Author's response to reviews

Title: Performance of Single-Balloon Enteroscopy for the Diagnosis and Management of Small Bowel Disorders Based on Clinical Manifestations

Authors:

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Author's response to reviews: see over
Point-by-Point Revision:

Reviewer 1 (Philipp Lenz)

Mayor comment:

1. Abstract: "Unlike the double balloon, single balloon enteroscopy allowed only limited visualization of the entire small intestine". The reviewer comment that there was no data support this statement.

   Answer: We agree, so we changed this statement to “Single-balloon enteroscopy permits visualization of the entire small intestine less often than does double-balloon enteroscopy.” (Abstract)

2. Introduction: "To overcome these limitations, SBE was developed by removing one of the balloons and using the hook/suction- and-pull technique instead of the balloon on the enteroscope, making it easier for the endoscopist to learn and perform". The reviewer comment that both balloon-assisted enteroscopy techniques have the comparable difficulty levels. The handling of the endoscope equipped with one balloon was supposed to be easier because the susceptibility to failure of the second balloon is avoid.

   Answer: We agree, so we changed the sentence to “To overcome these limitations, SBE was developed by removing the balloon on the enteroscope and using the hook/suction-and-pull technique in its place; the resulting endoscope, equipped with only 1 balloon, was supposed to be easier to handle.” (Introduction)

3. Introduction: "However, it remains controversial whether total enteroscopy is required to increase diagnostic yields and whether its impact on the management of small bowel disease are significant". The reviewer recommended to cite Xin L et al. study

   Answer: We have added this as reference 7. (References)

4. Material and Methods: "in our institute, insertion depth is not measured in centimeters; hence in our study, the insertion depth was estimated by the performers at the end of the procedure..."

   The reviewer ask the authors to specified how to identified the mentioned region.
Answer: The endoscopists estimated the depth by a combination of the mucosal pattern including the characteristics of the mucosal folds, and the location of the tip of the enteroscope as visualized by fluoroscopy. (A similar method for estimation of insertion depth was used in reference 17.)

5. Material and Methods: "Diagnostic yield was defined as a definite diagnosis and a positive finding that might be associated with the clinical presentation". The reviewer commented about the meaning of positive finding that might be associated with the clinical presentation.

Answer: We agree and changed this to “The diagnostic yield was defined as the percentage of procedures that produced either a definitive diagnosis or findings that could explain the clinical symptoms.” (Methods)

6. Results: "Of the patients, 22% underwent a retrograde procedure, whereas 77% underwent an antegrade procedure". The reviewer commented about explanation of the low number of combine enteroscopy and low retrograde route.

Answer: Most of the endoscopists who performed the procedures did not perform a second procedure if they thought that the first procedure had yielded a definitive diagnosis. The route of enteroscopy was chosen according to the suspected location of the lesion(s). As the jejunum was the most frequent site, the antegrade route was the first choice.

7. Only one patient underwent bidirectional procedure in the same setting, which was otherwise done as a sequential strategy?, How many patients were investigated by a combination approach?, not in the same setting, but subsequently?, what was the average time period between both investigation?

Answer: Only 1 patient underwent bidirectional enteroscopy during a single session. However, sequential bidirectional endoscopy was performed in 15 patients, within 7 days after the first procedure in 8 cases and within 7–30 days after the first procedure in 7 cases. The mean time between the 2 procedures was 11.3 days. (Added to the body text of the Results.)

8. Results: “Fluoroscopy was used in 71.7% of the procedures” What does the fluoroscopy rate seemed pretty high?

Answer: The endoscopists used fluoroscopy to aid in the correction of any loops formed during the procedure and also to help to localize the tip of the enteroscope.
9. Results: “The mean ± SD procedure duration was 82.4±43.2 minutes. While the mean procedure duration for the antegrade route was 81.8±41.2 min, that of the retrograde route was 78.3±34.7 min”. The procedure time were long compare to the literature. How did you define the beginning and the end of the examination.

Answer: The procedure time extended from the time when the scope was passed through the mouth until the scope had been completely withdrawn from the mouth (antegrade route) or from the time the scope was passed through the anus until it had been completely withdrawn from the anus (retrograde route). This means that the times in this study would be expected to be longer than those in some other studies in which the procedure was timed from the point at which the enteroscope was passed through the D-J junction (antegrade route) or the IC valve (retrograde route). (Explanatory text to this effect was added to the Methods).

10. Results: The reviewer suggested the authors to revise the whole passage, explaining the reason for the high “time to enteroscopy”, the comparison of the patients with and without clinical success especially for those with gastrointestinal bleeding.

