Peer Review File

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Reviewer A

This study was designed to identify risk factors for the occurrence of metachronous ovarian metastasis based on profile of clinicopathological parameters and expression of sex hormone receptors of operated GC patients with and without ovarian relapse
minor revision

1. Need a IRB number

Reply 1. Thank you very much for the kindly reminder. The IRB number was added accordingly.

Changes in the text: We added the IRB number as advised (see page 23, line 1167-1168)

2. Insert of inclusion and exclusion criteria in method section

Reply 2. Thank you very much for mentioning this point. We described the criteria in the *Patients and Methods* section of the **main** text and illustrated the criteria as **Figure 1**. However, we didn't describe it in the Method section of the abstract.

Changes in the text: We inserted the inclusion and exclusion criteria in Method section of the abstract as advised (see page 3, line 79-81). Furthermore, we mentioned that the criteria were illustrated as Figure 1 in the Patients and Methods section of the main text (see page 6, line 236).

3. How about explain the rule of ER beta in cancer or gastric cancer?

Reply 3. Thank you very much for bringing out this point. Your advice is highly appreciated. We realized that our explanation of the rules of ER beta was relatively insufficient in our manuscript, which may leave some doubts for both reviewers and readers. Therefore, we studied more publications and made certain changes in our paper accordingly.

Changes in the text: We have modified our text regarding the fundamental principles of ER beta in cancer as advised (see page 18, line 938-955).

Thank you for your efforts.

Sincerely yours.

Reviewer B

You showed some risk factors of MOMs in gastric cancer. I think this study is quite

informative to us. However, there is a problem to be addressed in this manuscript.

Major revisions

1. You classified pathological differentiation of primary tumors in three categories in the Table 1. If possible, would you show WHO pathological type (tub1, tub2, por1, por2, sig, etc.) in primary tumors?

Reply: Thank you very much for the comments and suggestions. We reviewed the WHO pathological type of the primary gastric lesions. There are 11 subtypes of adenocarcinoma of gastric cancer according to the 5th edition. However, some subtypes such as parietal cell carcinoma, hepatoid carcinoma and etc. were not witnessed in our samples. Accordingly, we classified these patients into five subgroups (1. Tubular; 2. Papillary; 3. Mucinous; 4. Signet-ring cell; 5. Mixed subtypes) which were seen in our samples.

Changes in the text: We have modified our text as advised (see Page 6, line 237-238) and updated the corresponding Table 1 (see Page 29, line 1302-1306).

2. Would you show status of SHRs and pathological type in resected MOM? Additionally, were those pathological findings same between primary lesion or MOM?

Reply: Thank you very much for this intriguing question. Your advice is well taken. As our statistical analysis highlighted the significance of ERbeta negativity on primary gastric lesion in the occurrence of MOM (illustrated in Table 3), we further performed IHC staining of ERbeta on the metastatic ovarian lesions of 47 GC-MOM patients undergoing oophorectomy to figure out if expression status of ERbeta was consistent between primary and metastatic tumor. For 8 ERbeta (+) patients, 7 ovarian tumors were ERbeta (+); for the other 39 ERbeta (-) patients, all ovarian tumors were ER (-), indicating the general consistency of ERbeta expression between paired tumors. However, the IHC staining of ERalpha and PR was missing due to the limited funding issue as well as the insignificance of these two SHRs in the occurrence of MOM. Regarding the WHO pathological type of metastatic ovarian tumors, we conducted pathological inspection and clarified that the pathological types were same between paired tumors.

Changes in the text: We have modified our text as advised (see Page 11, line 456-461; see Page 13, line 597-604), updated the corresponding Table 2 (see Page 31, line 1310-1312) and added a new supplementary Figure 1 (see Page 37, line 1338-1340).

Minor revisions

1. You described the p-value with the third decimal places in Table 1 and 3, while

more detailed p-values were noted in Table 4 and 5. I think the p-value should be written with the same decimal place in all Tables.

Reply: Thank you very much for pointing out this issue. We applied the same decimal place for all *P* values.

Changes in the text: We have modified our text as advised (See Page 34-36, Table 4 and Table 5).