Original Article

Impact of previous, simultaneous or intravesical recurrence bladder cancer on prognosis of upper tract urothelial carcinoma after nephroureterectomy: a large population-based study

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Background: Currently, the impact of previous, simultaneous, or subsequent bladder cancer on the prognosis of upper urinary tract urothelial carcinoma (UTUC) is controversial. We aimed to investigate the impact of previous, simultaneous or intravesical recurrence (IVR) bladder cancer on the prognosis of UTUC based on a large population-based cohort from the Surveillance, Epidemiology, and End Results (SEER) database.

Methods: A total of 8,431 UTUC patients diagnosed from 2004 to 2018 met the inclusion criteria were identified based on the SEER database. We evaluated the impact of bladder cancer on the prognosis of UTUC by Kaplan-Meier method and propensity score matching (PSM).

Results: In all, 6,831 patients only had UTUC (UTUC-only), 880 patients with previous or simultaneous bladder cancer (UTUC-Bca), 720 patients with IVR (UTUC-IVR). After adjusting baseline covariates that varied significantly among groups, we found UTUC-Bca cohort, regardless of tumor grade and stage, had poorer prognosis than UTUC-only cohort. In general, we demonstrated IVR had no significant impact on the prognosis of UTUC compared to PSM matched patients without IVR. However, subgroup analysis revealed that UTUC patients with subsequent MIBC recurrence or shorter interval (<20 months) between UTUC and IVR had worse prognosis compared with UTUC-only cohort.

Conclusions: UTUC patients with previous or simultaneous bladder cancer, IVR with MIBC, and shorter interval between UTUC and IVR were significant predictor for worse prognosis. Thus, more stringent postoperative surveillance and active treatment strategies should be considered for UTUC patients with those risk factors.

Keywords: Upper urinary tract urothelial carcinoma (UTUC); prognosis; bladder cancer; risk factor

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Introduction

Upper urinary tract urothelial carcinoma (UTUC) refers to ureter cancer and renal pelvis cancer, accounting for 5–10% of urothelial carcinoma. It is not rare for UTUC patients to have previous, simultaneous, or subsequent bladder cancer. Approximately 18.8–33.6% of UTUC patients have a previous bladder cancer history, and 8–13% of cases have concurrent bladder cancer at diagnosis (1-3). About

22–47% of UTUC patients may experience intravesical recurrence (IVR) after nephroureterectomy (RNU) (4,5). Currently, the impact of previous, simultaneous or IVR on the prognosis of UTUC is controversial.

It was reported that previous or concomitant bladder cancer was an independent predictor of IVR after RNU, but did not significantly affect the cancer specific survival (CSS) (6-8). Nevertheless, several studies revealed that UTUC patients with concomitant or bladder cancer history had worse prognosis, and was an independent risk factor (2,9,10). Meanwhile, IVR was also reported to have an adverse effect on the prognosis of UTUC (2,5,11). In contrast, studies showed IVR after RNU did not affect the prognosis of UTUC (12,13). Most of previous studies exploring the impact of bladder cancer on UTUC were conducted in small cohorts.

In the present study, we aimed to investigate whether UTUC patients with previous, simultaneous bladder cancer or IVR were prognostic factor affecting the prognosis of UTUC based on a large population-based cohort from the Surveillance, Epidemiology, and End Results (SEER) database. We present the following article in accordance with the STROBE reporting checklist (available at https://dx.doi.org/10.21037/tau-21-758).

Methods

Patient selection

Data was collected from the SEER database of the National Cancer Institute (https://seer.cancer.gov). We selected the database SEER 18 regs which was submitted in November 2020 (2000–2018). UTUC patients were identified by the International Classification of Diseases-O-3 (ICD-O-3) codes C64.9, C65.9, and C66.9 from January 2004 to December 2018. We further selected UTUC patients underwent RNU (surgery codes 40 or 50) and diagnosed with histological type of urothelial carcinoma by codes 8120 to 8139 based on ICD-O-3 codes. Exclusion criteria were as follows: (I) patients with other primary malignant tumors except bladder urothelial carcinoma; (II) patients with missing information on crucial covariates such as pathological information, follow-up data; (III) survival time ≤1 month; (IV) patients with both bladder cancer history and IVR. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Since identifiable patient information was not contained in the publicly available SEER database, no ethical approval and informed consent was required.

Data collection and definition

The demographic and clinical variables were collected from SEER database. The time from previous bladder cancer to UTUC was defined from the first diagnosis of bladder cancer to the first diagnosis of UTUC. Patients with simultaneous UTUC and bladder cancer were defined as the time interval between the diagnosis of UTUC and bladder was less than 1 month. IVR interval was defined from the first diagnosis of UTUC to the first detection of bladder cancer after RNU.

Statistical analysis

The chi-square test was performed to compare the distribution of categorical data. Kaplan-Meier method and log rank test to compare CSS between groups. Univariable and multivariable Cox proportional hazards models were performed to identify independent risk factors to predict CSS. In multivariable analysis, the backward step-down Wald selection method was utilized to select predictors (the entry and removal criteria were $P<0.05$ and $P<0.10$, respectively). Propensity score matching (PSM) analysis based on the nearest-neighbor matching principle with 1:1 ratio and a 0.02 caliper width was conducted to adjust the potential differences in the baseline characteristics of between two groups (14). Statistical significance was set at 0.05 with 2 sides. Statistical analyses were conducted using R software 4.0.4 (http://www.r-project.org).

