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ANSWERING REVIEWERS

Name of journal: World Journal of Clinical Cases

Manuscript NO: 52715

Title: Upper Esophageal Sphincter Abnormalities on High-resolution Esophageal
Manometry with Treatment Response of Type II Achalasia

Reviewer's code: 02441021

Position: Editorial Board

Academic degree: MD

Professional title: Professor

Reviewer's country: Egypt

Author's country: China

SPECIFIC COMMENTS TO AUTHORS

Excellent manuscript. Appreciable number of patients. Excellent methodology. Good results

Answer: Thank you for your objective comments.



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Name of journal: World Journal of Clinical Cases

Manuscript NO: 52715

Title: Upper Esophageal Sphincter Abnormalities on High-resolution Esophageal Manometry with Treatment Response of Type II Achalasia

Reviewer's code: 02155135

Position: Editorial Board

Academic degree: MD

Professional title: Associate Professor

Reviewer's country: Italy

Author's country: China

SPECIFIC COMMENTS TO AUTHORS

Thank you for the opportunity to review this manuscript. The authors have submitted a manuscript entitled "Upper Esophageal Sphincter Abnormalities on High-resolution Esophageal Manometry with Treatment Response of Type II Achalasia". The aims of this study were "• to analyze the types of UES abnormalities present and their frequency in consecutive patients with esophageal motility disorders undergoing HREM according to the current Chicago classification. • to determine the association between common clinical symptoms and UES abnormalities. • to assess the treatment-induced changes in LES and UES objective parameters to evaluate the treatment response among subjects with achalasia and UES dysfunctions. This is an intriguing topic of growing interest in the motility community. This single centre retrospective study enrolled 498 consecutive patients who underwent clinical HREM studies. The interesting work performed by the authors must be acknowledged, although there are some points to be clarified. I am wondering whether the decision to present data on presence/absence of UES

abnormalities and then divided into LES normal and LES abnormal groups in accordance with LES restP and LES IRP is appropriate or generates confusion into the Readers. Specifically the novel finding of this study was the analysis of HREM results after dilation beyond the clinical outcome. In Table 5, 17 patients were diagnosed as Achalasia type II and one as type III; however, in the results section you reported Treatment response among subjects with type II achalasia. and described: Ten subjects with achalasia were excluded from the analysis due to a lack of pre- or posttreatment manometric data (Fig. 1). I would like to know the patient with Type III achalasia was among the excluded patients? Did he undergo pneumatic dilation? in the results section Pg 11 line 5 Authors stated that This meant that the treatment was effective in every subject. In my opinion this comment should be transferred in the discussion. Moreover, I did not find in the methods the definition of an effective procedure based on HREM outcomes parameters. Authors wrote: Treatment response was defined qualitatively by Eckardt score and quantitatively by posttreatment HREM Please could you better explain what is the definition of favorable treatment response ? Table 7 is very difficult to follow and I am wondering if in only 8 subjects it is appropriate to perform a mixed analysis. Moreover, there is no description of this analysis in the statistical analysis paragraph.

Question: I am wondering whether the decision to present data on presence/absence of UES abnormalities and then divided into LES normal and LES abnormal groups in accordance with LES restP and LES IRP is appropriate or generates confusion into the Readers.

Answer: Thank you for your objective comments. LES restP is a mean cutoff value used in traditional esophageal manometry, however, LES IRP is a median cutoff value used in HREM. A median rather than a mean cutoff value among test swallows for the IRP is more logical. This is clearly stated in the current Chicago classification. According to

presence/absence of UES abnormalities, grouping in the current manuscript are as follows: group 1 is UES abnormal, and group 2 is UES normal; both groups are further divided into LES normal and LES abnormal subgroups in accordance with LES restP and LES IRP.

Question: I would like to know the patient with Type III achalasia was among the excluded patients? Did he undergo pneumatic dilation? in the results section Pg 11 line 5 Authors stated that This meant that the treatment was effective in every subject. In my opinion this comment should be transferred in the discussion.

Answer: The patient with Type III achalasia was among the excluded patients. He didn't undergo pneumatic dilation. We have transferred comments in the discussion section and in the results section. Thank you for your useful suggestions.

Question: Moreover, I did not find in the methods the definition of an effective procedure based on HREM outcomes parameters. Authors wrote: Treatment response was defined qualitatively by Eckardt score and quantitatively by posttreatment HREM Please could you better explain what is the definition of favorable treatment response ?

Answer: We have define an effective procedure and a favorable treatment response in the Methods section in revised manuscript. Thank you for your useful suggestions.

Question: Table 7 is very difficult to follow and I am wondering if in only 8 subjects it is appropriate to perform a mixed analysis. Moreover, there is no description of this analysis in the statistical analysis paragraph.

Answer: Frankly, number of subjects analyzed in Table 7 is small. So, certain variables are controlled for as between-subject independent variables. In future HREM studies, a large number of subjects are needed to enroll to elucidate the relationship between

treatment response and UES dysfunction in achalasia subtype. In addition, we have added description of Table 7 analysis in the statistical analysis paragraph in revised manuscript.

ANSWERING REVIEWERS

Name of journal: World Journal of Clinical Cases

Manuscript NO: 52715

Title: Upper Esophageal Sphincter Abnormalities on High-resolution Esophageal Manometry with Treatment Response of Type II Achalasia

Reviewer's code: 01799104

Position: Editorial Board

Academic degree:

Professional title:

Reviewer's country:

Author's country: China

Reviewer chosen by: Le Zhang

SPECIFIC COMMENTS TO AUTHORS

The authors found that UES abnormalities are not uncommon (almost 50%) in their HREM series. The statistical significance is associated with achalasia and ineffective esophageal motility. The former is assumed a compensatory phenomenon as reported by others. The latter may be an interesting finding that arouse further study during the HREM examination. They found that abnormal UES is associated with poor response to

pneumatic dilatation in type II achalasia. Though the case number is limited, they may evaluated those with poor response is related to disease duration and severity in which pneumatic dilatation is not a good choice for the treatment.

Answer: Thank you for your objective comments. Frankly, a large number of subjects are needed to enroll to elucidate the relationship between treatment response and UES dysfunction in achalasia subtype in future HREM studies.