Peer Review File

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Reviewer #1:

Comment 1: This manuscript should be conducted as ‘case series’ because the sample size is too small for the ‘original article’.

Reply 1: Thanks for Reviewer’ s suggestion. The incidence of MECPL emerging at AS is very low and the definition, diagnosis and treatment are still not widely recognized. Our study is one of the most included researches at present.

We are very sorry to know if "case series" the Reviewer said is equal to "case report", because we did not find "case series" in the manuscript categories of ATM. Thus, the manuscript is still conducted as “original article”, which follow the STROBE Checklist that the Editorial Office suggested. But if "case series" is equal to "case report", we will also follow the suggestion of Reviewers and Editorial Office to change the manuscript categories of our article, if it could be accepted.

Comment 2: Some patients who had such lesions have received surgical operation instead of performing ESD, and these situations may have led to selection bias.

Reply 2: It is really true as Reviewer suggested and we have added discussion in the limitation.

Changes in the text: We added the sentence in the Discussion. (see Page 14, line 15-16)

Comment 3: The authors should describe the total number of colorectal ESD during the study period.

Reply 3: Considering the Reviewer’s suggestion, we have searched the total number of colorectal ESD in our endoscopic center during the study period and we have presented the total number in the result.

Changes in the text: We added the description in the Results as advised. (see Page

10, line 7-8)

Comment 4: A protruded lesion should be resected by conventional techniques such as polypectomy or EMR even when the lesions emerge in anastomotic sites. Why did the authors perform ESD for these patients?

Reply 4: According to the guideline, protruded lesion could be removal by polypectomy or EMR, even ESD. The reason why we chose ESD for these three patients was present as follow:

1. The size of all these three protruded lesions were larger than 2 cm.

2. Saline solution was difficult to been injected into the submucosa because of severe submucosal adhesion of AS scar, which led to inadequate lifting of the lesion.

3. There existed some anastomotic nails under the protruded lesions. It was difficult to remove the lesion completely with metal snare.

Thus, ESD for protruded lesion was time consuming, but it was safer and more efficient to remove the lesions emerge in anastomotic sites.

Special thanks to you for your good comments.

Reviewer #2:

Comment 1: The first paragraph regarding AR is not closely relevant to this topic. I suggest deleting this part for the integrity of this paper.

Reply 1: We have re-written this paragraph according to the Reviewer's suggestion.

Changes in the text: We have modified our first paragraph as advised. (see Page 6, line 4-7)

Comment 2: The reference regarding 14 to 18 may not be necessary since the vast majority of endoscopic techniques employed is familiar to most endoscopists.

Reply 2: As Reviewer suggested, we have deleted the incorrect references and added another reference in this part.

Changes in the text: We have modified our text as advised. (see Page 7, line 12)

Comment 3: Please further clarify the definition of experienced endoscopists, the "1000 cases" is indicative of regular gastroscopy/colonoscopy or ESD?

Reply 3: We are very sorry for our negligence of clarifying the definition of experienced endoscopists. In our paper, the "1000 cases" is indicative of ESD procedure.

Changes in the text: We added the description in the Methods as advised. (see Page 8, line 6-7)

Comment 4: I highly doubt whether the endoscopist only used a dual knife for all procedures. How about other knives, such as TT-knife, Hybrid Knife?

Reply 4: It is really true as Reviewer said that other knives, such as TT-knife, Hybrid Knife could be used during ESD. Generally speaking, the endoscopists in our center prefered to using the dual knife routinely during all procedures of ESD, which also achieved good results. Of course, other knives were also used occasionally, but the frequency was very low.

Comment 5: I suppose it is better to demonstrate a comprehensive pathological picture of a resected sample with HE staining.

Reply 5: Considering the Reviewer's suggestion, we have added a comprehensive pathological picture of a resected sample with HE staining.

Changes in the text: We have modified Figure legends in the text. (see Page 21, line 17)

Changes in the figure: We have added new submissive pictures, named "Figure 2", in the text.

