

## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Gastroenterology*

**Manuscript NO:** 74937

**Title:** Usefulness of serum C-reactive protein and calprotectin for the early detection of colorectal anastomotic leakage: A prospective observational study

**Provenance and peer review:** Unsolicited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 02573214

**Position:** Editorial Board

**Academic degree:** MD

**Professional title:** Chief Doctor, Full Professor, Surgeon, Surgical Oncologist

**Reviewer's Country/Territory:** Italy

**Author's Country/Territory:** Portugal

**Manuscript submission date:** 2022-01-13

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2022-01-14 05:35

**Reviewer performed review:** 2022-01-15 07:47

**Review time:** 1 Day and 2 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input checked="" type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

<b>Peer-reviewer statements</b>	Peer-Review: [ <input checked="" type="radio"/> ] Anonymous [ <input type="radio"/> ] Onymous Conflicts-of-Interest: [ <input type="radio"/> ] Yes [ <input checked="" type="radio"/> ] No
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## SPECIFIC COMMENTS TO AUTHORS

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.

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**Peer-review model:** Single blind

**Reviewer's code:** 04164271

**Position:** Peer Reviewer

**Academic degree:** MD, PhD

**Professional title:** Associate Professor

**Reviewer's Country/Territory:** Japan

**Author's Country/Territory:** Portugal

**Manuscript submission date:** 2022-01-13

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2022-01-14 06:07

**Reviewer performed review:** 2022-01-22 08:18

**Review time:** 8 Days and 2 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

<b>Peer-reviewer statements</b>	Peer-Review: [ <input checked="" type="checkbox"/> ] Anonymous [ <input type="checkbox"/> ] Onymous
	Conflicts-of-Interest: [ <input type="checkbox"/> ] Yes [ <input checked="" type="checkbox"/> ] No

## SPECIFIC COMMENTS TO AUTHORS

Thank you for giving me an opportunity to review this paper. This is an interesting manuscript titled "USEFULNESS OF SERUM C-REACTIVE PROTEIN AND CALPROTECTIN IN THE EARLY DETECTION OF COLORECTAL ANASTOMOTIC LEAKAGE: A PROSPECTIVE OBSERVATIONAL STUDY." I enjoyed reading this paper which has a hypothesis that CRP and CLP may contribute to early detection of CAL after colorectal resection. I have several questions and concerns regarding the study. I am very pleased that the excellent analysis has yielded some interesting results. 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. 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. The day of Major CAL is day 5, what day is the time to start postoperative diet? Is Major CAL occurring after the start of postoperative diet? Is that also occurring before the meal starts? 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. In this paper, do the authors need Table 3?

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**Peer-review model:** Single blind

**Reviewer's code:** 03242621

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Associate Chief Physician

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** Portugal

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**Reviewer chosen by:** AI Technique

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**Reviewer performed review:** 2022-01-26 04:57

**Review time:** 11 Days and 17 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

<b>Peer-reviewer statements</b>	Peer-Review: [ <input checked="" type="checkbox"/> ] Anonymous [ <input type="checkbox"/> ] Onymous Conflicts-of-Interest: [ <input type="checkbox"/> ] Yes [ <input checked="" type="checkbox"/> ] No
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## SPECIFIC COMMENTS TO AUTHORS

The present study suggests that the combination of C-reactive protein and calprotectin test could possibly predict colorectal anastomotic leakage (CAL) early after colorectal surgery. CAL after surgery has a remarkable impact on patients' outcomes, but the plasma marker for early detection is relatively lacking. Many thanks for this article and its work since it provides a sizeable monocentric sample. I have some concerns regarding this study, 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. 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). 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. 4. Many grammatical issues need to be fixed professionally.