



PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 41467

Title: Prognostic Significance of Primary Tumor Localization in Stage 2 and 3 Colon Cancer

Reviewer’s code: 03656272

Reviewer’s country: Turkey

Science editor: Fang-Fang Ji

Date sent for review: 2018-08-13

Date reviewed: 2018-08-24

Review time: 11 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer’s expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The authors has designed a good study to define the effect of tumor location on the prognosis of stage 2-3 colon cancer. The recommendations are below. About abstract: In the “AIM” section, last sentence should define a purpose, not what you had done. In



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addition, the number of patients, timeline also should be mentioned in “results” section. In the results part; descriptive data about gender, age should be mentioned in the first sentences. You can change “log rank p” to only “p”. In addition, median length of survival should be added. The sentence “However, post-recurrence OS appeared to be worse in RCC patients.” Should be revised, because it is not statistically significant. It should be discussed in “discussion” section in the manuscript. The analysis concluded some prognostic factors, those should be added in the results and conclusion sections. About Introduction: In this section, there are too many preclinical data about colon cancer. It should be revised and made more clear. In addition there is no data about the new findings that has gained popularity in the last 3-4 years. The 2nd reference is written in 1990. Do we really need it? The last paragraph should include what your hypothesis was. You should mention about the background studies that conveyed you to work on that subject. In addition, you should mention why we need such a study. About Methods and results: The inclusion criteria should be more clear. For example, did you include patients less than 18? The “sex” should be changed to “gender”, because it was mentioned as “gender in tables. In table 3; surgical margin was not included in cox regression. However, it has a p value of 0.008. In st. analysis section, p values of $p < 0.250$ was determined as a cut off value for multivariate analysis, but their results in analysis are not present in tables. The mode of recurrences (Locoregional or systemic) are not present in results sections. The mode of recurrence can be an important determinant of OS2 difference in RCC and LCC. It should be included in the analysis and discussed. In addition, according to recent studies, instead of grouping adjuvant regimen into ox vs 5-fu based, it would be much better to group them by including capecitabine vs 5-Fu based. You have enough number of patients. While presenting results, it would be better to first write the univariate- multivariate of DFS, the univariate- multivariate of OS can be presented. Discussion section: In this part, first



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paragraph should summarize your purpose and what you had found. For example “In our study, we aimed to.....(1 sentence). We concluded that.....(short 1-2 sentences). In some parts “emergency surgery” was used as “presentation of ileus”. It can cause confusion. The discussion should focus on the adjuvant studies, the studies containing metastatic cases should be excluded.

INITIAL REVIEW OF THE MANUSCRIPT

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 41467

Title: Prognostic Significance of Primary Tumor Localization in Stage 2 and 3 Colon Cancer

Reviewer's code: 03004570

Reviewer's country: Turkey

Science editor: Fang-Fang Ji

Date sent for review: 2018-08-13

Date reviewed: 2018-08-16

Review time: 2 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good		<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	(General priority)	Peer-reviewer's expertise on the topic of the manuscript:
<input type="checkbox"/> Grade E: Do not publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Minor revision	<input checked="" type="checkbox"/> Advanced
		<input checked="" type="checkbox"/> Major revision	<input type="checkbox"/> General
		<input type="checkbox"/> Rejection	<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This manuscript is about the prognostic significance of primary tumor localization in patients with stage II and III colon cancer (CC). Its title reflects the main subject and key



