

## ANSWERING REVIEWERS



June 30, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: ESPS Manuscript No.11344-Review.docx).

**Title:** Long-term survival after resection of pancreatic cancer: a single-center retrospective analysis

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

**ESPS Manuscript NO:** 11344

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

**To the reviewer 181208**

(1) > *Survival curves used for the Cox multivariate analysis have not been provided and they should be added.*

We created the survival curves of multivariate analysis and submitted as Figure 1 and 2.

(2) > *In methods it is unclear how the cut-offs for the tumors markers were chosen. Also in the structured abstract medians are given for DUPAN and percentages for the rest of the significant variables.*

We wrote how the cut-offs for the tumor markers were chosen in “statistical analysis” in “MATERIALS AND METHODS” paragraph.

We changed the information of tumor markers into as follows; medians were given for all tumor markers both in the text and the tables because there was statistical variation in concentrations of tumor markers.

(3) > *No information is given on the site of the tumor (head vs tail) and presenting symptom e.g. jaundice vs pain) which have been previously suggested to be associated with outcomes.*

There was a great variation in tumor locations, ie. head, body, tail, uncus, head-body, head and tail, body-tail, head-body-tail..., and, we are afraid that the analysis would become too complicated. So, we refer to only operative procedures, ie. pancreatico-duodenectomy, distal pancreatectomy, total pancreatectomy, and excluded precise tumor locations from our analysis.

I'm really sorry, but there were few data about presenting symptoms of old cases, and we can't add them to the present analysis.

(4) > *The normal range of the tumor markers in the authors' institution should be given as well as the method/kit used.*

We wrote the normal range of tumor markers and the kit used in our hospital in “MATERIALS AND METHODS”.

(5) > *Information should be added if adjuvant radiation therapy has been used at all.*

In our hospital, adjuvant radiation therapy is not used for pancreatic cancer, so we added this information into the “RESULTS”.

(6) > *In table 1 it is unclear what the parenthesis in age represents. Median and range?*

I'm sorry. We used only “mean  $\pm$  SD” for age in all the tables.

(7) > *In table 2 it is not explained what MST means. Median Survival Time?*

Yes. We wrote that MST meant Median Survival Time in the footnote of Table 2.

(8) >In table 2 the numbers on tumor markers do not add up to the total number of patients. The rest is missing?

Yes. There were a few patients who didn't undergo examination of tumor marker, so their data of the concentration of tumor markers were missing. We wrote this information in the "RESULTS".

**To the reviewer 02446400**

(9) Results the Authors report mean concentrations of 4.5 +/- 6.4 (?) for CEA, 876 +/- 3755 (??) for CA19-9 and 1630 +/- 7756 (??) for DUPAN-2 marker. They seem no-sense data and don't match the values reported in Table1 and Table2.

We changed the information of tumor markers as written in (2).

**To the reviewer 02446363**

(10) In univariate analysis of prognostic factors (shown in Table 2), some variables that are well known to be associated with prognosis of pancreatic cancer, such as peri-neural invasion and tumor differentiation, were not included?

As you indicated, extrapancreatic neural invasion and portal invasion are often reported to be associated with prognosis of pancreatic cancer, so we added these factors into the present analysis. As a result, these two factors significantly influence survival in univariate analysis, and then, we put them into multivariate analysis.

I'm really sorry, but there were few data about tumor differentiation and we were not able to add this factor into the present analysis.

(11) Simultaneous evaluation of the parameters (as two independent ones) in multivariate analysis is not reasonable, because UICC stage covers T classification.

As you indicated, UICC stage covers T and N classification, so we excluded UICC stage in multivariate analysis, as shown in Table 3.

**To the reviewer 00504462**

(12) Can you explain the reason of the various kind of surgeries your surgeons performed? Were there any surgery criteria used?

In our hospital, three pancreatic surgeons determine operation modes for each patient according to the results of preoperative CT scan, MRCP or ERCP and EUS. When there is a possibility of portal invasion according to the preoperative examinations, we performed reconstruction of portal vein. It is difficult to know exactly whether there is extrapancreatic neural invasion or not, so neural dissection of SMA is performed for almost all patients. Actually, there is not a precise surgery criteria about the operation mode stated above and the effectiveness is controversial yet.

3 References and typesetting were corrected

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

Sincerely yours,

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