Reviewer’s report

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

Version: 3 Date: 20 January 2015

Reviewer: Peter C Thuss-Patience

Reviewer’s report:

The authors answered most of my questions. Thank you. Some last points, which I think are important have not been answered sufficiently in my view.. I think these obligatory points have to be addressed and changed in the manuscript, to avoid that similar questions I had are raised by the readers.

Obligatory:
Abstract and page 11 line 18
The way hypothyroidism is identified is still not consistently described in the manuscript.

In the answer letter to my previous question the authors wrote: “We did not identify hypothyroidism by L-thyroxine use but by the record of past medical history”. A similar sentence was included in the method section of the revised manuscript.

But in the abstract it is stated: “hypothyroidism determined based on the use of levothyroxine supplementation”. On page 11 line 18 it says: “the use of levothyroxine as a surrogate of the underlying hypothyroidism”

The article has to be clear and consistent about the way hypothyroidism was identified hypothyroidism: Either by L-thyroxine use (as you stated at page 11 and in the abstract OR by the medical records as stated in the answer letter and in the method section. Please clarify in the manuscript.

The possibility that patients may take L-thyroxine due to other reasons than hypothyroidism should be mentioned in the manuscript as a shortcoming of the analysis.

This clarification is obligatory before acception for publication

Obligatory:
At page 12 line 11 onwards it is said:
“Surprisingly, the survival benefit of hypothyroidism was not seen for surgical patients, however. We can only speculate why this may be the case. Low triiodothyronine syndrome, which is often observed postoperatively, has been reported to be associated with
unfavorable outcomes in surgery patients [19]. Thus, the survival benefit brought by the relatively earlier clinical stage of hypothyroidism patients might be offset by the addition of surgery, which might contribute to the reasons for the survival benefit of hypothyroidism was only observed in non-surgery patients in our study”

In my view this explanation is still not understandable even when reading the comments of the authors in their answer letter. Why should a low t3 syndrome offset the beneficial effect of hypothyroidism? Low T3 syndrome occurs in the same frequency in patients with and without preexisting hypothyroidism. Therefore a negative effect should occur in the surgical group with and without hypothyroidism. A difference between the groups due to hypothyroidism would not be altered by a low T3-syndome if it occurs at the same frequency in both groups. In addition to this, hypothyroid patients supplemented with L-thyroxine might even have a lower chance to get low T3 syndrome.

This is an obligatory change or clarification

Major: Page 7 line 10
It is said: “Since all the patients recorded as having hypothyroidism also regularly took 11 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 (see above).

Minor corrections:
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.

Page 23 line 2
English spelling error “Univaraite”

Page 24 line 5 “ age “ appears twice , delete one “age“

Page 9 line 14
Is has to be “table 2” not “table 3”

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”

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))

After these last obligatory corrections or clarifications have been made, I have no further comments.

Congratulations.

Level of interest: An article whose findings are important to those with closely related research interests.

Quality of written English: Acceptable.

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.