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Manuscript NO.: 32109

Response to Reviewers

Editor's Comments to the Authors

Step 1. Please revise your manuscript according to the reviewers' comments. All of the revisions that you make to the revised manuscript should be cited in the response letter and highlighted in the updated version of the manuscript.

Answer: We thank you for the opportunity to revise our manuscript. The revised manuscript, titled "32109-Manuscript Highlighted", is now resubmitted, with all changes highlighted using the Track Changes function in Microsoft Word.

Step 2. Please update the manuscript according to the Guidelines and Requirements for Manuscript Revision-Retrospective Study.

Answer: We have now revised our manuscript in accordance with the Guidelines and Requirements for Manuscript Revision-Retrospective Study.

Step 3. Please provide the scientific research process.

Answer: We have now included a scientific research process document, titled "32109-Scientific Research Process".

Step 4. Please provide an Audio Core Tip.

Answer: We have now included an audio core tip file, titled "32109-Audio Core Tip".

Step 5. Please subject the final title of the manuscript to Google Scholar search, and store screenshot images of the results.

Answer: We have now subjected our manuscript title to Google Scholar Search. The resulting screenshot images are included, titled "32109-Google Scholar". The Google Scholar search returned only two citations, which are abstracts on this study that we presented at the Digestive Disease Week Conference in 2016.

Step 6. Please provide the files related to academic rules and norms. The files related to academic rules and norms include the Institutional Review Board statement, informed consent statement, biostatistics statement, conflict-of-interest statement, and data sharing statement.

Answer: We have now included the relevant signed files, titled "32109- Institutional

Review Board Statement”, “32109-Informed Consent Statement”, “32109-Biostatistics Statement”, “32109- Conflict-of-interest Statement”, and “32109-Data Sharing Statement”.

Step 7. Please provide the approved grant application form(s) or funding agency copy of any approval document(s)/letter(s).

Answer: There were no funding sources for this study.

Step 8. Please revise the language of your manuscript. For manuscripts submitted by Non-Native Speakers of English, the authors are required to provide a language editing certificate, which will serve to verify that the language of the manuscript has reached Grade A.

Answer: This manuscript was written by native English speakers.

Step 9. Please sign the Copyright Assignment form. The Copyright Assignment form can be downloaded from the ESPS; you may find it under the "Files Download" area (please click on the "+" in front of the manuscript number to view the Files Download button).

Answer: We have now included the signed copyright assignment form, titled “32109-Copyright Assignment Form”.

Reviewer 1’s Comments to the Authors

This is very interesting and important topic and nicely written manuscript. It will be nice if the authors can provide some more information (or explanation) about technical characteristics of CAPS system and stuff needed for it: 1. Authors' statement: “The initial infusion rate is set by endoscopist.” Question: Who is continuing? Nurse or endoscopist? 2. Authors' statement: “The endoscopist can also titrate the maintenance infusion rate upwards or downwards during the procedure” Question: Does it mean that endoscopist monitors and control CAPS the whole time? What is nurse doing? Do you need one or two nurses during the procedure? 3. Authors' statement: “CAPS system was approved by the FDA for ASA I and ASA II patients”. The authors included also minor percent of patients with ASA III (and it is nicely explained). Question: Did you have some experiences with patients who suffer from chronic obstructive pulmonary disease (GOLD classification?), chronic heart failure (NYHA classification?) or morbid obesity? In conclusion; despite of several limitations, that were correctly described at the end of discussion, this is very interesting study that can help the endoscopist to improve everyday clinical practice. It will be also nice to read first experiences of NAPCIS method in the future. Best regards!

Answer: Thank you for your comments. To answer your questions: 1) The nurse maintains or changes the infusion rate by controlling the CAPS device, according to

verbal orders issued by the endoscopist; 2) There is one nurse in the endoscopy room, and his/her only role is to control the CAPS device in accordance with verbal orders issued by the endoscopist; there is also a technician in the room to assist with biopsies or polypectomies; 3) None of the CAPS patients had chronic obstructive pulmonary disease or chronic heart failure, since we specifically excluded such patients from the CAPS experience (instead, all patients with COPD or heart failure underwent their GI procedures with general anesthesia). In our study, there was a BMI cutoff of 40 for all CAPS and control patients, therefore even though many of the subjects were obese, there were no patients with severe obesity (BMI >40). These issues are now discussed in the Methods section of the paper.

Reviewer 2's Comments to the Authors

1. In Table 1, Mean procedure time looked like similar in both CAPS and MF group (22.2 +/- 10.5 vs. 22.8 +/- 9.3), but the P value was < 0.001. Were there any differences in the maximum time and minimum time? Please comment why there were significant differences in mean procedure time in the discussion.

Answer: Even though the absolute difference in procedure times was small, the difference was still statistically significant because of the large sample size (total of almost 5000 subjects in the two groups). The maximum procedure time for the CAPS group was 125 minutes, while the maximum procedure time for the control group was 101 minutes. These maximum procedure times are now listed in the Results section of the paper.