Results

Patient baseline characteristics

As shown in *Figure 1*, a total of 8,431 patients met the inclusion criteria were included for further analysis. Median age of the entire cohort was 72 years (IQR, 63–80 years). In all, 6,831 patients only had UTUC (UTUC-only), 880 patients had UTUC with previous or simultaneous bladder cancer (UTUC-Bca), 720 patients with IVR (UTUC-IVR). The demographic and clinical characteristics of these cohorts were listed in *Table 1*, notable differences were identified among these cohorts. Patients with only UTUC were more likely to be associated with higher tumor

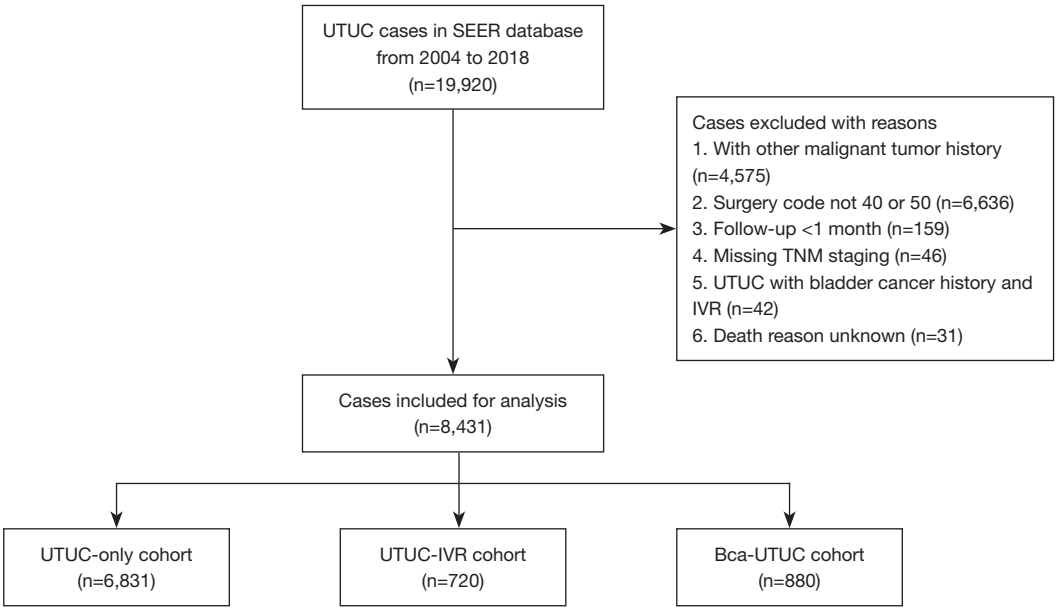

Figure 1 Flowchart illustrating patient selection from SEER database. UTUC, upper urinary tract urothelial carcinoma; SEER, Surveillance, Epidemiology, and End Results; IVR, intravesical recurrence.

grade and TNM stage, while UTUC-IVR cohort tended to be younger, with lower tumor grade and TNM stage.

Risk factors for UTUC prognosis

Detailed results of univariable and multivariable Cox regression analysis were displayed in supplementary Tables S1,S2, respectively. Multivariable Cox analysis revealed older age, bladder cancer history, carcinoma *in situ*, higher tumor grade and TNM staging were independent risk factors for CSS.

Impact of previous and simultaneous bladder cancer on UTUC prognosis

Overall, 820 had previous bladder cancer, 60 had simultaneous bladder cancer. The median time from first bladder cancer to UTUC was 47 months (IQR, 9–95 months). We found UTUC patients with previous or simultaneous bladder cancer had similar prognosis both before (P=0.86) and after (P=0.30) PSM analysis (Figure S1). As shown in *Figure 2A*, the CSS between UTUC-Bca cohort and UTUC-only cohort did not reach statistical significance. However, after adjustment of covariates that had significant difference in the baseline characteristics between two cohorts by PSM analysis, we found the CSS was significantly shorter for UTUC-Bca cohort (*Figure 2B*).

The influence of interval between previous bladder cancer and UTUC was assessed by smooth hazard ratio analysis. As shown in *Figure 2C*, the declining log hazard ratio curve indicated shorter CSS for patients who had earlier occurrence of UTUC after bladder cancer, but the impact of this was not obvious due to the small hazard ratio value. We further conduct X-title analysis and demonstrated the optimal cutoff value was around 5 years (Figure S2). We found the CSS of UTUC occurred within 5 years after bladder cancer [median: 49 months, 95% confidence interval (CI): 38–60 months] was similar to that of more than 5 years (median: 54 months, 95% CI: 35–73 months; P=0.13, *Figure 2D*). Furthermore, we found both low- (P=0.03) or high-grade (P<0.01) bladder cancer history, and previous muscle invasive bladder cancer (MIBC; P<0.01) or non-muscle invasive bladder cancer (NMIBC; P<0.01) had significantly adverse effect on the prognosis of UTUC (*Figure 3*).

