication of the revised manuscript in WJG.