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words are adequate. Some informations are not clear in the results section of the abstract; which p-value is there for right CC and for left CC respectively, both for DFS and OS? It is not clearly understandable. The manuscript describe the background of this topic, but there is not enough information, even in the discussion. The article contains 15 references only, this number is low for such a kind actual subject. PubMed contains more than hundred references when you enter "right versus left colon cancer". I recommend especially adding two more highly relevant references that you can find below (1,2). This is a single center retrospective trial containing the data of 942 patients followed up between 1995 and 2017 (22 years!). A propensity score matching analysis is recommended to minimize bias for this retrospective study. Figure-1 and Figure-2 show comparative DFS and OS in patients with stage II and III CC, according to adjuvant chemotherapy (CT) intake, but the number of patients not receiving adjuvant CT according to the stages separately is missing even in the manuscript. This number and its reason is highly important for especially stage III patients. It seems that only 241 patients received oxaliplatin-based CT for total patient population. The number of stage III patients is 375, so, what is the percentage of patients with stage III receiving oxa-based CT? What is the effect of this subgroup to DFS and OS? The number and completeness of adjuvant CT cycles effect also survival analysis in stage III, and these details are not in the manuscript. After all these revisions, manuscript worth to publish. 1.

Huang CW, Tsai HL, Huang MY, et al. Different clinicopathologic features and favorable outcomes of patients with stage III left-sided colon cancer. *World J Surg Oncol*. 2015 Aug 28;13:257. 2. Lee MM, MacKinlay A, Semira C, et al. Stage-based Variation in the Effect of Primary Tumor Side on All Stages of Colorectal Cancer Recurrence and Survival. *Clin Colorectal Cancer*. 2018 May 26.

INITIAL REVIEW OF THE MANUSCRIPT



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PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 41467

Title: Prognostic Significance of Primary Tumor Localization in Stage 2 and 3 Colon Cancer

Reviewer's code: 03551828

Reviewer's country: Japan

Science editor: Fang-Fang Ji

Date sent for review: 2018-08-13

Date reviewed: 2018-08-19

Review time: 5 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
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			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
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SPECIFIC COMMENTS TO AUTHORS

Dr. Sakin A et al presents the results of a retrospective study that is trying to assess the prognostic impact of primary tumor sidedness in locally advanced colon cancer. Though limited by data from single institute, it would provide additional findings for tumor



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sidedness topics in colorectal cancer. However, there are some concerns for study methods, analysis, and the results. 1. The authors should indicate the Figure regarding K-M curves of RCC vs. LCC in each stage, not stratified by adjuvant chemotherapy. In Stage II colon cancer, adjuvant therapy is not a standard of care; therefore, there would be no clinical impact in analysis of stage II RCC vs. LCC by adjuvant chemotherapy. 2. Please explain method of the multivariate analysis in the 'Statistical Analysis' section. Also, in the Table 3, some data may be missing (for instance, PT stage, pN, Surgical margin). 3. The authors reported, "Rate of mucinous adenocarcinoma histology, rate of LN number of ≥ 12 , mean number of LNs dissected were significantly higher in RCC group." These results may be different between Stage II and III. Therefore, it would be of interest to analyze them according to the Stage. 4. There was no statistically significant difference in median survival time after recurrence between RCC and LCC cases (log rank $p=0.092$). Previously, Kerr DJ et al have reported important findings using data of prospective adjuvant trials (Lancet Oncol 2016;17:1480-1482). They suggested that recurrences arising from right-sided primary tumors might have an inherently more aggressive phenotype or perhaps that they are more resistant to our current therapeutic options for advanced colorectal cancer than metastases arising from left-sided tumors. Please discuss this important point.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 41467

Title: Prognostic Significance of Primary Tumor Localization in Stage 2 and 3 Colon Cancer

Reviewer’s code: 03475590

Reviewer’s country: China

Science editor: Fang-Fang Ji

Date sent for review: 2018-08-13

Date reviewed: 2018-08-21

Review time: 8 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer’s expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This is a retrospective study included 942 patients with stage II and III colon cancer which were followed up in our clinics between 1995 and 2017. The results showed no association of tumor localization to either DFS or OS in patients with stage II or III colon



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cancer managed with or without adjuvant therapy. This results may help to make clinical decision in clinical. However, the variable in the survival figures should include the adjuvant therapy group or without adjuvant therapy group. The talbes and figures should be more professional for publish.

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