

March 11, 2015

Ya-Juan Ma
Science Editor, Editorial Office
World Journal of Gastroenterology

RE: Manuscript NO: 16174 revision 1

Dear Ya-Juan Ma:

We appreciate the constructive comments from your three reviewers. As suggested, we have made revisions to the manuscript long the lines of each of their comments. We have highlighted those in yellow to show where changes have been made and have made a point-by-point response to each of the reviewers.

This article was a reveiw of sphincter of Oddi dysfunction. The clinical background was well written and also mentioned about the latest studies and issues. However, authors should mention about the medication for SOD. What kind of medication might improve symptoms? For, sphincter of Oddi Type III, what kind of treatment should be performed?

In the initial manuscript on Page 10, the issue of medical therapies was discussed. There is very little published data on the use of these medications which I have cited. In addition, I had in the initial manuscript the use of antidepressant medications which has not been studied but which we commonly employ. We thought that would be useful for the reader. We also commented on the use of botulinum toxin in reference to this. I do not think there are any additional medications to cite. However, we have added an addition sentence to the end of that paragraph which is, I think, along the lines of what the reviewer wants. That is, use of medication since it appears that endoscopic treatments are likely not effective.

Overall the review is well-written, however certain changes/additions would further improve the quality of this review article. 1. Page 5- "Type II patients have abnormal liver tests and/or biliary dilatation but not both potentially suggesting a sphincter disorder" "and/or" should be changed to "or" 2. Page5- "In these patients manometric findings of sphincter hypertension can be found in to 55 - 65% (11-13)." add "up to 55-65%" 3. Page 6- rephrase the last paragraph regarding the reproducibility of the manometric findings to make it easier for readers to understand (Khashab et al. Endoscopy 2010;42:369-74. PMID 19967632) 4. Page 21- Delete reference #40 after reference #44 5. Author should make distinction regarding objective "biliary" AND "pancreatic" findings in Types I and II SOD. Also, difference in clinical presentations between biliary and pancreatic SOD/sphincter hypertension, and potential implications for treatment. Discuss selective vs. dual sphincterotomies in these 2 subgroups. 6.

The review article predominantly focuses on the advances in understanding of Type III SOD and lack of efficacy of sphincterotomy (based on EPISOD study), without significant discussion about newer studies and newer approaches for Types I and II, therefore, might be appropriate to the change the title of the review to focus on Type III .

- 1.) The change on Page 5 has been made.
- 2.) We have made the appropriate change.
- 3.) We have rephrased the paragraph in the hopes of making this clearer.
- 4.) Reference 40 at the end has been deleted. Number 40 in the text is correct.
- 5.) We have added the pancreatic findings to the biliary findings in Table 1. As noted, this manuscript principally focuses on Type III SOD. Thus we will leave the information regarding the pancreatic types in the table but not discuss them further. The issue of pancreatic SOD could be an entire manuscript in and of itself. I believe this is what the reviewer is referring to when discussing selective versus dual sphincterotomies.
- 6.) To our knowledge there is no new information on Types I and II SOD and thus this manuscript focuses on Type III SOD. The title has been changed as suggested.

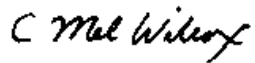
Comments for authors The Author tried to summarize the present situation of biliary SOD classification and treatment and succeeded it. This manuscript was well arranged based on the evidences and easily understandable. I have some requests for improving it more. Major comments 1. The author declared no COI. However, this manuscript has an aspect of the introduction of his RCT study (ref.7). Therefore, there is possibility not to fairly evaluate the value of the study. I will recommend describing his authority of the study anywhere in the manuscript. 2. Please put subtitles in each paragraph. 3. Many important papers related to SOD were appeared in the manuscript including retrospective and RCTs. Please summarize them into some tables for easy to understand. 4. The author mainly mentioned biliary SOD in the manuscript as "SOD". In the beginning part of the paper, the definition and the clinical criteria of SOD based on ROME III (eg. Gastroenterology. 2006;130(5):1498) should be explained. 5. Please put "RAPID scale" in the manuscript. Readers must be interested in it. Minor comments 1. Typo p.4 l.6 ""though" through? 2. Table 1 is not easy to understand. Please revise it (eg. both; eather; non, or 2; 1; 0).

- 1.) I understand the comment of the reviewer regarding conflicts of interest since I was involved in the EPISOD study.
- 2.) Subtitles have been added throughout.
- 3.) The most important papers are the two well done were on Type II SOD and those have been included in Table 2.
- 4.) The ROME criteria have been better explained on Page 3-4 and a new reference added.
- 5.) The rapid scale has now been discussed in the manuscript (see Page 8) and the appropriate reference has been added.
- 6.) Though has been changed to through.

7.) The Table has been adjusted to include pancreatic disease and hopefully by this addition it will be easier to understand.

We hope our changes have improved the quality of the manuscript. If there are any additional changes after your review, we will of course make them. I also need to send the audio core tip which I will do.

Sincerely,

A handwritten signature in black ink that reads "C Mel Wilcox". The signature is written in a cursive, slightly slanted style.

C. Mel Wilcox, M.D., M.S.P.H.
Professor of Medicine and Director
Division of Gastroenterology and Hepatology

CMW/sdd



**School of Medicine
Department of Medicine
Division of Gastroenterology and Hepatology**



April 9, 2015

Ya-Juan Ma
Science Editor, Editorial Office
World Journal of Gastroenterology

RE: Manuscript NO: 16174

Dear Dr. Ma:

We appreciate your review of our submission. You made one remark that you would like us to note that sphincter of Oddi type III does not exist in the tables. However, this conclusion is my conclusion based upon the literature. I believe it will be up to the next ROME Committee meeting where perhaps a reclassification is performed and they delete SOD Type III. Until then I believe the tables are accurate. The main point of the entire review is to raise the potential issue that we need to think of new approaches to the patient with right upper quadrant pain and normal imaging and laboratory tests rather than ERCP and manometry.

I hope my comments make sense and that we can leave the manuscript as is. Thank you for the opportunity to publish in the *World Journal of Gastroenterology*.

Sincerely,

C. Mel Wilcox, M.D., M.S.P.H.
Professor of Medicine and Director
Division of Gastroenterology and Hepatology