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ORIGINAL RESEARCH

Predictors of Intravesical Recurrence After Radical Nephroureterectomy and Prognosis in Patients with Upper Tract Urothelial Carcinoma

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Purpose: We investigate factors that may contribute individually to bladder recurrence and find out the potential candidate to receive postoperative single dose intravesical chemotherapy.

Materials and Methods: A total of 217 patients who were diagnosed with upper tract urothelial carcinoma (UTUC) underwent radical nephroureterectomy (RNU) between 2012 and 2016 in a single hospital. The possible risk factors that may contribute to development of bladder recurrence and overall survival were analysed. In order to find out the relationship between 1st bladder recurrence timing and outcome, we divided the 54 of 56 patients (2 patients with prophylactic intravesical chemotherapy excluded) with bladder recurrence after RNU into 2 groups, using the median time of 1st bladder recurrence and confirmed with the "minimum P-value" approach. The primary endpoint was the development of relapsing high-risk non-muscle invasive bladder cancer (NMIBC). The predictive factors of early recurrence and prognostic factors of survival were also analysed.

Results: Among 217 patients with UTUC under RNU, intravesical recurrence occurred in 56 (25.8%) patients after a median follow-up of 35.2 (1.18–83.34) months. On multivariable analysis, the preoperative ureter manipulation (p=0.009) was a significant predictor for the development of bladder tumours. As for overall survival, renal rein invasion (p=0.017), neutrophil to lymphocyte ratio (p=0.021), and main tumour size (p=0.015) were significant predictors. For 54 patients who developed bladder recurrence, the optimal cut-off point of early recurrence was determined to be 10 months after surgery (p=0.042). Preoperative ureter manipulation (p=0.005) and tumour located both pelvicalyceally and ureterically (P=0.042) were identified as independent factors associated with early recurrence. An end-stage renal disease history and surgical margin positive patient has more late bladder recurrence.

Conclusion: Bladder recurrence was common in UTUC after RNU. Early bladder recurrence was associated with more relapsing high-risk NMIBC and preoperative ureter manipulation was identified as an independent factor associated with early recurrence.

Keywords: intravesical recurrence, prognosis, radical nephroureterectomy, upper tract urothelial carcinoma

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Introduction

Upper tract urothelial carcinoma (UTUC) consists of renal pelvic and ureteral urothelial carcinoma (UC).[1] Unlike bladder UC, UTUC contributes to 5–10% of all urothelial tumours, with an estimated annual incidence of 1–2 cases per 100,000 population in the United States.[2] However, the incidence rate is higher in Taiwan. According to the Taiwan Cancer Registry Annual Report in 2016, the age-standardized incidence rate of

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UTUC per 100,000 population was 3.61 and 4.21 among men and women, respectively, which comprises up to 30% of all UCs in Taiwan.[3]

The standard surgical treatment of UTUC is radical nephroureterectomy (RNU) with bladder cuff excision. Despite treatment with standard surgery, tumour recurrence is common, especially intravesical recurrence (IVR). A meta-analysis showed that the incidence of IVR was 29%, with a median time of 22.2 months (range 6.7–56.5 months).[4] Previous studies have proposed the predictor of IVR, but the definite pathophysiology of bladder recurrence remains unclear. Two theories have been proposed to explain the possibility of frequent urothelial cancer recurrence: implantation of a tumour cell of monoclonal origin after intraluminal seeding[5] or field-cancerization theory[6] or both. Studies on prophylactic instillation of intravesical chemotherapy (IVCT) after RNU have been reported with the number needed to treat as 9 to reduce the risk of IVR.[7] However, considering the potential extravasation of chemotherapy, immediate instillation was not routinely performed for every high-risk patient. Therefore, accurate prediction of IVR is necessary to identify the best candidates.

The aim of this study was to investigate factors that may contribute individually to recurrence of bladder carcinoma and identify potential candidates to undergo prophylactic intravesical chemotherapy.

Materials and Methods

A total of 373 patients were diagnosed with primary UTUC between January 2012 and December 2016 at Linkou Chang Gung Memorial Hospital. The study protocol was approved by the Institutional Review Board at the Chang Gung Memorial Hospital (Taoyuan, Taiwan) (IRB: 201601299B0C602). The patients' consent to review their medical records was waived by the IRB of Chang-Gung Memorial Hospital due to retrospective study. The patient data confidentiality fulfilled the Declaration of Helsinki. The following were excluded from the study: 12 patients who were lost to follow-up within 3 months, 55 who received systemic chemotherapy, 52 who did not undergo surgical intervention, 6 who underwent concomitant radical cystectomy, 13 who did not receive standard radical nephroureterectomy, 7 who had double active cancer, and 10 who had previous/concurrent bladder UC. One patient underwent complete resection of the tumour during diagnostic ureteroscopy, and the final pathology of nephroureterectomy showed no residual malignant tumour. The clinical data of the remaining 217 patients were retrospectively reviewed.