Impact of IVR on UTUC prognosis

The median time to IVR after RNU was 14 months (IQR, 7–39 months). Compared to UTUC-only, UTUC-IVR had significantly longer CSS (*Figure 4A*). Yet it was worth noting that UTUC-IVR cohort was associated with lower tumor

Table 1 Patient characteristics

Variables	UTUC-only (n=6,831)	UTUC-IVR (n=720)	Bca-UTUC (n=880)	P value
Age, median (IQR)	72 (64–79)	72 (62–79)	75 (67–81)	<0.01
Gender, male/female	3,731/3,100	425/295	667/213	<0.01
Median CSS (95% CI)	81 (65–97)	NA	51 (38–64)	<0.01
Race, n (%)				
White	5,868 (85.9)	630 (87.5)	803 (91.3)	<0.01
Black	357 (5.2)	34 (4.7)	30 (3.4)	
Asian or other	606 (8.9)	56 (7.8)	47 (5.3)	
Location, n (%)				
Ureter	1,714 (25.1)	186 (25.8)	297 (33.8)	<0.01
Renal pelvis	5,117 (74.9)	534 (74.2)	583 (66.3)	
Side, n (%)				
Left	3,415 (50.0)	358 (49.7)	449 (51.0)	0.91
Right	3,407 (49.9)	362 (50.3)	430 (48.9)	
Both	9 (0.1)	0	1 (0.1)	
Histology, n (%)				<0.01
Papillary urothelial carcinoma	3,455 (40.6)	460 (63.9)	468 (53.2)	
Urothelial carcinoma	3,315 (48.5)	259 (36.0)	405 (46.0)	
Carcinoma *in situ*	61 (0.9)	1 (0.1)	7 (0.8)	
Grade, n (%)				<0.01
GI–II (low grade)	934 (13.7)	179 (24.9)	116 (13.2)	
GIII–IV (high grade)	5,427 (79.4)	488 (67.8)	687 (78.1)	
Gx	470 (6.9)	53 (7.4)	77 (8.8)	
T stage, n (%)				<0.01
Ta–1	1,844 (27.0)	288 (40.0)	255 (29.0)	
T2	1,027 (15.0)	132 (18.3)	181 (20.6)	
T3	3,071 (45.0)	270 (37.5)	356 (40.5)	
T4	809 (11.8)	25 (3.5)	73 (8.3)	
Tx	80 (1.2)	5 (0.7)	15 (1.7)	
Lymph node, n (%)				<0.01
Negative	5,521 (80.8)	656 (91.1)	724 (82.3)	
Positive	1,066 (15.6)	48 (6.7)	117 (13.3)	
Nx	244 (3.6)	16 (2.2)	39 (4.4)	
Metastasis, n (%)				<0.01
Negative	6,239 (91.3)	704 (97.8)	832 (94.5)	
Positive	551 (8.1)	10 (1.4)	42 (4.8)	
Mx	41 (0.6)	6 (0.8)	6 (0.7)	

UTUC, upper urinary tract urothelial carcinoma; IVR, intravesical recurrence; IQR, interquartile range; CSS, cancer specific survival; CI, confidence interval.

