

Lian-Sheng Ma, President and Company Editor-in-Chief
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Dear Prof. Lian-Sheng Ma

Thank you for your prompt reply revised all valuable comments concerning about our manuscript for us.

And I have revised our manuscript according to your reviewer's comments as soon as possible. Below I outline the revision that were made.

We hope the manuscript is now suitable for publication. And we look forward to your decision.

Thank you in advance for your consideration.

A. Suggestion of reviewer 1

1. The usage of "metaplastic polyp"

We deleted the word "metaplastic polyp" in the first line of introduction. This pointed was also by reviewer 2, 3.

2. The definition of SSA and SSP

We added the paper written by Dr. Quirke et al Virchows Arch 2011 as reference number 9 in reference page. And also the comments about the usage the word "adenoma" of SSA was described in page 4.

B. Suggestion of reviewer 2

1. The recommendation the title name about "sessile serrated lesion"

We changed the title name from "Sessile Serrated Lesions" to "Serrated Polyps". This pointed was also by reviewer 3.

2. About the definition of hyperplastic polyps (HPs) as a non-neoplastic lesions

We apologize very confused you about the phrase Line 1 to 3 in the introduction. It is afraid that it is confused to use this definition (HPs is non-neoplasia) by using this phrase. But HPs was defined as non-neoplastic lesions and it has been not indication for endoscopic treatment before the proposal the serrated adenoma in 1990 and SSA in 2003. So we used this phrase to explain the necessity of endoscopic treatment concerning about the serrated polyps as an introduction.

3. About the mentioned “MVHP is not common on proximal colon”

It is not correct above mentioned. Please see the table of Patai AV et al. World J Gastroenterol 2013. In general SSA is originated from MVHP at proximal colon. In contrast TSA is caused from GCHP at distal colon.

4. The inappropriate using about the using “I” or “my group” in manuscript

We appreciate to point out this inappropriate using these words. We changed the correct words at all.

5. The usage of “metaplastic polyp”

This pointed was also by reviewer 1, 3. And we deleted this word.

6. The change the word “gland cavities” to “crypts”

We replaced the “crypts” in page 3.

7. Replace the usage the word “tumor” to “polyp”

We changed “tumor” to “polyp” in page 7

8. Concerning about the “small sized “ polyp

We changed the more clearly about the size in page 9.

9. Histological description about TSA

We apologize the confusing about the histological criteria on TSA. Described the histological criteria in page 4 is the proposal about the serrated adenoma, which is defined as the neoplastic lesion by Longacre in 1990. At first, we wanted to introduce the criteria to differentiate them of SSA.

10. About the single entity of SSA/P

We changed this phrase as mentioned in page 5.

11. The usage of the word “non-neoplastic”

We changed “Non-neoplastic lesion” to “Most of HPs” in page 6.

12. Subchapter about the TSA and SSA/P

We changed the order of SSA/P and TSA as mentioned.

13. The necessity of additional revision and newly reference paper about for indication concerning about the endoscopic treatment.

We want to apologize for lack of explanation about the indication for treatment. And we changed the phrase, ‘there are no established rules ...’. And also, we described about the indication for endoscopic treatment in accordance with AGA and European guideline with additional flow chart about SSA/P in Table 2 as your suggestion and reviewer 1, 3 as well at page 8.

14. Inappropriate about the review of molecular pathway and Ki-67 expression

We deleted the phrase described about the molecular pathway including Ki67 explanation.

15. About the phrase “ 90% of SSA/P lesions are associated with cytological dysplasia”

We also want to apologize the difficult to understand from this phrase. We only wanted to describe the AFI findings about SSA/P with cytological dysplasia. In other words, it is suggested to possibility to differentiate neoplastic from non-neoplastic SSA/P lesion, if we use the AFI method. Therefore, we changed the explanation about the phrase, completely.

16. About reference

We deleted the reference number 53. This point was also suggested by reviewer 3.

17. About the Additional description about the histoogcal findings in Figure 1.

We added the histological description for HP findings in Figure 1 at page 15.

18. About the presentation of pathological findings by high power view at Figure 4-i

We replaced the high power view of pathological finding. We are very sorry for difficult to understand.

C. Suggestion of reviewer 3

1. The suggestion about the title name about “sessile serrated lesion”

We changed the title name from “Sessile Serrated Lesions” to “Serrated Polyps”. This problem was also pointed by reviewer 2.

2. The inappropriate using about the using “I” or “my group” in manuscript

We appreciate to point out this inappropriate using these words. We changed the correct words at all.

3. The usage of “metaplastic polyp”

This problem was also pointed by reviewer 1 and 2. So we deleted this term.

4. About the origin about SSA/P and TSA

We can agree with your mentioned, which is described about the differently pathway with TSA and SSA/P. We are thinking that SSA/P is originated from MVHP, too. In contrast, TSA is derived from GCHP as your description. And we appreciate for teaching some additional reference paper. But we deleted about the description about the molecular pathway including the findings about Ki-67 stain in accordance with reviewer 2 in this time.

5. About reference

We deleted the reference number 53 and 57. This point was also suggested by reviewer 3.

6. The necessity of additional explanation concerning about the endoscopic treatment in accordance with European guideline.

We appreciate for your valuable comment. We added the description about the

European guideline additional flow chart about SSA/P at Table 2 as your suggestion and reviewer 1, 2 at page 8.

7. Necessity to show the data concerning about the sensitivity, specificity and accuracy for the diagnosis of SSA/P by using IEE method.

We added the method for diagnosis of SSA/P with using the flow chart in Table 2. And also we added to show our data when using IEE observation in conclusion (page 10).

8. About the several misspelling and grammatical mistakes

We also very apologize for our insufficient ability using in English. Our manuscript has already checked up by native editing before the submitted. But we asked to check up our manuscripts again before this submitted of revised manuscript.

Sincerely yours,
Shoichi Saito

To Dear reviewer 1:

Thank you for your valuable suggestion for our manuscript. And I changed the several points in accordance with your indication. Please check up for them.

And we very, very agreed with your suggestion about the definition and usage the word "SSA". So we cannot understand the WHO classification, two divided into with and without cytological dysplasia for SSA/P. If we use the word "adenoma" for colon polyps, we can diagnose the neoplastic changed the polyp, not non-neoplasia at this moment.

I'd like to discuss with you much more about the problem. If it is possible, please let me know your e-mail address. Let's discuss at international digestive disease meeting, like DDW (Washington DC), UEG (Barcelona) and Japanese DDW (Tokyo) in next year. Again I appreciate for your kindness.