

We thank the reviewers and editors for their critical and insightful evaluation of our manuscript. The raised concerns are certainly of major importance, and we have tried to answer them accordingly. We believe the excellent reviewers' suggestions contributed to a much-improved presentation of our findings. Please note, that in addition to a point-by-point response to comments (answered below), we have additionally included minor formatting edits throughout the manuscript.

Comments from the Editors and Reviewers:

Reviewer #1:

**Scientific Quality:** Grade B (Very good)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Minor revision

**Specific Comments to Authors:** The authors retrospectively compared the short- and long-term outcomes between laparoscopic and open ICR for the treatment of ileocolic CD, found that the laparoscopic procedure had better short-term outcomes and comparable long-term outcomes compared to open group. While there are several points need to be clarified.

**1. The inclusion and exclusion criteria were not clearly stated in the manuscript.**

Thank you for your valuable comment. As the reviewer pointed out, we made effort to clarify the inclusion and exclusion criteria. Ileocolic resection included patients receiving resection of the ileum and colon with ileocolic anastomosis within the right/transverse colon. Patients who underwent previous bowel resection for CD, those without anastomosis, those with ileocolic anastomosis distal to the transverse colon and patients with missing data or loss to follow-up were excluded (Figure 1).

Page 6. Line 2 ~ 8. "Patients who underwent LICR or OICR for primary CD at Asan Medical Center in Seoul, Korea, from January 2006 to December 2017, were retrospectively identified. Ileocolic resection included patients receiving resection of the ileum and colon with ileocolic anastomosis within the right/transverse colon. Patients who underwent previous bowel resection for CD, those without anastomosis, those with ileocolic anastomosis distal to the transverse colon, and patients with missing data or loss to follow-up were excluded (Figure 1)."

**2. For the patients included in this study who underwent surgical treatment of ileocolic CD, what is the indication for the selection of laparoscopic or open ICR? The selecting bias may exist that patients with mild CD were likely to undergo the laparoscopic surgery, which could exert a tremendous influence on the short-term outcomes, especially the factors found statistically different in this study. The less penetrating behavior in laparoscopic ICR mentioned in the study might prove this hypothesis, which should be defined and illustrated in the manuscript.**

We agree with the reviewer in that a selection bias may exist and patients in the laparoscopic group is likely to have mild CD compared to the open group. Because this study is a retrospective study, we cannot be completely free from this in born limitation.

Laparoscopic and open surgery was selected for each patient according to surgeon preference. Important factor considered for selection of surgical method is the history of previous abdominal surgery with or without bowel resection. As patients with previous bowel resection were excluded, multiple factors such as age, general condition, and disease extent were taken in consideration.

To minimize the selection bias, we included covariates that have influence in selecting surgical methods and surgical outcomes in the PSM analysis. By using PSM, we could match patients in pairs to the closest baseline characteristics. The baseline clinical characteristics of the two groups before PSM showed difference in Montreal classification, disease duration, comorbidity, and indications for surgery. We were able to adjust these factors by performing PSM analysis (Table 1).

We are aware of the limits of PSM and have described it in the limitation section of discussion in the manuscript.

Page 15. Line 24 ~ 29, Page 16. Line 1 ~ 5. “The present study had several limitations. First, this study was a retrospective evaluation of patients at a single center. Randomized-controlled trials are required to specifically evaluate the ability of a laparoscopic approach to minimize postoperative complications. Although propensity-score matching can reduce selection bias, resulting in a situation similar to a randomized-controlled trial, our propensity-score matching models could not eliminate all selection biases. For example, the most frequent reasons for conversion to open surgery, such as adhesions and huge phlegmons, could not be calibrated by propensity-score matching analysis. Also, although the CDAI scores for both groups were moderate grade, the laparoscopic group presented significantly lower CDAI with 230.8

compared to 269.1 in the open group ( $p=0.008$ ). Inevitably, a randomized controlled trial is essential to evaluate the role of laparoscopic approach with more reliable evidence.”

