



**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Gastrointestinal Oncology

**Manuscript NO:** 39357

**Title:** C-reactive protein may be a prognostic factor for the whole gastroenteropancreatic neuroendocrine tumors group

**Reviewer's code:** 02454185

**Reviewer's country:** China

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2018-05-23

**Date reviewed:** 2018-05-23

**Review time:** 1 Hour

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input checked="" 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 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**

This is an article addressing a interesting question in the field: to identify independent predictors of survival outcome. Accurate prediction of the outcome is usually the priority in medical decision making. The major limitation of the study was that the



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authors only assessed independent predictors of survival outcome, they did not build a model (best showed as a nomogram) to make a prediction, which will be more clinically relevant. For independent predictors, they may have colinearity that one predictor contains part of the predictive information of another variable. specifically, I have the following comments: 1. "CRP affected the course of the progression in the worst way"---this statement is untrue. the comparison of predictors was not made in the abstract. the conclusion was not supported by data. 2. CRP is a non-specific inflammatory biomarker that can have prognostic value in various diseases, this should be mentioned in the introduction with reference (J Crit Care. 2014 Feb;29(1):88-92. ). 3. can you confirm that there was no studies being conducted before on GEP-NET? that you stated the study is a pioneer study. 4. for descriptive statistics, the normality of continuous variables should be checked before making comparison. cite a reference for the standard description of how to make statistical description and make univariate inference (Univariate description and bivariate statistical inference: the first step delving into data. Ann Transl Med. 2016 Mar;4(5):91. doi: 10.21037/atm.2016.02.11.). 5. for building a Cox regression model, how did you choose the covariates? there are many methods such as purposeful selection, stepwise and so on. But you need to state the exact method you have chosen for others to replicate the results. How did you perform ROC analysis? since the Cox model returns a outcome with a dimension of survival time. ROC curve was only applicable to binary outcome data. I suppose the authors have converted survival probability at certain time points, but this should be explicitly explained. insert a reference (Semi-parametric regression model for survival data: graphical visualization with R. Ann Transl Med. 2016 Dec;4(23):461. doi: 10.21037/atm.2016.08.61.) for the description of Cox modeling after the sentence "Cox proportional hazards test was made. " 6. in table 2 the authors need to clarify how statistical inference was performed. 7. If the authors want to compare the predictive



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performance of CRP and other variables, the ROC curves should be compared with Delong method. 8. I suggest to use nomogram to display the predictive of the model, this method can accommodate survival data and predict survival at any time point. see a tutorial for more details (Drawing Nomograms with R: applications to categorical outcome and survival data. Ann Transl Med. 2017 May;5(10):211. doi: 10.21037/atm.2017.04.01.)

#### **INITIAL REVIEW OF THE MANUSCRIPT**

##### ***Google Search:***

- The same title
- Duplicate publication
- Plagiarism
- [Y] No

##### ***BPG Search:***

- The same title
- Duplicate publication
- Plagiarism
- [Y] No



**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Gastrointestinal Oncology

**Manuscript NO:** 39357

**Title:** C-reactive protein may be a prognostic factor for the whole gastroenteropancreatic neuroendocrine tumors group

**Reviewer's code:** 00068723

**Reviewer's country:** Japan

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2018-05-23

**Date reviewed:** 2018-05-23

**Review time:** 3 Hours

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 type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input checked="" type="checkbox"/> Grade D: Fair	<input checked="" 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 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**

The authors investigated GEP-NET with clinicopathological data. They claimed that CRP was related with survival. This study was potentially useful because GEP-NET was a rare condition. Conclusion was interesting regarding CRP. But the presentation was



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immature, and was sometimes hard to evaluate. Table 1. It was not clear what “yes” or “no” of 5-year survival. Ethical statement was absent. Table 2. It was not clear how mitotic count and Ki-67 level were analyzed. The methods of analysis of Ki67 was not clear. If immunostaining was performed, the staining methods should be described. Representative photos should be presented. References were relatively old. It did not seem normal to show P value  $<0.05$  in red.  $P=0''.''02$  instead of  $0''.''02$ . Discussion was long. Discussion should be focused on the significance of the study.

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##### ***BPG Search:***

- The same title
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- Plagiarism
- No



**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Gastrointestinal Oncology

**Manuscript NO:** 39357

**Title:** C-reactive protein may be a prognostic factor for the whole gastroenteropancreatic neuroendocrine tumors group

**Reviewer’s code:** 02567564

**Reviewer’s country:** India

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2018-05-23

**Date reviewed:** 2018-05-26

**Review time:** 3 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 checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input checked="" 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 checked="" type="checkbox"/> Minor revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Major revision	<input checked="" 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**

The authors report results from a fairly large cohort of patients with GP-NET and report on predictors of outcomes in these cases. The study, although has strengths, is constrained by the improper English language usage. Therefore the revised version must



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address this issue. Major Introduction. The authors briefly report that CRP could be increased in solid malignancies. It is important at this stage to also mention that CRP is a non specific marker increased in many nonneoplastic abdominal conditions like IBD, abdominal infections like tuberculosis and that CRP could be normal in some individuals inspire of active disease. This could be clarified in discussion ( Serial C-reactive protein measurements in patients treated for suspected abdominal tuberculosis. Dig Liver Dis. 2018 Jun;50(6):559-562. ) Minor Abstract: the first sentence of the result section does not make sense “ determined by Ki-67 level and mitotic count and the level of CRP that one of the biochemical data.” Again many of the sentences in this section do not seem to make sens. Please let a English speaker see the paper Instead of reporting as “meaningful” better to use the word significant The discussion needs to be curtailed and should focus on the new findings of this study especially the CRP rather than factors which have been dealt well in previous publications.

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