

## Reviewer #1

**Conclusion:** Minor revision

**Specific Comments to Authors:** Thank you for inviting me to evaluate the observational study titled "Development of a warning score for early detection of colorectal anastomotic leakage: Hype or hope?". It is an interesting paper, the authors developed a predictive classification system [Early ColoRectAL Leakage (E-CRALL) score] from a prospective observational, single center cohort, carried out in a colorectal division from a non-academic hospital the score performance and CAL threshold from postoperative day (POD)3 to POD5 were estimated. The conclusion is that The E-CRALL score is an accessible tool to predict CAL at an early timepoint. Additionally, E-CRALL can reduce overall healthcare costs, mainly in the reduction of hospital costs, independent of whether a patient developed CAL. The information in this review is helpful to clinical communities. The paper is well arranged and the logic is clear, and. The cited literature is comprehensive and modern. The provided figure and tables are well composed and understandable. The quality of language of the manuscript is acceptable for me. So, I recommend to you that this manuscript may be accepted. There are some advices for author: 1) Is there a data bias in the research data of the colorectal department of a non-academic hospital, whether it has promotion value, because it is often affected by the level of surgeons, surgical methods, and technical conditions, such as whether to perform preventive ostomy, may significantly reduce colorectal anastomotic leakage. 2) Why are interleukin-6, ascites, and the examination of ascites not listed as variables in E-CRALL?

Dear Reviewer #1, thank you for your comments and suggestions.

Please, find below (and in the main file), our answers.

**1. Is there a data bias in the research data of the colorectal department of a non-academic hospital, whether it has promotion value, because it is often affected by the level of surgeons, surgical methods, and technical conditions, such as whether to perform preventive ostomy, may significantly reduce colorectal anastomotic leakage (CAL).**

We agree with you comment and are aware that data bias can be present in this context. However, our hospital is a reference center of colorectal disease, and our team perform approximately 400 colorectal resections with anastomosis every year. Furthermore, since 2015, we are a team of five surgeons mainly dedicated to colorectal procedure, which significantly reduces disparities in clinical decision, as performing or not a preventive ostomy. Additionally covering stoma was built in 23 (8.3%), 8 (8.5%) and 2 (8.0) patients of G1 (no complications), G2 (complications others than CAL) and G3 (CAL group), respectively, without statistical significance ( $p=0.99$ ) – vide our primary study, which can be consulted at <https://www.wjgnet.com/1007-9327/full/v0/i0/0.htm> - *Table 2 Patients' operative characteristics* – page 2763.

**2. Why are interleukin-6, ascites, and the examination of ascites not listed as variables in E-CRALL?**

In our primary study, which can be consulted at <https://www.wjgnet.com/1007-9327/full/v0/i0/0.htm>, we chose to assess only serum biomarkers, mainly because we no longer use abdominal drainage after colorectal surgery as a routine in our practice. The biomarkers chosen were C-reactive protein, procalcitonin, calprotectin, white blood cell count and eosinophil cell count.

## Reviewer #2

**Conclusion:** Minor revision

**Specific Comments to Authors:** Interesting job. Extreme current topic in colorectal surgery. Some clarifications 1. How was anastomotic leakage diagnosed? 2. Was a classification used for anastomotic leakage? If so, which one? 3. How was the anastomotic leakage treated? 4. It is necessary to mention the treatment in consideration of the fact that patients undergoing right colic resections and patients undergoing left colorectal resections were included. 5. Was abdominal drainage used at the end of the surgical procedure? 6. Were there protective ostomies? 7. Was a transanastomotic tube used in left colorectal resections?

Dear Reviewer #2, thank you for your comments and suggestions.

Please, find below (and in the main file), our answers.

### **1. How was anastomotic leakage diagnosed?**

CAL was defined in accordance with the following criteria: (1) Clinical: Enteric discharge from abdominal drain or wound, rectovaginal fistula, or anastomotic defect found by digital examination; (2) Radiological (CT): Extravasation of endoluminally administered contrast, intra-abdominal collection around the anastomosis, presacral abscess near the anastomosis or perianastomotic air, and free intraabdominal air; and (3) Surgical findings (reoperation): Necrosis of the anastomosis or signs of peritonitis and anastomotic defect.

### **2. Was a classification used for anastomotic leakage? If so, which one?**

Colorectal anastomotic leakage was classified into two categories: (1) Minor: Patients with CAL and Clavien-Dindo grade I or II, requiring no active intervention (radiological or surgical intervention) (Grade A of the International Study Group of Rectal Cancer definition); and (2) Major: All other patients with CAL - vide our primary study, which can be consulted at <https://www.wjgnet.com/1007-9327/full/v0/i0/0.htm> – page 2760.

### **3. How was the anastomotic leakage treated?**

In our research, seven patients (28.0%) were managed nonoperatively and two (8.0%) underwent radiologic drainage of intraabdominal collections. The remaining 16 patients (64.0%) required surgical intervention. Of the 16 reoperated patients, 10 (56%) had an anastomosis takedown with an end stoma and 6 (44%) received a defunctioning stoma vide our primary study, which can be consulted at <https://www.wjgnet.com/1007-9327/full/v0/i0/0.htm> – page 2762.

### **4. It is necessary to mention the treatment in consideration of the fact that patients undergoing right colic resections and patients undergoing left colorectal resections were included.**

We agree with your comment that there may be differences in the treatment of anastomotic leakage of right and left colorectal resection, but we chose not to highlight it because the main objective of this study was to develop a diagnostic tool. In our opinion, the choice of treatment adds nothing to our aims.

### **5. Was abdominal drainage used at the end of the surgical procedure?**

We follow ERAS protocol and no longer use abdominal drainage after colorectal surgery as a routine in our practice. The use of abdominal drain was dependent of intraoperative surgical team decision.

## **6. Were there protective ostomies?**

In our study, covering stoma was built in 23 (8.3%), 8 (8.5%) and 2 (8.0) patients of G1 (no complications), G2 (complications others than CAL) and G3 (CAL group), respectively, without statistical significance ( $p=0.99$ ) – vide our primary study, which can be consulted at <https://www.wjgnet.com/1007-9327/full/v0/i0/0.htm> - Table 2 Patients' operative characteristics – page 2763.

## **7. Was a transanastomotic tube used in left colorectal resections?**

In our research transanastomotic tube was not used.

## Science editor

The manuscript has been peer-reviewed, and it's ready for the first decision.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade C (Good)

Dear Science editor, thank you for your appraisal.

## **Company editor-in-chief**

I recommend the manuscript to be published in the World Journal of Gastrointestinal Surgery. Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the Reference Citation Analysis (RCA). RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/>.

Dear Company editor-in-chief, thank you for your comments and advice.

Following your suggestion, we did a search in the BPG tool (RCA - Reference Citation Analysis) and included two more references in our manuscript.