



# Large population-based study of upper tract urothelial carcinoma in China may provide further insight into the impact of bladder cancer on upper tract urothelial carcinoma's prognosis in Chinese population

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*Response to:* Li HK, Chung SD. Chronic kidney disease stages, intravesical therapy regimens, and regular cystoscopic follow up may also impact the survival of urinary tract urothelial carcinoma patients. *Transl Androl Urol* 2022;11:571-2.

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We appreciate the comment on our study on impact of previous, simultaneous or intravesical recurrence bladder cancer on prognosis of upper tract urothelial carcinoma (UTUC) after nephroureterectomy (1). We agree with Li and Chung that the incidence, carcinogenic factors, pathological characteristics of UTUC may differ between China and the U.S. For examples, it is reported that UTUC tends to be more female predominant in China, while it is more prevalent in males in the U.S. or European countries (2,3). Furthermore, tobacco smoking is a predominant risk factor for UTUC in the Western countries, but less than one fifth had this exposure in China (3). The use of traditional Chinese medicine containing aristolochic acid was more prevalent among Chinese, especially for female, and this may explain the observed gender differences among Chinese with UTUC (4-6). Moreover, UTUC tumors were found be more located in the ureter than in the renal pelvis (2). Several studies have revealed some distinctive prognostic factors to the Chinese population such as gender (3), tumor location (2,7) and aristolochic acid mutational signature (5).

Regarding several concerns raised in the comment, our reply may perhaps clarify some of them. We agree on that the chronic kidney disease (CKD) stage and dialysis history, regimens of intravesical chemotherapy and follow-up schedule play important roles in the prognosis of UTUC. Apart from these parameters mentioned by Li and Chung,

smoking history, diagnostic ureteroscopy, neoadjuvant or adjuvant chemotherapy that potentially have impact on the intravesical recurrence and survival are also absent in the SEER database. As a result, we were unable to balance these factors among groups in our analysis, and this was mentioned as the major limitations in our manuscript. Although it was reported that CKD was associated with worse overall survival, CKD had no effect on the cancer specific survival (CSS) (4,8,9). Since the primary outcome of the present study focused on CSS, CKD may not influence the conclusions of the present study. The present study is based on database from the U.S., some of our outcomes are in line with previous studies from Asian' cohort with large sample size (10). Furthermore, as with many registry-based retrospective studies, screening guidelines, surgical techniques, management patterns and follow-up schedules were unable to be standardized. Realistically, however, this heterogeneity reflects the variations of clinical practice in the real-world setting, and this may increase the generalizability of our results. Moreover, the conclusions of our study are strengthened by its large sample size and statistical method we used to balance the baseline and pathological factors that had significantly impact on the CSS of UTUC. Future study with large sample size and detailed clinicopathological information from national-wide cooperation in China may provide further insight into the characteristics of UTUC in Chinese population.

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