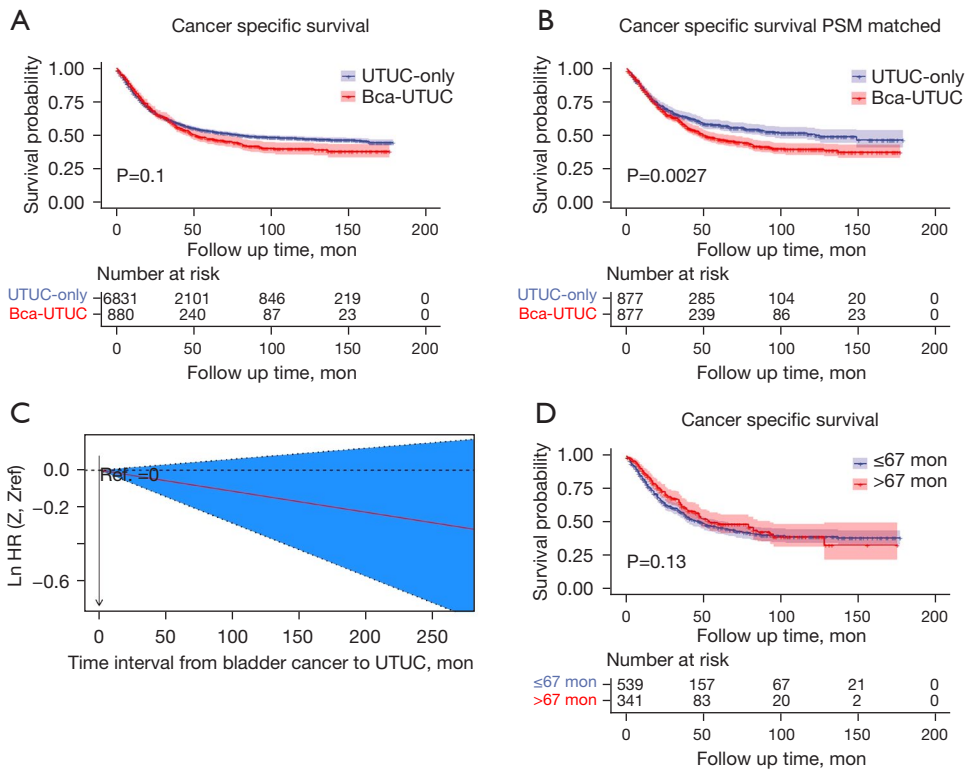

Figure 2 Kaplan-Meier survival curves showing CSS after RNU between UTUC-only cohort and Bca-UTUC cohort (A) and after PSM analysis (B); (C) smooth hazard ratio curve of interval between bladder cancer history and UTUC; (D) UTUC patients with different interval of bladder cancer history. UTUC, upper urinary tract urothelial carcinoma; PSM, propensity score matching; CSS, cancer specific survival; RNU, nephroureterectomy.

grade and TNM stage than that of UTUC-only cohort, we thus performed PSM analysis. After adjusting those covariates, we demonstrated IVR had no significant impact on the prognosis of UTUC compared to patients without IVR (*Figure 4B*). Furthermore, the interval between UTUC and IVR had significant impact on the prognosis (*Figure 4C*). Shorter interval suggested poorer CSS, especially for IVR occurred within 20 months after RNU (*Figure 4D*, Figure S3). Moreover, subgroup analysis revealed that patients with subsequent MIBC had worse prognosis compared to the baseline matched UTUC-only cohort (P=0.03), while the prognosis for patients with subsequent low grade bladder cancer (P=0.01) or NMIBC (P<0.01) was better than that of the UTUC-only cohort (*Figure 5*).

Discussion

In the present study based on the largest UTUC cohort from SEER database, we found that UTUC patients with previous or simultaneous bladder cancer were significantly correlated with inferior CSS compared with UTUC-only cohort. Meanwhile, IVR occurred within a short period of time or with MIBC after RNU was likely to predict a worse prognosis.

Currently, the EAU guideline stratified UTUC into low- or high-risk group based on preoperative clinicopathological variables. Patients with previous cystectomy for high grade bladder cancer was stratified as high-risk group (9,10,15). It was reported that 18.8–33.6% of UTUC patients had previous or simultaneous bladder cancer at RNU (1-3). In this study, we identified UTUC-Bca cohort tend to be more commonly associated with older age, lower tumor stage and grade compared with UTUC-only cohort, such distribution character was in line with previous study (2). Kuroiwa *et al.* (2) inferred this phenomenon was probably due to more meticulous clinical evaluation for patients with previously tumor history. After PSM analysis, we still found UTUC patients with previous or simultaneous

