

RE: 49160, entitled **Risk Factors for Recurrence after Bowel Resection for Crohn's Disease**

Dear editor,

Thank you for reviewing the above-referenced manuscript submitted earlier to your office. We would like to take this chance to express our appreciation to you and colleagues.

In accord with your and the Reviewer's comments, the manuscript has been revised accordingly, and the changes have been highlighted in Yellow in the revised manuscript. We feel that the revised manuscript has been strengthened by your and the Reviewer's suggestions and comments, and we are very appreciated of your and their time and effort. A point-by-point response to the reviewers' comments and suggestions has been prepared and follows this cover letter.

If there are any questions or problems for our revised manuscript, please feel free to contact us.

Sincerely yours,

Ping Lan

On behalf of all co-authors

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Responses to comments

Reviewer #1:

The authors report on a cohort of patients who have undergone surgery for Crohn's disease and have reported a number of factors which seem to predispose to early recurrence. The manuscript is a retrospective study with all of the potential shortcomings of this type of study. The follow up is also short. Despite this there does appear to be a useful message from the study. It is however worth noting that use of anti-TNF treatment and peri-anal Crohn's are likely indicators of disease severity. There are a small number of

grammatical/typographical errors that need addressing.

Response:

Thanks a lot for your comment and suggestion. Some grammatical/typographical errors have been revised.

Reviewer #2:

The retrospective manuscript is well written but something spelling error in the body of the text.

Response:

Thanks a lot for your comment and some spelling errors have been revised.

Reviewer #3:

This study aimed to evaluate the risk factors for recurrence after bowel resection in Crohn's Disease. Major points: 1. This study lacks novelty and is limited by small sample size. 2. Endoscopic and clinical recurrence are not clearly described. 3. Medication of patients after surgical resection is not provided. Minor points: 1. In the abstract, only results from the multivariate analysis should be included.

Response:

1. The sample size is indeed small. Further clinical study with more patients is needed to confirmed the result.
2. Endoscopic and clinical recurrence are described in the revised manuscript.
3. Medical therapy after surgery was deficient as some patients did not receive medical therapy in our hospital, so it was not considered at first when concepting and designing this study.
4. The result in the abstract have been revised.

Reviewer #4:

This is well designed, performed and written retrospective clinical study for the evaluation of risk factors for recurrence after bowel resection in Crohn's Disease' patients and its association with diagnostic age, disease behavior and preoperative use of anti-TNF treatment. The authors investigated altogether 64 patients with Crohn's Disease who received intestinal resection. The authors give a sufficiently clear overview about the study background and raised clearly the aim of the study, which is fulfilled. The statistical analysis was specified sufficiently well. The material studied is large enough and allows to draw the conclusions. The Results are presented clearly and have been discussed well. The paper is supplied with 2 Tables and one Figure which give very good overview about the results and are presented very clearly and correctly. The authors found that diagnostic age, disease behavior and preoperative use of anti-TNF were independent prognostic factors for endoscopic recurrence. Complication with perianal lesions was an independent prognostic factor for clinical recurrence. This paper has also important clinical outcome because pay attention on possible risk factors for recurrence after bowel resection in patients with Crohn's disease.

Response:

Thanks a lot for your comment.

Reviewer #5:

This manuscript deals with risk factors for recurrence after bowel resection for Crohn's disease. It provides a case series of 64 patients and may be seen as local quality control rather than scientific research. The follow-up period is short. No innovations are presented. A thorough stylistic/linguistic revision is recommended (perhaps changes were made after the editing process or the authors did not take up all the suggestions); e.g., "Patients diagnosed Crohn's Disease and received intestinal resection between April 2007 and December

2013 were included in this study"; "...complication with perianal lesions (P=0.032) and preoperative use of immunomodulatory (P=0.031) were significantly correlated with clinical recurrence"; etc. The reference list also requires revision (in order to be consistent with the guidelines of the journal); DOIs/PMIDs are not included.

Response:

Thanks a lot for your comment and suggestion. Some stylistic/linguistic revision have been made. The reference list has also been revised according to the guidelines.

Reviewer #6:

This is very interesting paper about recurrence risk factor for crohn's disease after surgical treatment. Author concluded age, anti-TNF, perianal lesion and Disease behavior are risk factor for crohne's disease after surgical treatment. Manipulation of the bacterial flora is an attractive mode of preventing postoperative recurrence, as specific bacteria including bacteroides, fusobacteria and E. coli have been found in increased amount in the neo-terminal ileum. . However, a small study with VSL#3 did note that patients receiving the probiotic had less severe endoscopic recurrence (lower Rutgeerts score) and reduced levels of pro-inflammatory cytokines. (Madsen K, A Randomized Controlled Trial of VSL#3 for the Prevention of Endoscopic Recurrence Following Surgery for Crohn's Disease. Gastroenterology. 2008;134:A-361.) Nitroimidazole antibiotics including metronidazole and ornidazole have been shown to decrease the risk of clinical and severe endoscopic recurrence. The overall rate of recurrence was low which was attributed to the widespread metronidazole use, although in combination with azathioprine endoscopic recurrence was less frequent and less severe. (D'Haens Therapy of metronidazole with azathioprine to prevent postoperative recurrence of Crohn's disease: a controlled randomized trial. Gastroenterology.

2008;135:1123–1129.) I ask some questions to author. 1. Please comment about the relationship between patients receiving probiotic and recurrence. 2. Please comment about the relationship between antibiotics and recurrence. 3. Author concluded recurrence risk factor is age. How old is age. 4. Disease behavior: perforation, fistula, mesenteric ischemia Please comment what kinds of disease behavior are risk factor. 5. I think perianal lesion of crohn's disease is difficult to treatment. Please comment what kinds of surgical treatment of perianal lesion do you perform.

Response:

Thanks a lot for your comment and suggestion.

1, 2. Information about probiotic and antibiotics was deficient so they were not considered at first when concepting and designing this study.

3, 4. The details of age and disease behavior were added in the revised manuscript.

5. We mainly performed thread-drawing drain for perianal lesion of Crohn's Disease.