Author's response to reviews

Title: Rebleeding rate after interventional therapy directed by capsule endoscopy in patients with obscure gastrointestinal bleeding

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Version: 2 Date: 10 March 2008

Author's response to reviews: see over
Dear Dr. Bucceri,

Thank you for your letter concerning the above-mentioned manuscript. I received your letter on February 26 and have revised the manuscript accordingly. I am pleased to note the favorable comments of the reviewers and have made the necessary corrections, as described in detail on the following pages. I hope that these corrections will meet with the reviewers’ approval.

First I would like to address the Editorial concerns.

Thank you for your useful suggestion. We have added an Acknowledgements section between the Author’s contributions section and the Reference list.
I have carefully corrected some types and grammatical errors.
Response to Reviewer 1 (Dr. McAlindon)

Thank you very much for your useful suggestions. We have made several revisions to our manuscript, which we feel has been greatly improved as a result.

Major 1: I am not absolutely clear if “therapeutic intervention” and “specific medical therapy” are considered separately – I think they are, but perhaps this needs to be clarified further.

According to your suggestion, we have clarified the definitions of “therapeutic interventions” and “specific medical therapy”. In this study, we used the words “specific medical therapy” to indicate a specific “drug” therapy that has been accepted as an established drug therapy such as the use of mesalazine for Crohn’s disease. As the phrase “specific medical therapy” is confusing, we have changed this phrase to “specific drug therapy”. We have defined that “therapeutic intervention” includes “specific drug therapy” in this study. We have added this information to the Results sections.

Major 2: One of the main messages is that therapeutic intervention reduces rebleed rate, but there are no details about these two groups of patients. Perhaps patients did not undergo intervention because they had significant co-mobidity (eg advanced heart failure) and were on aspirin or anticoagulants. One would expect that this kind of patient would be at high risk of rebleed. i.e. is it the intervention that helps, or is it that those who do not undergo intervention are a high risk group? This should be addressed.
As you mentioned, it is important to consider the selection of the patients that underwent interventions. Patients who had significant co-morbidity and were on aspirin or anticoagulants might have a high risk of rebleeding. In a recent report, Sidhu et al. demonstrated that co-morbidity was a significant predictive factor of a positive diagnostic yield [Sidhu R, et al. Am J Gastroenterol 2007;102:1329-30], and this result might be related to the rebleeding rate in this patient population. However, in the present study, the main reasons for not undergoing “further interventions” were the CE findings were too small to justify further interventions (n = 10), the absence of clinical rebleeding for a notable period (n = 10), co-morbidity (n = 4), and patients’ refusal (n = 3) and only 1 of the 4 patients who had co-morbidities developed rebleeding. Moreover, none of the patients did not undergo “therapeutic intervention” because of co-morbidity or the use of aspirin/anticoagulants. Therefore, co-morbidity and the use of aspirin/anticoagulants did not affect the decision to undergo intervention and were not associated with a high risk of rebleeding in this study. We have added this information to the Results and Discussion sections.
Response to Reviewer 2 (Dr. Garcia-Compean)

Thank you very much for your useful suggestions. We have made several revisions to our manuscript, which we feel has been greatly improved as a result.

1. – The title of the manuscript does not reflect entirely the content of the manuscript. I recommend for example: “Rebleeding rate after interventional therapy directed by CE in patients with obscure gastrointestinal bleeding” since modification of the natural history of OGIB was given by the effect of the therapy and not for the CE per se.

According to your suggestion, we have changed the title of the manuscript (“Rebleeding rate after interventional therapy directed by capsule endoscopy in patients with obscure gastrointestinal bleeding”).

2. – Authors excluded patients with swallowing disorders and pacemaker implantation. I suggest authors to point out in discussion section that these conditions are no longer contraindications for performance of CE.

According to your suggestion, we have added the following sentences to the Discussion section.

“While swallowing disorders and pacemaker implantation were regulated as exclusion criteria in the present study, these factors are no longer regarded as contraindications for the performance of CE. Actually, none of the patients considered for enrollment in the present series had suspected swallowing disorders or implanted pacemakers”.
3. – Range values of time of follow up and haemoglobin values were not given.

We have added the range values for the follow-up period and the haemoglobin values in the Results section.

4. – In table 2 definitions of abbreviations should be given in the bottom of the table. Table must be auto explained.

According to your suggestion, we have included the definitions of the abbreviations used in the table at the bottom of Table 2.

5. – The diagnostic yield of CE in the study was 95%, although relevant findings were found in 58%. These relevant findings maybe correspond to the named P2 lesions proposed by some authors (3). Make some comments in discussion.

According to your suggestion, we have added the following comments in the Discussion section.

“Moreover, when lesions observed at CE were divided into highly relevant (P2) or less relevant (P0, P1) according to the possibilities of their being responsible for the GI bleeding, highly relevant lesions were more frequently classified in true-positive cases and led more frequently to therapeutic decisions, compared with less relevant lesions [Saurin et al. Endoscopy 2005;37:318]. The named P2 lesions proposed by some authors corresponded to significant findings of the present study. These results suggest that this classification of CE findings may assist clinicians in making appropriate therapeutic
decisions and may improve the clinical outcome of patients with OGIB.”

6. – Complications due to procedure and rate of incomplete studies were not précised.

The complications arising to CE and the rate of incomplete studies have been stated in the Results section.

7. – In discussion section in the paragraph of limitations authors may state that this was not a randomized trial, posttherapy values of haemoglobin were not given.

According to your suggestion, we have added this information to the Discussion section in the paragraph describing the study’s limitations.

8. – Finally I suggest authors to include in the manuscript references of published studies having similar aims and compare their results with those of them.

According to your suggestion, we have cited some published reports [Garcia-Compean D et al. Gastroenterol Clin Biol. 2007;31:806, Delvaux M et al. Endoscopy 2004;36:1067] and have added the following paragraph to the Discussion section.

“In this study, we evaluated the clinical impact of CE for directing interventional therapy in patients with OGIB and reported the long term results of this strategy using the rebleeding rate as the primary outcome. This important issue has been rarely studied to date; however, some previous reports have described similar results. Recently, Garcia-Compean et al. reported that a significantly reduced rate of recurrent bleeding (6%) was observed in patients with positive CE findings who underwent specific
treatment in a study of 40 patients with OGIB [Garci-Compean D et al. Gastroenterol Clin Biol. 2007;31:806]. Delvaux et al. also reported similar results: among 18 patients who were treated for intestinal lesion that were detected by CE, only one patient (5%) relapsed during a 1 year follow-up period [Delvaux M et al. Endoscopy 2004;36:1067]. Although the details of their treatments were not exactly the same as ours, their results were very similar."

I would like to thank the reviewers for their helpful comments, and hope that the revised manuscript is acceptable for publication in BMC Gastroenterology.

Hiroki Endo