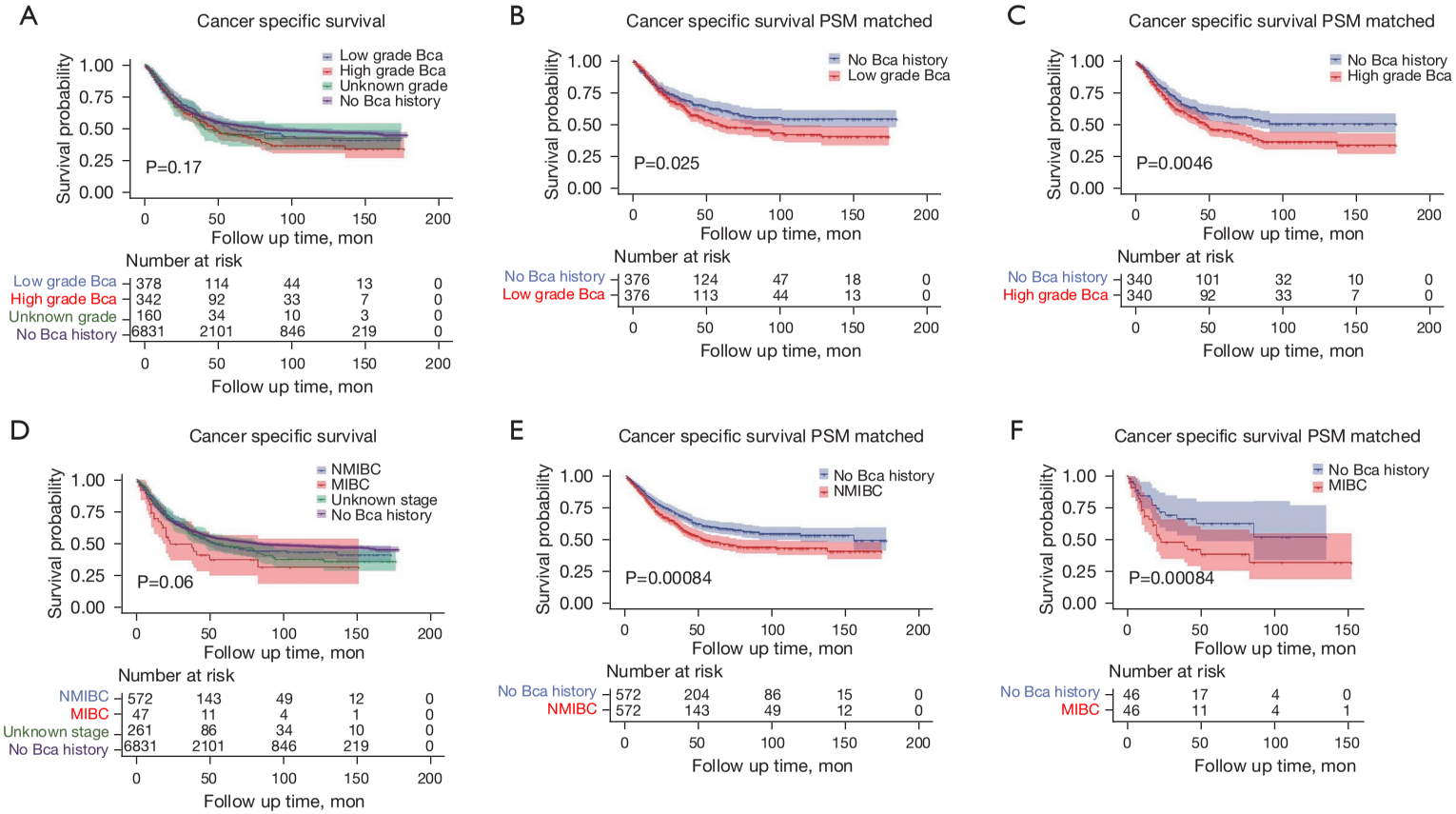

Figure 3 Subgroup analysis comparing prognosis for UTUC-Bca cohort and UTUC-only cohort using Kaplan-Meier survival curves. (A) CSS of different bladder tumor grade of UTUC-Bca cohort and UTUC-only cohort; CSS of low grade (B) and high grade (C) bladder tumor of UTUC-Bca cohort and UTUC-only cohort after PSM; (D) CSS of different bladder tumor stage of UTUC-Bca cohort and UTUC-only cohort; CSS of NMIBC (E) and MIBC (F) of UTUC-Bca cohort and UTUC-only cohort after PSM. PSM, propensity score matching; NMIBC, non-muscle invasive bladder cancer; MIBC, muscle invasive bladder cancer; UTUC, upper urinary tract urothelial carcinoma; CSS, cancer specific survival.

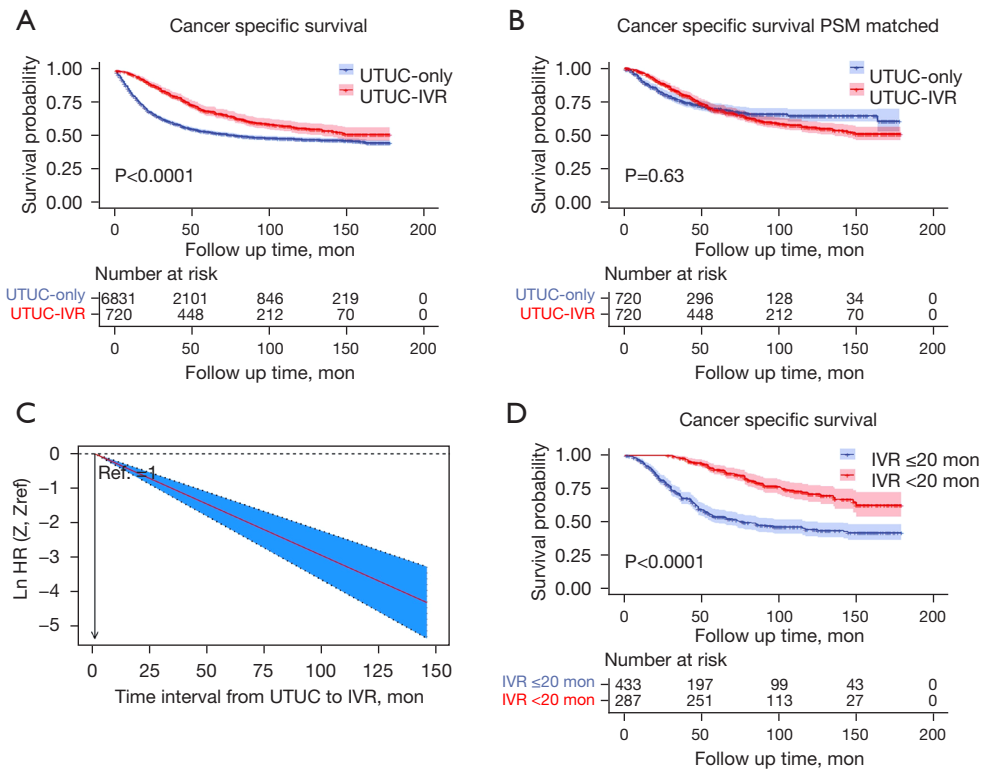

Figure 4 Kaplan-Meier survival curves analysis of UTUC-only cohort and UTUC-IVR cohort (A) and after PSM analysis (B); (C) smooth hazard ratio curve of interval between UTUC and IVR; (D) Kaplan-Meier survival curve comparing UTUC patients with different interval of IVR. UTUC, upper urinary tract urothelial carcinoma; IVR, intravesical recurrence; PSM, propensity score matching.

bladder cancer, regardless of tumor grade and stage, had significantly worse CSS. Meanwhile, the interval between UTUC and bladder cancer history has little impact on prognosis, which indicated bladder cancer history was a persistent risk factor even if it was a long time ago. In line with our findings, Kuroiwa *et al.* (2) included 2,668 patients underwent RNU and revealed that patients with previous or simultaneous bladder cancer had significantly shorter overall survival than patients without it.

