

Peer Review File

Article Information: <https://dx.doi.org/10.21037/tau-23-133>

Response to Reviewer

a) Major:

1. Representative value of each blood inflammation marker (HRR, AGR, and others) such as mean, median, range, standard deviation should be summarized in a Table and be described in the manuscript.

Response: Thank you for your suggestion. We have created a table (Table 2) that summarizes representative values of blood inflammation markers and described it in the manuscript.

2. Page 7, lines 16-21: Pathological grading and staging must be performed according to the latest references (2022 WHO classification and AJCC 8th edition, also needs reference no.). Regarding the selection of a dominant lesion in cases with concurrent renal pelvic and ureteral lesions, the order of priority among grade, stage, and size is unclear in the present manuscript.

Response: We strongly appreciate your comments. The grading and staging criteria used in present study have been updated to 2022 WHO classification and AJCC 8th edition. In addition, tumor location was consistent with the location of dominant lesion determined in the following order of priority: stage, grade, and size.

3. Page 13, lines 1-10: Authors refer to a close prognostic significance between pT2 and pT3 tumors. Because heterogenous prognostic data in pT3 tumor in the renal pelvis as compared to that in the ureter has been discussed, subgroup analysis of renal pelvic and ureteral tumors would clarify this point. In addition, line 8-10, is this suggestion for all cases or only high-risk subgroup in Figure 7?; please describe in detail.

Response: This advice is invaluable to us. We then conducted a subgroup survival analysis for patients with pT3 renal pelvis carcinoma, pT3 ureteral carcinoma, and pT2 UTUC. Sadly, there was no statistically significant difference in OS between the three subgroups. It might be due to the relatively small sample size. The Kaplan-Meier curve, if available, should be used as Supplemental Figure 1.

Regarding the suggestion in lines 8-10 of page 13, we apologized for this vague description. Actually, the suggestion was applied to all cases according to Figure 3C.

4. Page 14, lines 9-19: UTUC and bladder urothelial carcinoma is histologically similar but embryologically and molecular genetically different tumors. Data of ref. 13 and 39 should not be treated as same, and need to be explained separately in the manuscript.

Response: Admittedly, it isn't very rigorous to confuse UTUC with urothelial carcinoma of bladder(UCB). We have chosen to delete the citation of UCB (including ref. 13) after careful consideration to avoid drawing misleading conclusions.

5. Regarding X-tile analysis, detail descriptions are necessary in Figure 7A and the manuscript for better understanding.

Response: Thanks for your advice. According to your comments, we have described Figure 7A in greater detail and briefly introduced X-tile in the Statistical Analysis section.

b) Minor:

1. There are many misuses and grammatical errors in the manuscript. Correction of the paper by a native English speaker is recommended.

Response: We revised the whole manuscript carefully to avoid language errors. And we consulted a professional editing service to check the English. These changes will not influence the content and framework of the paper. And here we did not list the changes but marked in red in the revised paper. We appreciate for Editors/Reviewers' warm work and hope that the correction will meet with approval.

2. There are multiple terms to express "development cohort" in the manuscript: "training set", "primary cohort", and "primary sample", etc. Please unify the terms.

Response: "Primary cohort", "development cohort", and "training set" were unified into "training cohort".

3. Page 9, lines 14-16: It is unclear that each data is from either of the two cohorts (sets)

Response: We appreciate you reminding us. The language problem has been modified.

4. Page 12, lines 13 and 14: Does "independent predictors of UTUC" mean poor prognosis of UTUC patient?

Response: Both risk factors and protective factors are independent predictors. Thus we would like to offer a more detailed description here: The findings suggested that in addition to advanced T staging and positive surgical margin, low AGR (≤ 1.588) and low HRR (≤ 1.020) were independent risk factors of UTUC.