



ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 17436

Title: Mucosal healing including the small intestine predicts clinical outcome in Crohn’s disease

Reviewer’s code: 03254791

Reviewer’s country: United States

Science editor: Jing Yu

Date sent for review: 2015-03-10 18:50

Date reviewed: 2015-03-12 21:39

Table with 4 columns: CLASSIFICATION, LANGUAGE EVALUATION, SCIENTIFIC MISCONDUCT, CONCLUSION. It contains checkboxes for various review criteria like 'Grade A: Excellent', 'Priority publishing', 'Google Search', etc.

COMMENTS TO AUTHORS

The study's efforts to validate an endoscopic scoring system using newer technology is important. It is somewhat limited by its retrospective nature that only includes those patients who have been pre-selected to undergo DBE. Abstract—Should define double balloon enteroscopy as “DBE” as is not standard definition known to all. Describe the DBE technique as all may not be familiar with this technique. At our institution we utilize transoral DBE. As such, methods describing length from ileocecal valve “on the oral side” is confusing. I would either describe length of bowel IC valve OR if from oral route length of bowel from mouth. Transanal approach and length of bowel from IC valve “on oral side” is very confusing. Table 1—Given limitation of study that includes only those patients who were ordered DBE—should include more demographics about their disease. E.g. disease location at diagnosis, disease behavior, duration of disease, duration of disease, presence of SB disease by wireless capsule endoscopy, by radiography e.g. MRI, CT scan fluoroscopy. Inclusion of #lesions is misleading. Recommend including # patients that have findings. Also define “lesions”. As only 39/76 could have lesions identified at 80cm, there must be multiple



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lesions described for each patient. This is misleading. Add headings for tables and N plus percentage for better comparison. SES-CD may have been less predictive b/c of your population is self-selected and likely biased toward including patients that have mainly small bowel disease. Would include this in your discussion.



ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 17436

Title: Mucosal healing including the small intestine predicts clinical outcome in Crohn’s disease

Reviewer’s code: 03029622

Reviewer’s country: Ireland

Science editor: Jing Yu

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Table with 4 columns: CLASSIFICATION, LANGUAGE EVALUATION, SCIENTIFIC MISCONDUCT, CONCLUSION. It contains checkboxes for various review criteria like 'Grade A: Excellent', 'Duplicate publication', 'Plagiarism', etc.

COMMENTS TO AUTHORS

Small bowel mucosal healing is a “hot topic” currently. This paper is thus a timely one in attempting to define the role of DBE in this expanding area. The authors perform a small retrospective study of patients with established Crohn’s disease undergoing DBE. The concept of small bowel mucosal healing scoring systems is important. I would suggest this paper is suitable for publication with some changes. Minor revisions A. Introduction 1. Suggest change anti-TNF antibodies to monoclonal antibodies as newer non anti-TNF agents available. 2. The sentence “To date, however, a method of evaluating MH in CD which includes the small intestine has not been established” should be modified. SBCE and MRE have both been shown to be capable of assessing mucosal healing. This should be mentioned in the introduction. B. Results 1. Some of the terminology is confusing. The authors should try to make reference to distance travelled proximally from ileo-caecal valve. The use of the term “oral” is unnecessarily confusing. 2. The authors make no mention of any small bowel imaging performed prior to DBE. It would be interesting to know if (a) mucosal disease/strictures had been identified prior to DBE and (b) more proximal disease was identified. 3. Faecal



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calprotectin levels would be interesting if available C. Discussion 1. DBE is not always widely available. It would be nice to know where the authors feel DBE fits into the overall paradigm of CD treatment ie. Should it be performed on every patient diagnosed with CD or in selected cases. Major revisions A. Results 1. The authors state that the mSES-CD is better at predicting surgery free survival compared to SES-CD. This would seem apparent as strictures tend to occur in the narrower small bowel lumen. There are a large proportion of patients (39%) in this study that had strictures at the time of DBE. Despite small numbers, a sub-group analysis of those patients without strictures would be interesting to see if (a) mSES-CD is still more predictive of surgery free survival and (b) CRP correlated more closely with mSES-CD.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 17436

Title: Mucosal healing including the small intestine predicts clinical outcome in Crohn's disease

Reviewer's code: 01514813

Reviewer's country: Italy

Science editor: Jing Yu

Date sent for review: 2015-03-10 18:50

Date reviewed: 2015-04-13 22:07

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

To me, the biggest problem of this study is the lack of clarity on the aim of the study. As indicated in the abstract while the aim of the study was to evaluate the clinical utility of a new endoscopic score, the title introduces the concept of mucosal healing as a prediction of clinical outcome. Since, there is no evidence of mucosal healing (namely patients received only one assessment of their inflammatory lesions, and there is no before and after treatment study) it is incorrect to define an endoscopic score <4 as "mucosal healing". In my opinion, the study indicates that the endoscopic study of the small bowel allows a more accurate definition of the presence and degree of inflammation of the anatomical lesions. As that it could be useful in predicting the need for surgery where previous studies showed contrasting results on the utility of endoscopy for this prediction (Jauregui-Amezaga A, et al. Gut Published Online First: December 16, 2014 as 10.1136/gutjnl-2014-308101; Allez M, et al. Am J Gastroenterol 2002;97:947-53) To substantiate their findings the AA should: ? specify if physicians who recommended surgery were blinded or not to the endoscopic assessment and discuss the consequences ? show the total number of patients who underwent surgery and their



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disease's location and extension ? Introduce in the graph of Figure 2 , at each time point, the total number of patients at risk for surgery and the number of patients undergoing surgery . In addition: The Title has to be changed according to the defined major aim (clinical utility of the new score). Previous studies on endoscopy utility for predicting intestinal surgery should be discussed and contrasted with the AA results. These include also findings on Infliximab therapy and disease duration recognized in previous studies and confirmed in the present study as factors influencing surgery.