Answer: We have re-written this part of the manuscript as follows: “The diagnostic yield was only 42.9% in the overt GI bleeding group and 54.0% in the occult GI bleeding group. These results were not consistent with those of previous Western studies, which reported diagnostic yields of as high as 78% in patients presenting with GI bleeding [4, 5]. In addition, the most common cause of bleeding was erosions and ulcers; this was similar to the findings of other Asian studies but different from those of the Western studies, in which angiodysplasia was the most common finding. Therefore, we hypothesized that the difference in diagnostic yield might be related to the different etiologies of GI bleeding. We suspect that a prolonged time interval between clinical presentation and enteroscopy, i.e., time to enteroscopy, could produce false-negative findings. Therefore, we determined the time to enteroscopy in this study, which was 49.3 ± 104.9 days overall. The reason for this prolonged time to enteroscopy was related to our health system. The patients who were referred for SBE in our hospital (a university-based tertiary care center located in the central part of Thailand) came from all over the country. In general, it takes some time to make arrangements for such referrals. However, in the patients with overt GI bleeding, the time interval between the onset of bleeding and the day on which enteroscopy was performed did not differ significantly according to whether a definitive diagnosis was achieved (p= 0.08). Therefore, the time to enteroscopy might not be directly related to the diagnostic yield. The previously mentioned hypothesis would also suggest that the low diagnostic rate in this study might be related to the etiology of the bleeding itself, which was most frequently found to be erosions and ulcers. However, the time to enteroscopy in this study was rather prolonged, which may have allowed the lesions to heal and disappear.”(Discussion)
11. Please related your description of the relevant finding to “Xin L, Liao Z, Jiang YP, Li ZS, indications, detectability, positive findings, total enteroscopy, and complications of diagnostic double-balloon endoscopy; a systematic review of data over the first decade of used. GIE 2011;74:563-70

Answer: We have re-written this part of the manuscript as follows: “In comparison with the results of a meta-analysis of the performance of DBE by Xin L et al. in 2011 [18], the results from the study showed that the most common indication for enteroscopy was suspected mid-GI bleeding (62.5%), followed by symptoms/signs only (7.9%), small-bowel obstruction (5.8%), and Crohn’s disease (5.8%). The pooled detection rates were 68.1%, 68.0%, 53.6%, 63.4%, and 85.8% for overall, suspected mid-GI bleeding, symptoms/signs only, Crohn’s disease, and small-bowel obstruction, respectively. Inflammatory lesions (37.6%) and vascular lesions (65.9%) were the most common findings in patients with suspected mid-GI bleeding in Eastern and Western countries, respectively. The pooled rate of total enteroscopy by combined or antegrade-only approaches was 44.0%. GI bleeding was also the most frequent indication in the present study, but our detection rate for GI bleeding was lower. However, the causes of bleeding in this study were predominantly inflammatory rather than vascular lesions, similarly to those in other reports from Eastern counties. The rate of total enteroscopy in this study was very low” (Discussion)

12. Discussion” However, the area of interest was achieved in approximately 80.7% of the time, and an overall diagnosis could be made using these procedures in approximately 42.8% of the time, which is similar to that in other SBE studies that reported approximate 37–61%” the reviewer suggested for citation...

Answer: This has been addressed in the References and in the Discussion with “which is similar to the rates of 37–61% reported elsewhere for SBE [3,5,11-14].”

13. Discussion: “in addition, these result was comparable with those of DBE studies that reported diagnostic yield of approximately 43-52%. Please cite...

Answer: This has been addressed in the References and in the Discussion with “In addition, this result was comparable with those of DBE studies that reported diagnostic yields of approximately 43–72% [5,12].”

14. Discussion/Results: Diagnostic yield in overt GI bleeding was 42.9%

Answer: We have rewritten this part of the manuscript (Discussion).
15. Please note down the clinical setting of the hospital performing the enteroscopy in this study.

**Answer:** We have noted this information in the Discussion as follows: “The patients who were referred for SBE in our hospital (a university-based tertiary care center located in the central part of Thailand)…."

**Reviewer 2 : Peter Green**

1. **There is the extensive duplication of the results and tables.**

   **Answer:** We have revised the tables and the results to reduce duplication.

   (Table 1 has been abbreviated and the Results revised.)

2. **How many patients were taking NSAID?**

   **Answer:** There were 22 patients with history of NSAID therapy at the time of clinical presentation. We had already analyzed these data but found no significant relationship with the results. Therefore, we did not mention it.