Author's response to reviews

Title: Time Esophageal pH<4 Overestimates the Prevalence of Pathologic Esophageal Reflux in Subjects with Gastroesophageal Reflux Disease Treated with Proton Pump Inhibitors

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Author's response to reviews: see over
Responses to Editor and Referees

Responses to Editor

1. We have removed the Figures and Tables from the body of the text and have created a separate file for each Figure.
2. We have reviewed the manuscript for English spelling, grammar and syntax. We have also shortened the Discussion.
3. We have added an Acknowledgements section on p17 (highlighted in red) that describes the funding for this paper.
4. All changes in the paper have been highlighted in red.

Responses to Referee 1 (Dr. Numans)

Major Compulsory Revisions

1. We have added more description of integrated acidity on p 4 (highlighted in red). On p 9 (highlighted in red), we have pointed out how our definition of pathologic esophageal reflux differs from that based on the temporal association of reflux episodes with symptoms of GERD.
2. On p 10 (highlighted in red), we have pointed out that from the clinical standpoint, our findings affect the interpretation of esophageal pH recordings, but not the indication for such measurements.

Minor Essential Revisions

We gave this comment a good deal of thought. The paper has 18 values for the AUC and 95% confidence interval from the ROC analyses. As we see it, no one analysis is more relevant than any others and including a graph would not provide any important information beyond the AUC and 95% CI. In the second paragraph on p 7, we discuss the meaning of ROC analyses in general and the references given seem to us to indicate that no additional information would be provided from a graph. We also consulted two of our statistical colleagues who agreed that providing one or more graphs would not add important information beyond the AUC and 95% confidence interval.

Discretionary Revisions

We have attempted to make the Discussion more concise my omitting some paragraphs that seemed less important and by shortening and re-wording several sentences.
Responses to Referee 2 (Dr. Fein)

Major Compulsory Revisions

1. We have added more description of integrated acidity on p 4 (highlighted in red).
2. On p 10 (highlighted in red), we have pointed out that from the clinical standpoint, our findings affect the interpretation of esophageal pH recordings, but not the indication for such measurements. We believe that for patients being treated with a PPI, integrated esophageal acidity should be calculated instead of time esophageal pH<4, because this will reduce the possibility of reaching a false conclusion that esophageal acid exposure is abnormally high.