

July 19, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 11947-review.doc).

**Title:** Per-oral endoscopic myotomy: major advance in achalasia treatment and in endoscopic surgery

**Author:** David Friedel; Rani Modayil; Stavros N. Stavropoulos

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 11947

The manuscript has been improved according to the suggestions of reviewers:

1. Revision has been made according to the suggestions of the reviewer
  - a. Clarification- Per oral endoscopic myotomy is a NOTES procedure. POEM, at least as performed by Pinghong Zhou's team in Shanghai, Dr. Stavropoulos's team at Winthrop and few other centers around the world involves complete incision of the muscularis propria of the esophagus to the level of mediastinal pleura or pericardium in the chest and cardia fat pad in the abdomen. As such, we believe that it does represent a NOTES intervention and so do other NOTES experts. At the pre-eminent international annual NOTES meeting in the United States, the annual meeting organized by NOSCART, there has been an entire section dedicated to POEM for the past several years. At the opening remarks at this year's NOSCART meeting delivered by David Rattner (NOTES Going Forward: Is There a Future?) and Rob Hawes (NOTES at 10 years: A Perspective), POEM figured prominently as one of the (few) success stories of NOTES. Lest there be a perception of Western bias in this, at the NOSCART meeting, Phillip Chiu, the pre-eminent surgeon and NOTES visionary from Hong Kong tasked with reviewing the state of NOTES in Asia, offered POEM as the main major development in NOTES in Asia. We work with an expert surgeon, we agree with the reviewer and have done so for many years. Dr. Stavropoulos is part of a multidisciplinary POEM team at Winthrop that includes Collin Brathwaite a very experienced laparoscopic bariatric surgeon and robotic surgeon. Furthermore, Dr. Stavropoulos is in constant collaboration with other minimally invasive surgeons whether it be as director and co-faculty with surgeons H. Inoue and P. Zhou at the annual POEM/EFTR/STER live course at Winthrop, co-chair of the annual NOSCART course in

2014 and 2015 with the other co-chairs being minimally invasive surgeons and NOTES pioneers John Romanelli (transvaginal cholecystectomy and POEM) and Patricia Sylla (transanal NOTES), or as invited POEM speaker at many surgical meetings including the annual meeting of SAGES in 2014, the meeting of the New York General Thoracic Surgery Club in 2014 and the Eastern Cardiothoracic Surgical Society Meeting in 2014.

- b. The title has been changed to include the word achalasia as recommended by the reviewer. We also included NOTES in a more oblique fashion
- c. We changed "incision-free" to "purely endoscopic" in the abstract.
- d. In response to the reviewer's comment-POEM procedure can be a good alternative to conventional laparoscopic or open surgery, we changed the following statement: " With the advent of NOTES (Natural Orifice Transluminal Endoscopic Surgery) in 2004, there has been an impetus to develop endoscopic less invasive alternatives to surgical procedures." We changed this statement to: "With the advent of NOTES (Natural Orifice Transluminal Endoscopic Surgery) in 2004, there has been an impetus to develop endoscopic less invasive alternatives to the traditional transcutaneous surgical procedures."
- e. Clarification regarding including discussion of oncological minimally invasive approaches in this review. Given the rarity of achalasia, POEM runs the risk of being perceived as a "niche" intervention with limited broader clinical impact. This could not be further from the truth as it popularized ESD in the United States and gave rise to offshoots of submucosal endoscopy (including STER, peroral pyloromyotomy and tunnel assisted esophageal ESD) that cover a much broader swath of pathology than esophageal motility disorders. The section on "POEM offshoots" that the reviewer refers to is small compared to the entire manuscript and thus appropriately proportioned to expose the reader to this phenomenal growth in tunnel based interventions spawned by POEM. A review on POEM would be incomplete without providing this broader perspective on this remarkable innovation.
- f. Reviewer comment: "There is no surgical intervention which eliminates surveillance requirement for any GI cancer after single application." This statement by the reviewer does not apply to our manuscript since our statement reads as follows: "Furthermore, by achieving en bloc resection of these small low risk tumors it allows definitive histologic confirmation (including mitotic rate) of their benign nature and eliminates the need for life-long surveillance." We speak of benign tumors such as leiomyomas, not GI cancers as stated by the reviewer. Current US NCCN guidelines recommend life-long surveillance of subepithelial tumors less than 2 cm in size. However, if such tumors are removed by STER (at current mean

procedure times as little as 20-30 minutes) and proven to be benign (e.g. leiomyoma), then no further surveillance is required.

g. We changed the conclusion to say POEM has the potential to be the preferred modality for achalasia.

2. References and typesetting were corrected
3. Headings were formatted according to the recommendation of the editor.
4. Abstract was revised to be informative rather than indicative
5. Title and running title were revised according to the recommendation of the editor

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

Sincerely yours,

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