Comment 6: In statistical analysis, I think some data is expressed as a range (median). Please correct it.

Reply 6: We are very sorry for our incorrect expression in statistical analysis and we have corrected them in both Manuscript and Table.

Changes in the text: We have modified our text as advised. (see Page 10, line 12-

14, 20 and Page 11, line 10 and Page 14, line 20).

Changes in the table: The incorrect expression in Tables 1-3 also have been corrected.

Comment 7: It is inappropriate to state suspicious microperforation (n=0, 0%). From my point of view, the author should imply "No microperforation was observed."

Reply 7: We have made correction according to the Reviewer's comments.

Changes in the text: We have modified our text as advised. (see Page 11, line 7).

Comment 8: The sentence "which is inconsistent with nature and invasion depth of the original tumor in those patients completely cured by standard treatment after CRC curative surgical resection with negative resection margins." is confusing. Please improve it.

Reply 8: We have re-written this sentence according to the Reviewer's suggestion.

Changes in the text: We have modified our text as advised. (see Page 11, line 16-20).

Comment 9: The authors are supposed to discuss the reason why postoperative hemorrhage is relatively higher than the regular ESD procedures. Can this phenomenon be attributed to more severe fibrosis at AS due to previous curative operation? Please provide related references within the discussion.

Reply 9: As Reviewer suggested, we searched for references but there was no evidence that severe fibrosis is associated with postoperative hemorrhage. Besides, a meta-analysis confirmed that there existed no significantly difference on postoperative bleeding between suture line and non-suture line lesions. The sample size is too small to confirm that postoperative hemorrhage is relatively higher than the regular ESD procedures. Thus, we re-wrote this part and provided new references within the discussion.

Changes in the text: We have re-written this part in Discussion (see Page 12, line 15-17)

Comment 10: The additional figure clearly demonstrating the endoscopic procedure of peeling MECPL and removing of AN is inevitably required.

Reply 10: Considering the Reviewer's suggestion, we have added additional clear figures to demonstrate the endoscopic procedure of peeling MECPL and removing of AN.

Changes in the text: We have modified Figure legends in the text. (see Page 21, line 10-15)

Changes in the figure: We have added new submissive pictures, named "Figure 1", in the text.

Comment 11: The conclusion is too heavy, please shorten this part.

Reply 11: We have shortened this part according to the Reviewer's suggestion.

Changes in the text: We have deleted a long sentence in Conclusions. (see Page 15, line 7-13).

Special thanks to you for your good comments.

Reviewer #3:

Comment 1: intro "80%-90% of resultant 5-year mortality rate. [5]" >> please note the mortality rate reported in ref-5 [J Surg Oncol. 2016;114:228] was 1/3 [6 of 18].

Reply 1: We have re-written this part according to the Reviewer A's suggestion and the ref-5 was deleted in our manuscript.

Changes in the text: We have deleted this sentence in text. (see Page 6, line 5-7).

Comment 2: Ref-13 "MD MW, Ph.D. MKM, MD YH, et al." or "Wada M, Kato M, Hirai Y, et al."?

Reply 2: We have made correction according to the Reviewer's comments.

Changes in the text: We have modified our text as advised. (see Page 18, line 9).

Comment 3: ref-22 "22. MD SN, MD IO, MD MM, et al." >> or "Nonaka S, Oda

I, Makazu M, et al.”?

Reply 3: We have made correction according to the Reviewer’s comments.

Changes in the text: We have modified our text as advised. (see Page 19, line 18).

Comment 4: Supplement Table 2-3 Detail information of each patient>> Suggest to change as “Supplement Table 2 Detail pathological information of each patient” & “Supplement Table 3 Detail operative information of each patient” to avoid duplicated table titles

Reply 4: We have made correction according to the Reviewer’s comments.

Changes in the Supplemental Table: We have modified our Supplemental Table as advised.

Special thanks to you for your good comments.