Reviewer #1

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

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

1. Page 3, line 29 − 31 Abstract, in the Results section, 'The length of hospital stay was markedly higher in the group that developed CAL (median of 21 vs. 13 and 7 days)'. It isn't very clear since 21 is for G3; readers might have no idea about the median length of hospital stay for G1 and G2, respectively. Meanwhile, P-value is missing.

We rewrote the sentence and included P-value.

2. Page 6, line 13, the Definitions section, the current definition for CAL is without any proper citation; As mentioned in the Discussion section, page 16, line 11 − 13, 'Third, we chose a comprehensive definition of CAL, recently defined by van Helsdingen et al.[47] to include all patients with CAL, minimizing selection bias '. I would suggest a knowledge-based definition for CAL (reference 47).

We included the reference suggested in this section.

3. My greatest concern is that 'All patients received prophylactic antibiotic. ' (page 7 line 22 − 23). It's possible that not every patient needs a prophylactic antibiotic treatment, and on the other hand, overuse of the antibiotic itself and the class of antibiotics could interfere with the results of inflammatory markers, such as CRP, WBC, etc.

Patients received prophylactic antibiotic accordingly to hospital infection control committee protocol.

4. Many grammatical issues need to be fixed professionally.

We did another professional proofreading to fix those issues.

Reviewer #2

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

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

However, in what order should this test method recommended by the authors be utilized in combination with other tests in clinical practice? For example, if this test method value is abnormal on the third postoperative day, then CT should be added and fasting should be managed.

The aim of this study was to identify the accuracy of biomarkers to early detect anastomotic leakage. We found that the combination of some biomarkers can predict the presence of anastomotic leakage. This hypothesis will be tested in our next study.

Does this test method change the way the authors monitor for the occurrence of postoperative CAL? I think the authors need to propose a method for postoperative management by using this test method in clinical practice.

That is the aim of our next prospective study. Currently, we still follow the institution protocol.

The day of Major CAL is day 5, what day is the time to start postoperative diet?

We follow ERAS protocol and its recommendations for starting diet, as well as clinical assessment.

Is Major CAL occurring after the start of postoperative diet? Is that also occurring before the meal starts?

As we followed ERAS protocol, all patients had already started the diet.

If this test can detect signs of Major CAL before the start of the postoperative meal, it would be considered an excellent test, but if CAL occurs after the start of the postoperative meal, the need for this test would be limited. Because even in Major CAL, 61.1% are diagnosed by CT.

As previously mentioned, we follow ERAS protocol and its recommendations for starting diet early on the postoperative period. This test can early warn for CAL development and be useful for timely and proper management.

In this paper, do the authors need Table 3?

We believe that this table is important to show the way different clinical situation can influence morbidity and mortality.

Reviewer #3

This prospective observational study provides relevant evidence about postoperative more feared colorectal complication such as colorectal anastomotic leakage. The study demonstrated the importance of some biomarkers, such as C-reactive protein and calprotectin, to improve early diagnosis accuracy of anastomotic postoperative leak. I would like emphasize the importance of 5 days' hospital stay, at least, after colorectal surgery (procalcitonin had the best predictive effect on postoperative day 5; the mean C-reactive protein value on postoperative day 5 were significantly higher in the group that developed leakage compared with the group without complications). This study may aid the scientific society to improves ERAS (Enhanced Recovery After Surgery) protocol to reduce postoperative recovery and complications, and consequently improves patient's satisfaction and outcome after surgery.

Dear Reviewer #3, many thanks for your comments. We appreciate your idea of using our hypothesis in ERAS context and to improve outcomes after surgery.

Science editor

Dear Science editor, thank you for your comments and suggestions.

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

Please add in what order this test method recommended in this manuscript should be used in conjunction with other tests in clinical practice; it is recommended that this test method be used in clinical practice to suggest an approach to postoperative management.

The biomarkers studied, in particular the combination of CLP and CRP plasma levels, may be included in a standard postoperative surveillance programme as a warning tool for CAL. In case of "positive test", this protocol recommends abdominal and pelvic CT scan or early reoperation in case of imaging dubious or negative, to reduce the time to CAL detection and enabling prompt management.

In addition, please arrange the Figures in the main text in order, and the pictures of the supplementary materials are another part.

We reorganized the files as requested.

Company editor-in-chief

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

We attached the figures in a single Power Point file as requested, as well as we reviewed the settings of tables.

Also, we added the copyright information in all our original figures.