### **3. Please define the PSM criteria in the Methods section.**

We are sorry for the unclear delivery of the important PSM criteria. As the reviewer recommended, we have defined the PSM analysis in the Methods section. Propensity scores were estimated by multiple logistic regression analysis. All pre-specified covariates were included in the full non-parsimonious models. The covariates included demographic characteristics (age, gender, BMI, smoking history, previous history of abdominal surgery, previous history of comorbidity, and ASA score), disease-related variables (Montreal classification, disease duration, perianal CD, family history of CD and extra-intestinal CD manifestations), and treatment-related variables (preoperative hemoglobin and albumin concentrations, preoperative RBC transfusions, preoperative medications, and indications for surgery). These variables were selected as they can affect the selection of surgical approach and perioperative outcomes. The operative approach was entered into the regression model as a dependent variable. A 1:1 “nearest neighbor”, case–control match without replacement was used by a medical statistician (JB Lee).

Page 8. line 15 ~ 26, Page 9. Line 1 ~ 6. “Propensity score matching analysis

To minimize the impact of selection bias for the surgical approach and potential confounding in this observational study, patients who underwent LICR and OICR were subjected to propensity-score matching, with rigorous adjustment for significant differences in patient characteristics. Propensity scores were estimated by multiple logistic regression analysis. All pre-specified covariates were included in the full non-parsimonious models. The covariates included demographic characteristics (age, gender, BMI, smoking history, previous history of abdominal surgery, previous history of comorbidity, and ASA score), disease-related variables (Montreal classification, disease duration, perianal CD, family history of CD and extra-intestinal CD manifestations), and treatment-related variables (preoperative hemoglobin and albumin concentrations, preoperative RBC transfusions, preoperative medications, and indications for surgery). These variables were selected as they can affect the selection of surgical approach and perioperative outcomes. The operative approach was entered into the regression model as a dependent variable. A 1:1 “nearest neighbor”, case–control match without replacement was used. The discrimination and calibration abilities of the propensity-

score model were 0.7332 by C-statistics and  $p = 0.1219$  by Hosmer-Lemeshow statistics. Following propensity-score matching, short- and long-term results were compared in the two groups.”

#### **4. The perioperative Crohn's Disease Activity Index for the patients enrolled in the study was recommended to be compared between these two groups if possible.**

We agree Crohn's Disease Activity Index (CDAI) is an important variable associated with severity of CD. As the reviewer recommended, we have collected the eight variables to calculate perioperative CDAI: number of loose stools, abdominal pain, general well-being, extraintestinal complications, antidiarrheal agents used in the previous 7 days, abdominal mass, hematocrit, and body weight. The CDAI score were compared between open and laparoscopic groups by T-test. Laparoscopic group had significantly lower CDAI ( $230.8 \pm 9.5$  versus  $269.1 \pm 10.8$ ,  $p=0.008$ ) in the matched set. Although PSM analysis was used to minimized selection bias, it seems that patients with low severity in the laparoscopic group were selected.

CDAI scores range from 0 to 600. A score of less than 150 corresponds to relative disease remission; 150 to 219, mildly active disease; 220 to 450, moderately active disease; and greater than 450, severe disease<sup>[1]</sup>. Although the CDAI scores were lower in the laparoscopic group, the grades of CDAI scores were both moderate (220 to 450). In South Korea, the national insurance policy permits usage of biologics to patients with CDAI scores higher than 220. Thus, we believe the laparoscopic and open group can be considered to have a comparable severity of CDAI in regard to grading from mild to severe. We acknowledge that the difference in CDAI scores is an important information for interpreting our results and described this limitation in the discussion section.

Page 10. Line 6 ~ 11. “Crohn's Disease Activity Index (CDAI) scores were compared between the two groups. LICR and OICR group both presented a moderate grade in CDAI score ( $230.8 \pm 9.5$  and  $269.1 \pm 10.8$ , respectively). Because the demographic data differed between the OICR and LICR groups, these patients were subjected to 1:1 propensity-score matching to reduce selection bias. A total of 102 pairs was therefore included in the propensity-score matched population.”

