



PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 68183

Title: Intertwined leukocyte balances in tumours and peripheral blood as robust predictors of right and left colorectal cancer survival

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05370992

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: Spain

Manuscript submission date: 2021-05-16

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-05-18 01:47

Reviewer performed review: 2021-05-20 02:56

Review time: 2 Days and 1 Hour

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 Grade E: Do not publish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 type="checkbox"/> Grade B: Minor language polishing <input checked="" 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 type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No



Peer-reviewer statements	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 manuscript is interesting. “Intertwined leukocytes balances in tumours and peripheral blood as robust predictors of right and left colorectal cancer survival.” A prospective study of patients with colorectal cancer found differences in prognosis after surgical intervention between patients with RCRC and LCRC colorectal cancer. However, it requires some answers to comments particularly related of the prognosis. #Core tip: This was a prospective study involving 65 patients with colorectal cancer, seeking to find robust predictors of survival after surgical intervention, amongst the leukocytes balances in peripheral blood and tumour tissues. A number of these variables are shown to predict OS and RFS, in both RCRC and LCRC patients, thus allowing to improve pre- and postoperative patient’s treatments. Method: Paraffin-fixed samples of tumour and peritumour tissues were assessed for leukocytes concentrations by immunohistochemical detection of CD4, CD8 and CD14 markers expression. Q:How to improve pre-operative patient’s treatments? #CONCLUSION: Easily obtainable variables at preoperative consultation, defining the status of leukocytes balances between peripheral blood and tumour tissues, are reported as robust predictors for OS and RFS of both RCRC and LCRC patients. Q: The leukocytes of tumour tissues were easily obtainable variables at preoperative consultation? #Patient selection:They were surgically treated according to each patient’s condition for right (caecum, ascending or transverse colon) or left (descending or sigmoid colon) hemicolectomies followed by anastomosis, with partial hepatectomy if 8 synchronous metastasis was presented. Q:What was the outcome of these 8 patients? Are they considered as influencing factors? #RESULTS:They ranged from stages 0 to IV, based on tumour-nodes-metastasis (TNM)



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

classification, 28 (43.1%) of them presenting metastasis (either synchronous or metachronous at the time of surgery); and approximately a half, 30 (46.1%), received adjuvant therapy after surgery. Q: 28 (43.1%) of them presenting metastasis (either synchronous or metachronous at the time of surgery);30 (46.1%), received adjuvant therapy after surgery.What effect did they have on the outcome of the follow-up?
#Patients' progression follow-up: The survival analysis, with a median follow-up of 26 months,... Patient selectionwere recruitedfrom January 2017 to September 2019.
Q: What was the end date of the follow-up? How to get "mean follow-up of 26 months"?
METHODS: Ratios of leukocytes concentration in blood and tissues were calculated, and evaluated for their predictor values for OS and RFS with Spearman correlations, Cox univariate and multivariate proportional hazards regression, followed by the calculation of the Receiver Operating Characteristic (ROC) and Area Under the Curve (AUC), and the determination of Youden s optimal cutoff values for those variables which significantly correlated with either RCRC or LCRC patient s outcome. Q: C-index was calculated?



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Peer-review model: Single blind

Reviewer's code: 04723746

Position: Peer Reviewer

Academic degree: MD

Professional title: Deputy Director

Reviewer's Country/Territory: China

Author's Country/Territory: Spain

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Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-05-17 09:43

Reviewer performed review: 2021-05-23 15:48

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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
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SPECIFIC COMMENTS TO AUTHORS

1. Will postoperative chemotherapy affect overall survival time and RFS? 2. The case collection is from 2017 to 2019. Not every patient has a 4-year follow-up period, so the survival chart should indicate the number of cases 3. CD14 includes mCD14 and sCD14. How to distinguish between mCD14 and sCD14 when detecting CD14 by immunohistochemistry? Does CD14+ alone represent monocytes well?



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Peer-review model: Single blind

Reviewer's code: 05106340

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Spain

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Reviewer performed review: 2021-05-27 01:34

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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
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SPECIFIC COMMENTS TO AUTHORS

This prospective study reporting value of combining circulating leukocytes ratios and tissues infiltrated leukocyte ratios on predicting OS and RFS of both RCRC and LCRC patients. The study is well conducted and presented. Major point: 1. As a prospective cohort study, whether this clinical trial has been registered on clinicaltrials.gov or similar. The corresponding website and registration number must be showed in the manuscript. 2. The heterogeneity of the tumor is relatively strong, and the degree of tumor infiltrating cells in different lesion may be different. In the study, is there any corresponding material standard when selecting the tumor tissues of the enrolled patients for immunohistochemistry? Is the middle part or the tumor edge to be selected? Whether these parts can represent the overall infiltration situation, the author needs further explanation. 3. The author found that all six indicators are related to the patient's prognosis. How to evaluate the prognosis when these 6 indicators conflict in patients? The author should build a model for integrated evaluation such as nomogram.