

World Journal of Gastroenterology

Editorial Board

Re: Gastroesophageal reflux disease and non-esophageal cancer

ESPS Manuscript NO: 12897

Dear Editor,

We want to thank the reviewers for their comments. Please find a point-by-point response to the reviewers' comments. The manuscript has now been revised accordingly.

All suggestions were taken into consideration. Changes are highlighted in the text.

We hope the revised manuscript may now pass the high standards scrutiny of the Journal editorial board to allow its publication.

Sincerely,

The authors

Reviewer 1.

In this review, the authors try to discuss existing data on the possible association between gastroesophageal reflux disease and extra esophageal cancers. They quote possible pathophysiological mechanisms and epidemiological studies and they conclude “that laryngeal and pharyngeal tumors are highly associated to GERD. Oral and lung cancers probably also connected to GERD”. Someone can assume, based on pathophysiological and epidemiological data, that there is a probable association but not clear evidence. As the authors emphasize “the majority of papers are far from ideal to prove a relationship of extra esophageal cancers and gastroesophageal reflux disease”.

It should be mentioned that not all studies show a relationship and that even in studies showing positive association this is not too strong.

The sentence was added verbatim to the discussion section.

Also it should be emphasized that it is very difficult to have convincing evidence with these studies as many factors such as smoking, alcohol consumption, diet, obesity etc may play a role.

This was previously mentioned in the discussion.

Moreover proportional increase in the incidences of two separate diseases do not necessarily indicate etiological relationship.

The sentence was added verbatim to the discussion section.

On the other hand, true diagnosis of GERD is questionable as only clinical data were used in previous studies.

This was previously mentioned. The section was improved.

I think that this review should be written in a more critical way with the title of the article in questioned form. The authors should discuss existing evidence but also analyze weaknesses and problems in interpreting data from the studies on this topic that have been published so far.

Several additions were done in a critical way. The title was sustained since it does not affirm for the association.

Reviewer 2.

The topic is interesting, however strong conclusions cannot be drawn due to lack of published studies. Current conclusions of the article are not based on sufficient background of good quality data.

We absolutely agree with the reviewer. The limitations of the data were stressed according to reviewer 1 suggestions.