Page 15. Line 24 ~ 29, Page 16. Line 1 ~ 5. “The present study had several limitations. First, this study was a retrospective evaluation of patients at a single center. Randomized-controlled trials are required to specifically evaluate the ability of a laparoscopic approach to minimize

postoperative complications. Although propensity-score matching can reduce selection bias, resulting in a situation similar to a randomized-controlled trial, our propensity-score matching models could not eliminate all selection biases. For example, the most frequent reasons for conversion to open surgery, such as adhesions and huge phlegmons, could not be calibrated by propensity-score matching analysis. Also, although the CDAI scores for both groups were moderate grade, the laparoscopic group presented significantly lower CDAI with 230.8 compared to 269.1 in the open group ( $p=0.008$ ). Inevitably, a randomized controlled trial is essential to evaluate the role of laparoscopic approach with more reliable evidence.”

Reviewer #2:

**Scientific Quality:** Grade B (Very good)

**Language Quality:** Grade A (Priority publishing)

**Conclusion:** Accept (General priority)

**Specific Comments to Authors:** I read the manuscript with extreme attention. Very interesting study Well written introduction Comprehensive materials and methods The results are well illustrated Complete and exhaustive discussion Clear tables.

Thanks for your comments.

**(1) Science editor:**

1 Scientific quality: The manuscript describes a retrospective cohort study of the short-term and long-term outcomes of laparoscopic versus open ileocolic resection in patients with Crohn's disease. The topic is within the scope of the WJG. (1) Classification: Grade B and Grade B; (2) Summary of the Peer-Review Report: The authors retrospectively compared the short- and long-term outcomes between laparoscopic and open ICR for the treatment of ileocolic CD, found that the laparoscopic procedure had better short-term outcomes and comparable long-term outcomes compared to open group. It is very interesting and well written. However, the inclusion and exclusion criteria were not clearly stated. The questions raised by the reviewers should be answered; and (3) Format: There are 5 tables and 2 figures. (4) References: A total of 42 references are cited, including 6 references published in the last 3 years; (5) Self-cited references: There are 3 self-cited references. The self-referencing rates should be less than 10%. Please keep the reasonable self-citations that are closely related to the topic of the manuscript, and remove other improper self-citations. If the authors fail to address

the critical issue of self-citation, the editing process of this manuscript will be terminated; and (6) References recommend: The authors have the right to refuse to cite improper references recommended by peer reviewer(s), especially the references published by the peer reviewer(s) themselves. If the authors found the peer reviewer(s) request the authors to cite improper references published by themselves, please send the peer reviewer's ID number to the editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately. 2 Language evaluation: Classification: Grade B and Grade A. A language editing certificate issued by Bioedit® LTD was provided. 3 Academic norms and rules: The authors provided the Biostatistics Review Certificate, and the Institutional Review Board Approval Form. Written informed consent was waived. The STROBE Statement needs the page number. No academic misconduct was found in the Bing search. 4 Supplementary comments: This is an invited manuscript. No financial support was obtained for the study. The topic has not previously been published in the WJG. 5 Issues raised: (1) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor; and (2) The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text. 6 Recommendation: Conditional acceptance.

We reviewed the self-cited references. One reference (number 10) included one of our co-authors Yu CS. However, the article was based on a nationwide registry and the other authors were not from our center. Also, reference number 44 was written by Ye BD who is a physician at our center. The study was mostly undergone by the gastroenterology department. Therefore, we believe only reference number 41 is strictly a self-cited reference. We reviewed our manuscript in effort to eliminate non-reasonable self-citations and these 3 articles were independently related to our topic. As the number of self-cited reference is below 10% we hope to keep these articles in our study.

We added pages for the STROBE checklist as recommended.

We added a the "Article Highlights" section and reviewed the text according to reviewers' comments.

**(2) Editorial office director:**

**(3) Company editor-in-chief:**

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Gastroenterology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

Reference

- 1      **Gajendran M**, Loganathan P, Catinella AP, Hashash JG. A comprehensive review and update on Crohn's disease. *Dis Mon* 2018; **64**: 20-57 [PMID: 28826742 DOI: 10.1016/j.disamonth.2017.07.001]