Author’s response to reviews

Title: Comparison of clinicopathologic characteristics, epigenetic biomarkers and prognosis between renal pelvic and ureteral tumors in upper tract urothelial carcinoma

Authors:

Dong Fang (fdmailbox@126.com)
Shiming He (shiminghe@bjmu.edu.cn)
Gengyan Xiong (xgy13537221@163.com)
Nirmish Singla (nirmish.singla@phhs.org)
Zhenpeng Cao (shenhaiyuanhang@sina.com)
Lei Zhang (zl070501@126.com)
Xuesong Li (pineneedle@sina.com)
Liqun Zhou (zhoulqmail@sina.com)

Version: 2 Date: 16 Jan 2018

Author’s response to reviews:

Response to Editors and Reviewers

Dear editors and reviewers:

We thank you very much for giving us an opportunity to revise our manuscript. We have studied comments carefully and have made correction which we hope meet with approval.

Editor Comments:

In addition might be worthwhile to present a multivariable analysis for survival analysis as Invariable/KP analysis carries less importance when multiple factors involved

Response: In previous submission we place multivariable analysis for patients’ survival at Supplementary files. In this revision we have moved the tables out of supplementary files. (Table 3 & Table 4, Page 8 Line 9)

Do you have any data re tumour size? was MMC used after RNU? please report this
Response: If you mean tumor size, we did make that comparison based on the longest tumor diameter. In Table 1, the median tumor size was 3.58±2.15 and 3.27±2.41 in renal pelvic tumor and ureteral tumor (p= 0.001)

No prophylactic MMC or THP was used in this group of patients. Patients were enrolled between 1999 and 2011, by which no consensus of prophylactic intravesical instillation was made. (Page 4, Line 45)

Reviewer’s Comments:

1. A major limitation of the current study is how patients are characterized into one of two groups based on tumor location even if a patient has tumor in both locations.

2. How many patients had tumors in both locations?

3. Can you generate an analysis with three groups (renal pelvis only, ureteral only, renal pelvis and ureter)?

Response: Thanks for this comment. Please allow us to answer these three questions together.

We acknowledge that there might be some confusion due to the enrollment of patients with tumors in both the ureter and the renal pelvis. There are 41 patients (6.7%) in our cohort. (Question 2)

Actually there are many previous similar studies grouped patients into renal pelvis vs ureter, based on the main tumor location. We defined the MAIN location mainly based on tumor stage, since tumor stage is the most important risk factor for prognosis. Besides, since urothelial carcinoma could synchronously be present in multiple places, even if we only noticed one tumor on general pathological examination, there might already be some tissues that carcinogenesis has occurred. Thus we think it might be acceptable to categorized patients based on the main tumor.

Besides, in those with tumors on both locations, we select the tumor tissue on the main location for experiment on methylation status (for example, a patient with tumors on both location and we judged the main location is renal pelvis; thus we performed MSP on the tissues of the renal pelvic tumor and the corresponding methylation status was noted), therefore we guess it makes sense. (Question 1)

Of course, we firmly agree that an analysis with renal pelvis only and ureter only would be more persuading. Thus, at the end of the Results part, we added a further analysis. Rerunning the dataset by grouping patients into renal pelvis only, ureteral only, renal pelvis and ureter, no significant changes were found. We also investigated what if we delete patients with tumors in both locations, the results were similar. (Page 8, Line 36) (Question 3)

Besides we made some correction about writing mistake (especially for some names of the genes) and an update about Acknowledgements and funds. Hope for your understand.
We appreciate reviewers very much for the positive and constructive comments and suggestions. Looking forward to hearing from you.

Thank you again for your consideration and assessment.