However, conflicting results have been reported regarding the impact of previous or simultaneous bladder cancer on the prognosis of UTUC. Several studies indicated that UTUC patients with history of bladder tumor was an independent predictor of IVR but had no effect on non-bladder recurrence or CSS (6-8). Nuhn *et al.* (16) showed that previous MIBC rather than NMIBC was an independent risk factor for CSS. It should be noted that these studies were usually based on relatively small sample size and short-term follow-up.

IVR is common despite the recommendation of single post-operative dose of intravesical chemotherapy after RNU (15). Currently, the impact of IVR on the prognosis of UTUC prognosis remains debatable. Xylinas *et al.* (17) reported that existence of IVR, which included NMIBC and MIBC, was not correlated with recurrence free survival or CSS. On the other hand, Yamashita *et al.* (18) revealed that IVR had an adverse impact on the prognosis of patients with non-muscle invasive UTUC. Kuroiwa *et al.* (2) found that among UTUC patients with pT0–2 disease, those with IVR had significantly shorter survival than patients without IVR, while in patients with pT3–4 disease IVR was not associated with worse survival (17,19,20). It was noteworthy that clinicopathologic characteristics difference may existed between UTUC-IVR and UTUC-only groups in these studies. As a result, the poorer survival of UTUC-IVR group in the previous studies could be attributed to these confounding factors.

In our research, UTUC-IVR group did not show difference in terms of CSS compared with UTUC-only group after PSM analysis. Further subgroup analysis

