

March 25, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 7171-review.doc).

**Title:** Can composite performance measures imply survival of patient with colorectal cancer?

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

**ESPS Manuscript NO:** 7171

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

We have made a major revision of resubmitted manuscript to respond the suggestions of the reviewers.

Following described more specific details about the author's responses.

(1) *Question 1a. In some places the text refers to the tables, but no explanations appear there as well.*

**Answer:** We made a major revision of resubmitted manuscript to resolve this problem. A new table (Table 1) was added for clear explanation.

Category	Measure	Description	Global priority*	Weight**		
				Cohort 1	Cohort 2	Cohort 3
Pre-treatment (PT)	PT1	CRC patients with pre-operative chest X-ray and abdominal ultrasound, CT scan, or MRI	0.144	0.213	0.193	0.213
	PT2	Early stage of CRC	0.104	0.154	0.140	0.154
Treatment (T)	T1	CRC patients with history of surgical resection that were checked by colonoscopy or barium enema LGI series with sigmoidoscopy within six months peri-operatively	0.030	0.044	0.040	0.044
	T2	Patients with non-metastatic CRC offered curative resection or neoadjuvant therapy within six weeks of diagnosis	0.057	0.084	0.077	0.084
	T3	Patients with stage I to III CRC who underwent wide surgical resection with a “negative margin”	0.133	0.197	0.179	0.197
	T4	CRC patients who underwent surgery with pathology reports on tumor and node stage	0.116	0.172	0.156	0.172
	T5	Patients with stage I to III CRC with twelve or more lymph nodes examined in pathology reports	0.092	0.136	0.124	0.136
	T6	Patients (<70 y) with stage III CRC who received chemotherapy within eight weeks after surgery	0.069		0.093	
Follow-up (F) ***	F1	CRC patients (stages I – III) survived after five post-operative years	0.101			
	F2	RC patients (stages I – III) experienced no local recurrence after five post-operative years	0.082			
	F3	CRC patients expired within 30 days after surgery	0.073			
Sum of priorities (or weights)			1.001****	1.000	1.000	1.000

Question 1b. *In other places, a reference is mentioned as to one of the methods used to develop the CPS, but no where is this manuscript there is an explanation regarding this method. For example, the concepts of analytic hierarchy process (AHP) and fuzzy AHP are not clearly explained and the corresponding tables (additional file, tables 2-4) added only to my confusion when reading the manuscript instead of clarifying the topic. Another example is the mentioning of questionnaires sent to experts in order to develop the AHP, but no where it is mentioned what the questions in these questionnaires are.*

**Answer:** (a) In the revised manuscript, we exclude the fuzzy AHP to avoid lacking explanation explicitly. So we included five methods only in the revised manuscript. Furthermore, we made a major revision of **Performance measures and AHP questionnaire in METHODS section**. The concept of AHP was revised in **AHP calculation of the CPS in METHODS section** as following

“The AHP method was developed by Thomas L. Saaty to solve complex problems involving multiple criteria and features an ordinal pair-wise comparison of attributes ranging from a score of 1 (equal importance) to 9 (extreme importance)<sup>[18]</sup>. The AHP technique results in priorities of attributes (weights of performance measures) that add up to 1. This method was used by Richman *et al.* for the selection of prostate cancer treatments<sup>[26]</sup>. Among the five methods used in the present study, it is the only one that requires experts’ choices in a questionnaire survey.”

(b) Because the development of performance measures and AHP questionnaire has been published in our prior publication, we just made citation in the text. Length of the original AHP questionnaire spanned about 14 pages (A4 size). ”

(2) Question 2. *Even though explanations as to the methods are vague and unclear, the manuscript is overloaded with data that add to the confusion and makes reading it very challenging. Both the text (in the results section) and the tables are packed with numbers and it is very difficult to differentiate the essence and the subordinate*

**Answer:** The manuscript has undergone major revision to rewrite the text (in the results section) and the tables to void what reviewer’s comment of reading text difficult. The last paragraph in **RESULTS section** was revised as following in order not to be packed with numbers:

“ The CPS values calculated by each of the five methods are presented in Table 3, ranging from 0 to 1 for all methods except PCA. CPS values derived with the equal weight method were strongly correlated with values derived using the AHP and PCA methods in cohort 1, and with the AHP method only in cohorts 2 and 3 (Table 4). The relationships between CPS values derived from each of the five methods and patient survival are summarized in Table 5, including hazard ratios (HR) estimated after controlling for confounders. Five-year OS in cohort 1 was significantly associated with CPS values derived with the 70% standard, equal weight, AHP, and PCA methods (HR: 0.76, 95% confidence interval [CI]: 0.59 – 0.98; HR: 0.32, 95% CI: 0.14 – 0.74; HR: 0.32, 95% CI: 0.14 – 0.73; and HR: 0.85, 95% CI: 0.78 – 0.92, respectively, all  $P < 0.05$ ). Similar results were found for the five-year DSS and DFS (except marginal significance for DFS by the 70% standard method). These data indicate that a patient with a higher CPS in cohort 1 had an increased probability for five-year survival. For patients in cohort 2, the CPS values derived with the AHP method were significantly associated with five-year OS or DSS, and values derived with the equal weight method were only associated with the DSS. There were no significant associations between five-year survivals and CPS values for patients in cohort 3. Moreover, CPS values derived with the all-or-none method gave no prediction for five-year survival. The goodness-of-fit model analysis using AIC showed that the best method for predicting five-year survivals, with the lowest AIC values, was the PCA method, followed next by the AHP and equal weight methods

(Table 6).”

Table 6 (original Table 5) was reshaped in the form similar to new Table 4, 5 and aimed to facilitate reader easier understanding.

		Method				
Cohort	Survival	All-or-none	70% standard	Equal weight	AHP	PCA
1	OS	12.819	8.544	6.002	5.895	0.000
	DSS	8.823	2.412	3.047	1.691	0.000
	DFS	9.406	6.023	4.921	3.434	0.000
2	OS	NA	14.655	11.914	11.205	0.000
	DSS	NA	4.593	1.363	0.000	2.520
	DFS	NA	2.385	0.246	0.000	1.605
3	OS	0.843	0.483	0.000	0.105	0.750
	DSS	1.053	0.380	0.000	0.421	1.507
	DFS	0.617	0.543	0.000	0.177	0.659

(3) *Question 3. The quality of the English syntax is poor throughout the manuscript, which adds to the confusion and lack of clarity when reading it. Even if the content would have been in a quality good enough to be published, this manuscript would have needed thorough English copyediting.*

**Answer:** We have requested English copyediting service by Ameditor Inc. (one of four English language editing companies recommended by your advice). Now we have certificate of grade A of the language.

3 References and typesetting were corrected

Thank you again for considering publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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