Author's response to reviews

Title: Improvement of endocytoscopic findings after per oral endoscopic myotomy (POEM) in esophageal achalasia; Does POEM reduce the risk of developing esophageal carcinoma?

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Author’s response to reviews: see over
Reviewer 1’s report

Title: Improvement of endocytoscopic findings after per oral endoscopic myotomy (POEM) in esophageal achalasia; Does POEM reduce the risk of developing esophageal carcinoma?

Version: 4 Date: 7 November 2012 Reviewer: P. Marco Fisichella Reviewer’s report:

Nice manuscript, well written. Interesting research idea, very original. Minor flaws in the retrospective study design. Discussion, tables and figures are appropriate. No revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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

Reviewer 2’s report

Title: Improvement of endocytoscopic findings after per oral endoscopic myotomy (POEM) in esophageal achalasia; Does POEM reduce the risk of developing esophageal carcinoma?

Version: 4 Date: 25 December 2012 Reviewer: Tsutomu Nomura Reviewer’s report: Major Compulsory Revisions

This study aims to evaluate the effectiveness of POEM in patients with esophageal achalasia. The authors claim that POEM is an effective and less invasive treatment for achalasia and may reduce the risk of esophageal carcinogenesis.

For the benefit of the reader, however, several points need clarifying and certain statements, which are given below.

1) In discussion, page 10/33, line 5-7 #Inoue et al. reported that there was no recurrence after the POEM procedure in their 17 case series of achalasia[10].

#In their report (reference No 10), the mean follow-up period was 5 months. More long follow-up period should be needed to claim#there was no recurrence after the POEM procedure#.
I’m afraid there still is no report regarding longer observation after POEM enough to verify the low recurrence rate. I added the reference of 43 cases report (Japanese manuscript) also from Inoue and his colleagues that has a little longer observation period. I inserted “short-term results” along with the 17 cases report.

2) In discussion, page 11/33, line20-21

Expression of the Ki-67 protein is associated with the clinical course of mucosal inflammation[25].

In the report (reference No 25), I could not find the description. In abstract, they mentioned that the expression of the Ki-67 protein is associated with the clinical course of cancer (breast and prostate), but did not mention of correlation with mucosal inflammation.

Thank you for pointing that out. As you mentioned Dr. Scholzen’s paper clarified the correlation between ki-67 expression and cell proliferation ability. So I made following alteration.

clinical course of mucosal inflammation

Expression of the Ki-67 protein is associated with the clinical course of cell proliferation that is closely linked to tissue inflammation[27].

3) In discussion, page 11/33, line21

They suggested

They are Dr. Leeuwenburgh? Dr. Scholzen?

That meant Dr. Leeuwenburgh. I changed from “they” to “Leeuwenburgh and his colleagues”.

4) The authors should discuss about the relationship between patients characteristic (type, dilation, duration of disease etc.) and the results of endocytoscopy, Ki67 and p53.

To our knowledge, the endoscopic nuclear counts appeared to be correlated only with dysphagia symptom before the procedure. The degree of dilation and type was strongly relevant to the duration after onset. Meanwhile, some patients received repeated balloon dilation, which could influence the status of inflammation on the surface mucosa. It is assumably difficult to refer the direct correlation between patients’ characteristic and both endocytoscopic and immunohistochemical results. I added the following sentences.

“There were no significant correlation between endoscopic nuclear counts and patients’ characteristics such as degree of dilation, type, and duration of dysphagia symptom.
However, statistically significant correlation between endocytoscopic nuclear counts and Eckardt score before the procedure was observed ($r=0.7937$, 0.3699~0.9441, $p<0.01$).

5) The authors should check the references. #reference 12 #Dis Esophagus, 2011##Dis Esophagus,2012 Apr;25(3):235-41. doi #? #reference 28#American journal of gastroenterology##Am J Gastroenterol#?

→Thank you for the kind assistance. I made the correction on the reference No 12. Regarding reference No.28, I'm afraid that is the correct state of the manuscript. It seems to be the abstract from the congress of American Gastroenterological Association. The abstract was sited in several articles and I hope this quotation does not violate the provision of your journal.

**Level of interest:** An article of importance in its field

**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.