Author’s response to reviews

Title: Prognostic significance of the combination of preoperative hemoglobin and albumin levels and lymphocyte and platelet counts (HALP) in patients with renal cell carcinoma after nephrectomy

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Author’s response to reviews:

Dear Editors and Reviewers:

Thank you very much for your letter and for the reviewers’ comments concerning our manuscript entitled “Prognostic significance of the combination of preoperative hemoglobin and albumin levels and lymphocyte and platelet counts (HALP) in patients with renal cell carcinoma after nephrectomy” (ID: BURO-D-17-00103). Those comments are all valuable and very helpful for revising and improving our paper. We have studied those comments carefully and have made corrections which we hope meet with approval. The main corrections and the response to the reviewer’s comments are as following:
Reviewer reports:

Mükremin Uysal (Reviewer 1): Please include all comments for the authors in this box rather than uploading your report as an attachment. Please only upload as attachments annotated versions of manuscripts, graphs, supporting materials or other aspects of your report which cannot be included in a text format.

Please overwrite this text when adding your comments to the authors.

Response: Thanks for your comment. We change this in the revised manuscript.

Ramy Youssef Yaacoub (Reviewer 2): The authors studied the prognostic significance of preoperative HALP in patients with RCC after nephrectomy in 1360 patients. They concluded that HALP was independent prognostic factor for CSS.

The study is important and should be considered for publications after few revisions:

1) The authors needs more detailed explanation on how they determined the cutoff value for HALP

Response: Thanks for your comment.

The X-tile software was able to compare the P values of different cut-off values for a continuous variable and determine the best cut-off value with the most significant P value.

We added this in the Patients and Methods: Statistical analysis section.

2) The authors needs to explain how they selected factors included in multivariate analysis as Table 3 shows many factors but multivariate analysis included only some factors. Of note some
other factors showed significance in univariate analyses included in the table but it seems that they were not included in the multivariate analysis.

Response: Thanks for your comment. We found that we did not explain this clearly. Actually, the variables with significant P values in the univariate analysis were included in the Cox proportional-hazards regression multivariate survival analyses. Because we chose the COX Forward LR method which will only output the significant variables. This was why some variables did not have HR and P values in the multivariate survival analyses. In the revised manuscript, we added this in the Patients and Methods: Statistical analysis section.

3) I recommend adding % in table 2

Response: Thanks for your comment. We add the % in the revised manuscript.

James J. Hsieh, MD PhD (Reviewer 3): It is a single institute report on a new prognostic platform (HALP) by Peng et al. HALP is likely reflecting nutritional status. Overall, it is of interests since all these parameters are easily obtained on most RCC patients.

Major comments

1. (Abstract) It is very erroneous to state HALP is better than TNM without validation and controlled for all variables, which needs to be removed. They should check if HALP further subcategorize TNM, which would be of value.

Response: Thanks for your comment. We found that we did not explain this clearly. Actually, the nomogram in this paper did included TNM stage, Fuhrman grade and HALP score. This should be that the model including TNM stage, Fuhrman grade and HALP score was more accurate.
than only use of TNM staging. Thanks very much for this comment. In the revised manuscript, we correct this in the abstract section and the results section.

2. (Background line 11) A contemporary RCC review such as Hsieh et al. Nature Reviews Dis Primer 2017 (PMID 28276433) is needed.

Response: Thanks for your comment. We added this in the revised manuscript.

3. (Background line 27) A recent report by Senbabaoglu et al. on RCC immune signature and clinical outcome Genome Biology 2016 (PMID 27855702) should be cited.

Response: Thanks for your comment. We added this in the revised manuscript.

4. It is sarcomatoid transformation, not sarcomatous...

Response: Thanks for your comment. We change this in the Results section: Patient characteristics and Table 1&2 of revised manuscript.

5. SIGN, please cite the original paper or the RCC review.

Response: Thanks for your comment. We added this in the Discussion section of revised manuscript.