Format for ANSWERING REVIEWERS

January 18, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 15236-review.doc).

Title: Improved Specimen Adequacy Using Jumbo Biopsy Forceps in Patients with Barrett's Esophagus

Author:

Jan Martinek, Jana Maluskova, Magdalena Stefanova, Inna Tuckova, Stepan Suchanek, Zuzana Vackova, Jana Krajciova, Marek Kollar, Miroslav Zavoral, and Julius Spicak

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We thank the reviewer for his constructive review. Here we present our point-by-point response to the reviewer´s comments:

1. We agree with the reviewer that the number of biopsies per forceps could have been more similar. However, we estimated (not determined) the number of biopsies beforehand as described in the manuscript and this estimation had not always been accurate. The main reason for this discrepancy was lower number of biopsies with jumbo forceps. The mucosal defects after biopsies with jumbo were sometimes quite large and we felt there is no need for additional sampling with jumbo. Discrepancies among the remaining three large capacity forceps (108-121) are rather small.
2. We agree with the reviewer and described our results in "results section" more accurately. In addition, all principal results are displayed in our Tables 1 and 2 and Figure 3.
   - **Text change: "More than two thirds of biopsies, taken with jumbo forceps, were adequate (71%); this was significantly more compared to the large capacity forceps (forceps A - 26%, forceps B – 17%, forceps C – 18%). Muscularis mucosae was present in 80% of the samples obtained by jumbo forceps. We obtained significantly bigger specimen using the jumbo forceps (2.4 mm) compared to the large capacity forceps (forceps A - 2 mm, forceps B – 1.6 mm, forceps C - 2 mm)."**
3. On average, 11.8 biopsies were taken from each patients, range 4-25. We added this statement into the results section.
   - Text change: **A total of 436 biopsies were taken, this represents on average 11.8 biopsies per patient (range 4-25).**
4. Both physicians who took biopsy specimen have been experienced endoscopists with a high

level of expertise. We agree that discrepancies among studies could be, partially, explained by different expertise of physicians. However, even the study showing "bad results" with jumbo forceps (Gonzales et al., GIE 2010, 72:935-40) mentioned a high level of experience of endoscopists. Thus, we rather think that the use of a therapeutic endoscope in the study of Gonzales may explain unfavorable results with Jumbo forceps in contrast to our study where we used a standard endoscope. This point has already been discussed in the first version of our manuscript.

5. We agree with the reviewer that we detected quite high number of patients with IEN. We have changed a discussion on that issue. We underline that this higher IEN detection could not have influenced our primary endpoints (specimen adequacy).
   - Text change:

   Second, there was a selection bias: we detected a high proportion of patients with IEN (both low and high grade IEN; 65%). Our department is a referral center providing endoscopic treatment for patients with BE; hence, this explains higher percentage of patients with IEN as compared to other studies (19%[5], 40%[11], 49%[19]). In addition, the use of tri-modal endoscopy with targeted biopsies (in some patients) may also explain the higher frequency of IEN detection.
6. Each specimen was independently assessed by two "esophaghus-specialized" pathologists (as mentioned in the method section) and any discrepancies were settled by the consensus. Honestly, only minimum discrepancies had been raised during the study.
7. There was a calculation error in Table 2, thank the reviewer for finding it and we apologize for this. We corrected this mistake accordingly.
8. We added the following paragraph to the discussion to clarify the significance of IEN detection
   - Text change:

   The main aim of the surveillance of patients with BE is the early detection of IEN or EAC, allowing less invasive endoscopic treatment. Although it is yet to demonstrate any benefit in a randomized control trial (RCT), endoscopic surveillance is recommended (a RCT is underway in the UK). Nevertheless, several studies have suggested that the patients with BE, who undergo surveillance, benefit from early-stage cancer diagnosis and improved survival[13-15]; however, no association was found between reduced risk of death from EAC and endoscopic surveillance[16].

9. We also performed manuscript editing according to requirements from editorial office. The language of the manuscript was revised by the professional language agency. As mentioned by the reviewer, the language quality is good.

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

Jan MARTINEK, MD, PhD, AGAF
IKEM
Department of Hepatogastroenterology
Prague, Videnska 1958
140 21 – Czech Republic
Fax: +240-2-6136-2615
E-mail: jan.martinek@volny.cz