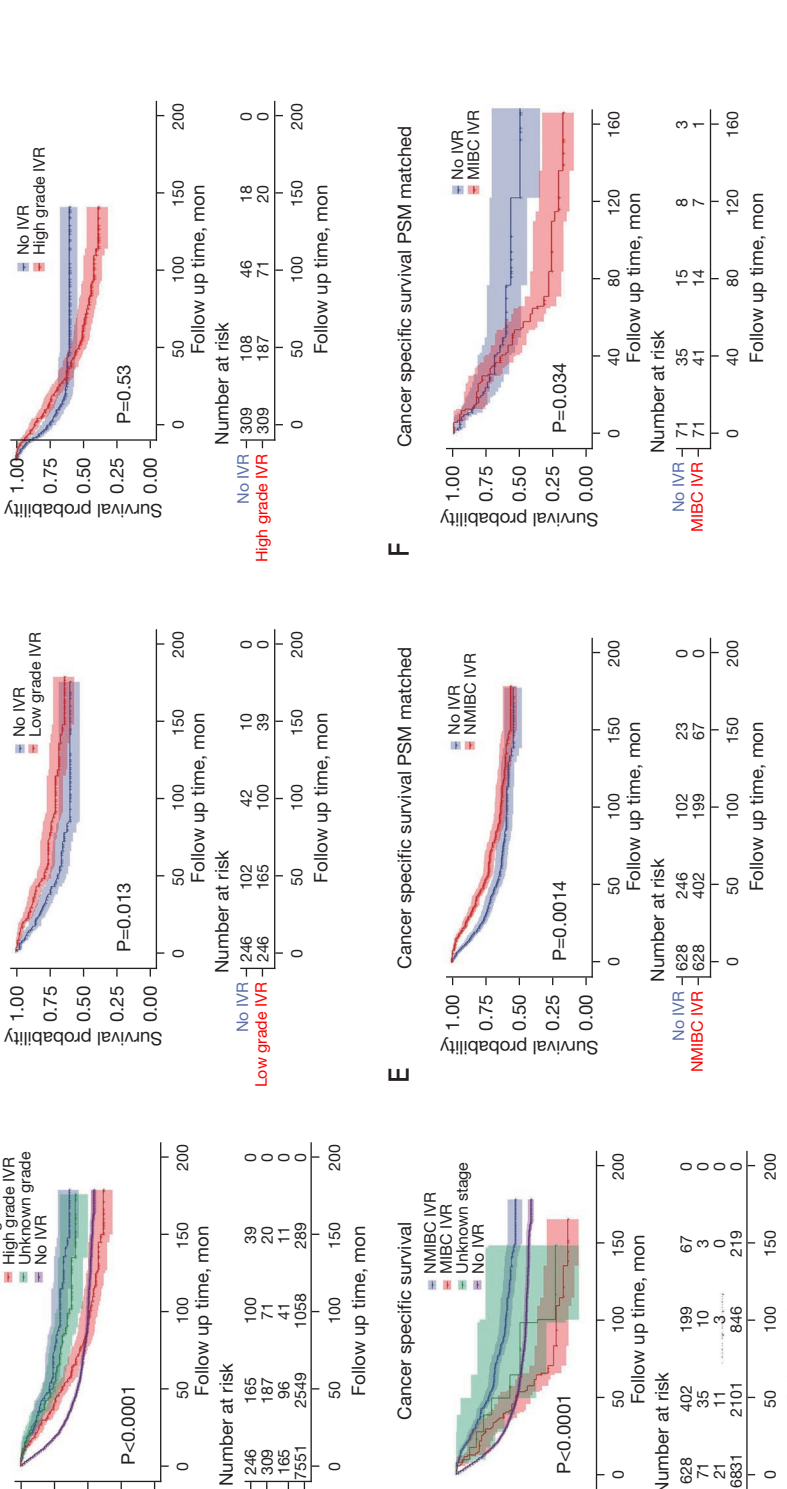

Figure 5 Subgroup analysis comparing prognosis for UTUC-IVR cohort and UTUC-only cohort using Kaplan-Meier survival curves. (A) CSS of different bladder tumor grade of UTUC-IVR cohort and UTUC-only cohort; CSS of low grade (B) and high grade (C) bladder tumor of UTUC-IVR cohort and UTUC-only cohort after PSM; (D) CSS of different bladder tumor stage of UTUC-IVR cohort and UTUC-only cohort; CSS of NMIBC (E) and MIBC (F) of UTUC-IVR cohort and UTUC-only cohort after PSM. IVR, intravesical recurrence; PSM, propensity score matching; NMIBC, non-muscle invasive bladder cancer; MIBC, muscle invasive bladder cancer; UTUC, upper urinary tract urothelial carcinoma; CSS, cancer specific survival.

suggested that UTUC with subsequent MIBC recurrence had significant poorer survival than that of UTUC-only group. Meanwhile, those with shorter interval between UTUC and IVR was associated with significantly worse prognosis. Interestingly, UTUC patients with low grade or NMIBC IVR was associated with favorable survival outcomes. Intraluminal seeding theory and field effect theory have been proposed to explain the potential pathophysiological mechanisms after RNU (21,22). The phenomena in this study may be explained by the theories of intraluminal seeding, because the heterogeneity of IVR reflected the aggressiveness and prognosis of UTUC tumor. Several genetic studies also showed a monoclonal origin of recurrence bladder tumors and primary UTUC with intraluminal seeding (23-26). As a result, it is necessary to apply intravesical chemotherapy or bacillus Calmette-Guerin instillation to prevent early recurrence after RNU, and stringently follow UTUC patients with cystoscopy to avoid IVR progressing to MIBC.

Despite the large sample size and long-term follow-up of the present study, several unavoidable limitations of this study should be noted. First, this registry-based retrospective study and its intrinsic biases must be acknowledged. This study included patients from 2004 to 2018, and the treatment and follow-up protocol for UTUC varied in different places and changed over time. For example, early single post-operative dose of intravesical chemotherapy (24–48 h) after RNU, which significantly decrease the rate of IVR, was not done in all centers, and some centers delayed intravesical instillation by up to one week to administer a cystogram confirming there is no perforation (27,28). Second, the respective incidence of UTUC patients with previous or simultaneous bladder cancer and IVR was 12.8% and 10.5%, both were lower than previously data in literature. Potential bias thus may exist. Third, information for several clinical variables in SEER database is absent, such as smoking history, diagnostic ureteroscopy, neoadjuvant or adjuvant chemotherapy.

Conclusions

UTUC patients with previous or simultaneous bladder cancer was a significant predictor for worse prognosis, and IVR with MIBC was an independent risk factor for CSS. Furthermore, shorter interval between UTUC and IVR indicated poorer prognosis. Thus, more stringent postoperative surveillance and active treatment strategies should be considered for UTUC patients with those risk factors.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

