Author's response to reviews

Title: Impact of comorbidities and use of common medications on cancer and non-cancer specific survival in esophageal carcinoma

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Author's response to reviews: see over
Ms. Cherry Battad                              February 2, 2015
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RE:  MS:  1243825290147828

Title: Impact of comorbidities and use of common medications on cancer and non-cancer specific survival in esophageal carcinoma

Dear Editor,

Thank you for reviewing the above-referenced manuscript submitted earlier to your office. We would like to take this chance to express our appreciation to you and colleagues. And we are also very appreciated of the reviewers’ time and effort.

In accord with the Reviewer’s comments and suggestions, the manuscript has been revised accordingly. All the comments have been carefully addressed. All changes have been highlighted in red. A point-by-point response has also been prepared and follows this cover letter.

If there are any questions or problems for our re-submission, please feel free to contact me.

Sincerely yours,

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Response to comments of the Reviewer: Peter C Thuss-Patience

1. The way hypothyroidism is identified is still not consistently described in the manuscript.

   Sorry for the inconsistent description of “hypothyroidism”. We identified hypothyroidism by the record of past medical history but not by the use of levothyroxine. And it is also true that all the patients recorded as having hypothyroidism regularly took levothyroxine. We have revised the manuscript to make a consistent description of “hypothyroidism”. (See the 15th to 17th line of page 3, and the 20th to 21st line of page 11 in the revised manuscript)

   And we admit that there is a possibility that patients may take L-thyroxine due to reasons other than hypothyroidism. We have mentioned it in the revised manuscript. (See the 12th to 14th line of page 13 in the revised manuscript)

2. The explanation for the survival benefit of hypothyroidism was only observed in non-surgery patients is not understandable.

   Thanks for raising this question.

   We admit that we don’t have direct evidence to support that postoperative “low T3 syndrome” occurs more frequently in patients with preexisting hypothyroidism than those without. We also can’t explain why the survival benefit of hypothyroidism was not seen for surgical patients, which will need further studies. So we have deleted that paragraph. (See the 11th to 13th line of page 12 in the revised manuscript)

3. It is said: “Since all the patients recorded as having hypothyroidism also regularly took levothyroxine, hypothyroidism/levothyroxine was considered one variable in analysis”. As was told in the answer letter there is some overlap of patients taking thyroxine due to other reasons. This has to be mentioned in the manuscript.

   We admit that there is a possibility that patients may take L-thyroxine due to reasons other than hypothyroidism. We have mentioned it in the revised manuscript. (See the 12th to 14th line of page 13 in the revised manuscript)

4. Page 9 line 13: English: “Other factors that were showed significant an impact on OS, EC-specific survival or non-EC specific survival in univariate analysis were listed in the footnote of Table 3.

   Thank you for pointing out this error. We have revised it to say: “Other factors which showed a significant impact on OS, EC-specific survival or non-EC specific survival in univariate analysis were listed in the footnote of Table 2.” (See the 13th to 15th line of page 9 in the revised manuscript)
5. **Page 23 line 2: English spelling error: “Univaraite”**

   Sorry for the spelling error. We have corrected it into “Univariate”. (See the 2nd line of page 22 in the revised manuscript)

6. **Page 24 line 5 “age” appears twice, delete one “age”**

   Both “the interaction of age with surgery” and “age” are the factors that showed a significant impact on EC-specific survival. They were related but two variables in our analysis. The first “age” appears in the phrase of “the interaction of age with surgery”, the second “age” is “age” itself.

7. **Page 9 line 14: Is has to be “table 2” not “table 3”**

   The Reviewer is right that it should be Table 2 there. Many thanks for the correction. (See the 16th line of page 9 in the revised manuscript)

8. **Page 9 line 16 I would recommend to include a sentence here which explains the multivariate analysis: for example: “all parameters included in the multivariate analysis are listed in the footnote of table 3”**

   Good suggestion. We have added the sentence in our revised manuscript to say “All the parameters included in the multivariate analysis were listed in the footnote of Table 3”. (See the 15th to 16th line of page 9 in the revised manuscript)

9. **You should state in the manuscript what you mean by AF. You did not answer this question in the answer letter. If you included all types of AF (intermittent, persistent). I suggest, simply state it in the manuscript (eg: AF (any type included, intermittent or persistent))**

   Thank you for pointing this out. Actually, we don’t have the specific data on the types of AF for every patient. We can only say that we included all types of AF, but most of them were intermittent AF. We have added this information in the revised manuscript. (See the 16th to 17th line of page 6 in the revised manuscript)