Author’s response to reviews

Title: Predominant Global Glomerulosclerosis in Patients of Upper Urinary Tract Urothelial Carcinoma with Pre-existing Renal Function Impairment is a Predictor of Poor Renal Outcomes

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Author’s response to reviews:
Reviewer 1
Q1: Sampling of kidneys: manuscript says "complete sections were taken" How was heterogeneity addressed?

Ans1: Thanks for your constructive comments. Kidney specimen were thoroughly excision and representation, section are taken from the non-tumorous area, which is at least 1 cm distance from the tumor. (Page 6, line 5)

Q2: table 1 and table 2 should define CKD as pre-existing or not?

Ans2: They were both defined as pre-existing CKD. Based on reviewer’s comment, we revised these in Table 1, Table 2 and all the associated content in revised manuscript.

Q3: Tables busy and difficult to digest. Able to convert some to figures?

Ans3: We appreciate your comments, and we have converted old Table 2 to Figure 3 to make it more clear and easy to be understood by readers.

Q4: would add sentence to the conclusion that may lend consideration to routine histologic evaluation of the non-tumorous kidney.

Ans4: We have made this revision by reviewer’s suggestion. (Page 18, line 2)

Q5: line 20, why is unilateral Nx encouraged in patients with AAN. Should it be bilateral?

Ans5: In AAN patients, once UTUC was found, and then unilateral nephrectomy was performed instead of prophylactic bilateral nephrectomy, because we hope to preserve the function of contralateral kidney to avoid immediately entering dialysis after bilateral nephrectomy. This paragraph has been deleted since it has little association with our study.

Reviewer 2

Q1: Good descriptive cross sectional study aiming to look at renal histopathology in patients with RCC and UTC. The major flaw in this kind of study is the presence of confounders such as AA use and chronic illnesses such as hypertension and diabetes which could be causes of CKD thereby causing the said histopathological changes. No correction for these factors has been
done. Only association can be established from a study of this nature and appropriate correction for confounding needs to be considered.

Ans1: We thank the reviewer for the insightful comments. After discussion, we re-analyze preexisting CKD, abnormal GGS and TI score by multivariate logistic regression and multivariate linear regression with these confounding factors followed by reviewer’s comments. Then we replace old Table 3 by new Table 2 and Table supplements. Associated content are written into the revised manuscript.

Q2: The discussion is too long, (all over the place) and varied and mostly not directly related to the present study. Kindly make it a bit more coherent and concise sticking to information that is relevant to the study conducted. The reasons why UTC was more prevalent in females in the Taiwanese is also a matter of readers interest and this can be highlighted in further detail by the authors.

Ans2: Based on reviewer’s comment, we have re-organized the content of discussion. We delete those parts not directly related to our study, and more emphasize on gender (Page 15, paragraph 2).