References

1. Yu LC, Chang CH, Huang CP, et al. Prognostic Significance of Primary Tumor Location in Upper Tract Urothelial Carcinoma Treated with Nephroureterectomy: A Retrospective, Multi-Center Cohort Study in Taiwan. J Clin Med 2020;9:3866.
2. Kuroiwa K, Inokuchi J, Nishiyama H, et al. Impact of Previous, Simultaneous or Subsequent Bladder Cancer on Prognosis after Radical Nephroureterectomy for Upper Urinary Tract Urothelial Carcinoma. J Urol 2019;202:1127-35.
3. Xylinas E, Kluth L, Passoni N, et al. Prediction of intravesical recurrence after radical nephroureterectomy: development of a clinical decision-making tool. Eur Urol 2014;65:650-8.
4. Elalouf V, Xylinas E, Klap J, et al. Bladder recurrence after radical nephroureterectomy: predictors and impact on oncological outcomes. Int J Urol 2013;20:1078-83.
5. Wu J, Xu PH, Luo WJ, et al. Intravesical Recurrence After Radical Nephroureterectomy of Upper Urinary Tract Urothelial Carcinoma: A Large Population-Based Investigation of Clinicopathologic Characteristics and Survival Outcomes. Front Surg 2021;8:590448.
6. Milojevic B, Djokic M, Sipetic-Grujicic S, et al. Prognostic significance of non-muscle-invasive bladder tumor history in patients with upper urinary tract urothelial carcinoma. Urol Oncol 2013;31:1615-20.
7. Pignot G, Colin P, Zerbib M, et al. Influence of previous or synchronous bladder cancer on oncologic outcomes after radical nephroureterectomy for upper urinary tract urothelial carcinoma. Urol Oncol 2014;32:23.e1-8.
8. Yoo S, You D, Song C, et al. Risk of Intravesical Recurrence After Ureteroscopic Biopsy for Upper Tract Urothelial Carcinoma: Does the Location Matter? J Endourol 2017;31:259-65.
9. Mullerad M, Russo P, Golijanin D, et al. Bladder cancer as a prognostic factor for upper tract transitional cell carcinoma. J Urol 2004;172:2177-81.
10. Rouprêt M, Colin P, Yates DR. A new proposal to risk stratify urothelial carcinomas of the upper urinary tract (UTUCs) in a predefinitive treatment setting: low-risk versus high-risk UTUCs. Eur Urol 2014;66:181-3.
11. Jiang Y, Yao Z, Zhu X, et al. Risk factors and oncological outcome for intravesical recurrence in organ-confined upper urinary tract urothelial carcinoma patients after radical nephroureterectomy: A propensity score-matched case control study. Int J Surg 2020;76:28-34.
12. Elawdy MM, Osman Y, Taha DE, et al. Risk factors and prognosis of intravesical recurrence after surgical management of upper tract urothelial carcinoma: A 30-year single centre experience. Arab J Urol 2017;15:216-22.
13. Lee CH, Ku JY, Jeong CW, et al. Predictors for Intravesical Recurrence Following Radical Nephroureterectomy for Upper Tract Urothelial Carcinoma: A National Multicenter Analysis. Clin Genitourin Cancer 2017;15:e1055-61.
14. Reeve BB, Smith AW, Arora NK, et al. Reducing bias in cancer research: application of propensity score matching. Health Care Financ Rev 2008;29:69-80.
15. Rouprêt M, Babjuk M, Burger M, et al. European Association of Urology Guidelines on Upper Urinary Tract Urothelial Carcinoma: 2020 Update. Eur Urol 2021;79:62-79.
16. Nuhn P, Novara G, Seitz C, et al. Prognostic value of prior history of urothelial carcinoma of the bladder in patients with upper urinary tract urothelial carcinoma: results from a retrospective multicenter study. World J Urol 2015;33:1005-13.
17. Xylinas E, Colin P, Audenet F, et al. Intravesical recurrence after radical nephroureterectomy for upper tract urothelial carcinomas: predictors and impact on subsequent oncological outcomes from a national multicenter study. World J Urol 2013;31:61-8.
18. Yamashita S, Ito A, Mitsuzuka K, et al. Clinical implications of intravesical recurrence after radical nephroureterectomy for upper urinary tract urothelial carcinoma. Int J Urol 2016;23:378-84.
19. Belhadj Y, Grande P, Seisen T, et al. Bladder mapping of tumour recurrence after radical nephroureterectomy for upper tract urothelial carcinoma and its influence on oncological outcomes. BJU Int 2019;123:618-23.
20. Marchioni M, Primiceri G, Cindolo L, et al. Impact of diagnostic ureteroscopy on intravesical recurrence in patients undergoing radical nephroureterectomy for upper tract urothelial cancer: a systematic review and meta-analysis. BJU Int 2017;120:313-9.
21. Jones TD, Wang M, Eble JN, et al. Molecular evidence supporting field effect in urothelial carcinogenesis. Clin Cancer Res 2005;11:6512-9.
22. Takahashi T, Kakehi Y, Mitsumori K, et al. Distinct microsatellite alterations in upper urinary tract tumors and subsequent bladder tumors. J Urol 2001;165:672-7.
23. Habuchi T, Takahashi R, Yamada H, et al. Metachronous multifocal development of urothelial cancers by intraluminal seeding. Lancet 1993;342:1087-8.

24. Hafner C, Knuechel R, Stoehr R, et al. Clonality of multifocal urothelial carcinomas: 10 years of molecular genetic studies. Int J Cancer 2002;101:1-6.
25. Hirano D, Okada Y, Nagane Y, et al. Intravesical recurrence after surgical management of urothelial carcinoma of the upper urinary tract. Urol Int 2012;89:71-7.
26. Takahashi T, Habuchi T, Kakehi Y, et al. Clonal and chronological genetic analysis of multifocal cancers of the bladder and upper urinary tract. Cancer Res 1998;58:5835-41.
27. National Comprehensive Cancer Network Guidelines Version 5.2021. Bladder cancer 2021. Available online: https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1417
28. O'Brien T, Ray E, Singh R, et al. Prevention of bladder tumours after nephroureterectomy for primary upper urinary tract urothelial carcinoma: a prospective, multicentre, andomized clinical trial of a single postoperative intravesical dose of mitomycin C (the ODMIT-C Trial). Eur Urol 2011;60:703-10.

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