Format for ANSWERING REVIEWERS

April 30, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 17580-Review.doc).

Title: Hospitalization for esophageal achalasia in the United States

Author: Daniela Molena, Benedetto Mungo, Miloslawa Stem, Anne O Lidor

Name of Journal: *World Journal of Gastrointestinal Endoscopy*

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Thank you for the positive review of our manuscript. We have responded directly to all points raised by each reviewer (reviewer's comments in *italic*, followed by our response in **bold**). Please find attached the revised manuscript with highlighted changes (highlighted in yellow).

Reviewer#1

This study provides a useful general overview of the trends and outcomes of achalasia management. And the research suggests that a timely and effective relief of esophageal obstruction may avoid future complications brought by the natural history of the disease. However, the abstract should be consistent with the text content,e.g. in abstruct,"about half (48.6%) underwent Heller myotomy, 2.4% underwent esophagectomy and 49% had endoscopic or other treatment.", but in the text,"15,567 Heller patients (49%), 785 esophagectomy patients (2.5%), and 15,417 non-surgical patients (48.5%) ". About Group 3, in Material and Methods, endoscopic and other treatment should be described.

We appreciate your positive feedback. Per your suggestion, we have fixed the percentages and now all of them are consistent throughout the abstract and text. In regards to Group 3, there were a variety of treatments these patients underwent, including EGDs, esophageal dilation, PEGs, and Botox injection. We have mentioned most common procedure types these patients underwent in the first paragraph of the results section and included a table in appendix.

Reviewer#2

The manuscript Nationwide treatment and outcomes in patients hospitalized for esophageal

achalasia in the United States by Daniela Molena and coauthors represents a clinically important analysis of NIS database. The study is retrospective with all potential biases of that kind of study. It must be emphasised in the conclusion that results of the study does not represent the comparison of endoscopic and surgical treatment of patients with achalasia. All younger patients without comorbidities treated with endoscopis ballon dilatation in an outpatient setting are excluded from this retrospective analysis. My suggestion to the authors is that they should divide patients in group three to those treated with ballon dilatation from those treated with injection therapy.

We thank the reviewer for their thoughtful consideration. This is a good point. We acknowledge that it would be insightful to identify patients treated with balloon dilation from those treated with injection therapy. However, there are two issues preventing us from clearly identifying these patients. 1) NIS only includes in-hospital data (no outpatient treatment is recorded). This important limitation has been included in our discussion. 2) NIS uses ICD-9 coding system for procedures (not CPT codes) and there is no specific code for pneumatic balloon dilation with a 30 mm balloon, as described in the landmark study by the European Achalasia Trial Investigators (*Boeckxstaens GE, Annese V, Des Varannes SB, et al. (2011) Pneumatic dilation versus laparoscopic heller's myotomy for idiopathic achalasia. N. Engl. J. Med 364:1807-1816*). There exists a code of 42.92 for dilation of esophagus, but there is no way to know if these dilations were merely routine dilations versus true pneumatic dilations. Additionally, botox injection represented only small portion of our non-surgical group. Although it would be very interesting to do so, for these reasons, we cannot compare outcomes in by subgroup in our non-surgical group. We have also included this explanation in our limitations section and changed the conclusion to emphasize that we are not comparing endoscopic and surgical therapies.

Reviewer#3
This study is a retrospective analysis of outcomes in patients hospitalized for espophageal acalasia. It is based on the use of a database with ICD 9 diagnosis. The study is well conducted, the number of patients considered is elevated and statistical analysis is correct. However we must evidentiate the used programme is only an administrative database predisposed to errors depending on inaccurately entered ICD-9 codes and on the lack of other clinical informations such as the stage of patients' disease at admission or achalasia treatments preceding the admission. Moreover, the results obtained are known and influenced by a variety of factors not reported (age at diagnosis, disase severity, comorbidity).

We thank the reviewer for this comment. We agree that the administrative nature of NIS database is prone to errors and lacks detailed clinical information. We already pointed out this limitation in the discussion. Age at diagnosis and comorbidity measured by Charlson score were reported in Table 2 and included in the adjusted analysis in Table 4. Unfortunately, disease severity is not recorded by NIS.

Reviewer#4
This retrospective review of a large database has produced some important conclusions. The paper is

also well-written. I have following suggestions- 1. It would have been more meaningful if the data in group-3 was sub-divided into- Pneumatic dilation group versus others (botulinum, etc). The statistical analysis re-run after this grouping would have provided more practical results. This is because, pneumatic dilation is equivalent to surgical myotomy.

This is a good point. However, as we already explained in response to Reviewer#2, NIS only collects in-hospital data and there is no specific ICD-9 code for pneumatic balloon dilation with a 30mm balloon.

Reviewer#5
In this study, Molena et al. conducted nationwide study on treatment and outcomes in patients with esophageal achalasia in the US. This is a carefully done study based on a large number of medical records and the findings are of considerable interest. I have no serious criticism regarding methodology, results and interpretation of results.

We thank the reviewer for their kind words.

Reviewer#6
The authors have done a valuable review on surgical treatment options in Achalasia. the study design, discussion and conclusion are fine.

We thank the reviewer for their positive feedback.