To determine the relation between bladder recurrence free survival time and prognosis, 54 patients with current IVR were analysed (2 patients were excluded owing to prophylactic intravesical chemotherapy). The timing of IVR was within postoperative 24 months, and the median time was 10 months. Therefore, we grouped the patients with bladder recurrence into early and late recurrence, using the median time of 1st bladder recurrence and confirmed with the "minimum P-value" approach. The "minimum P-value" approach, which was performed using the log rank test for the time to relapsing high-risk NMIBC after radical nephroureterectomy, was used to determine the best cut-off with which to divide up patients based on the time to relapsing high-risk NMIBC after radical nephroureterectomy. The minimum P-value approach has been proposed as a means of reducing the risk of missing a significant association in previous studies.[16,17] Further analysis was performed between the two groups.

UTUC was diagnosed by intravenous urography, computed tomographic urography, magnetic resonance imaging, or diagnostic ureteroscopy. Preoperative cystoscopy was performed in all patients to rule out concurrent bladder tumour. Regional lymph node dissection was not routinely performed in our cases.

According to the Clinical Practice Guidelines in Oncology (NCCN Guidelines), the standard management of upper tract urothelial carcinoma is standard RNU, included nephroureterectomy and ipsilateral bladder cuff excision. Several techniques has been described for bladder cuff excision; in our hospital, an extravesical approach was selected. When performing the extravesical approach of bladder cuff excision, the distal ureter is freed towards the bladder to the point of intramural ureter. The cuff of bladder is removed en bloc with the ureter by applying a clamp to the bladder wall and excising the full intramural portion of the ureter. We defined the bladder cuff excision by reviewing the operation record. All of the surgical records showed bladder cuff removed.

In our institute, cystoscopy was performed every 3 months after RNU for the first 2 years. The interval of cystoscopy was extended to every 6 months in the 3rd and 4th years after surgery, and then annually thereafter. Compared to the European Association of Urology (EAU) and National Comprehensive Cancer Network (NCCN) follow-up guidelines, we follow a more intensive cystoscopic examination. Bladder recurrence was defined as tumours identified on

Table 1 Clinicopathologic Characteristics of Patients with UTUC Treated by RNU

	Total=217	No Recur=161	Early Recur=27	Late Recur=29
Patient-specific factor				
Age, yr (%)				
<60	42 (19.4)	30 (18.6)	6 (22.2)	6 (20.7)
>60	175 (80.6)	131 (81.4)	21 (77.8)	23 (79.3)
Gender, n (%)				
Male	79 (36.4)	53 (32.9)	12 (44.4)	14 (48.3)
Female	138 (63.6)	108 (67.1)	15 (55.6)	15 (51.7)
ESRD, n (%)	21			
No	196 (90.3)	149 (92.5)	25 (92.6)	22 (75.9)
Yes	21 (9.7)	12 (7.5)	2 (7.4)	7 (24.1)
Hydronephrosis, n (%)				
Absent	84 (38.7)	66 (41)	10 (37.0)	8 (27.6)
Present	133 (61.3)	95 (59)	17 (63.0)	21 (72.4)
Neutrophil to lymphocyte ratio, n (%)				
<3.8	187 (96.2)	140 (87)	23 (85.1)	24 (82.8)
≥3.8	30 (13.8)	21 (13)	4 (14.9)	5 (17.2)
Platelet to lymphocyte ratio, n (%)				
<133	150 (69.1)	107 (66.5)	21 (77.8)	22 (75.9)
>133	67 (30.9)	54 (33.5)	6 (22.2)	7 (24.1)
Tumour-specific factor				
Location, n (%)				
Kidney	129 (59.4)	98 (60.9)	11 (40.7)	20 (69)
Ureter	66 (30.4)	48 (29.8)	10 (37.0)	8 (27.6)
Kidney and ureter	22 (10.1)	15 (9.3)	6 (22.2)	1 (3.4)
T stage, n (%)				
<T2	119 (54.8)	91 (56.5)	12 (44.4)	16 (55.2)
≥T2	98 (45.2)	70 (43.5)	15 (55.6)	13 (44.8)
Histology type, n (%)				
Infiltrating	144 (66.4)	109 (67.7)	18 (66.7)	17 (58.6)
Papillary	73 (33.6)	52 (32.3)	9 (33.3)	12 (41.4)
Grading, n (%)				
Low	53 (24.4)	38 (23.6)	8 (29.6)	7 (24.1)
High	164 (75.6)	123 (76.4)	19 (70.4)	22 (75.9)
Tumour focality, n (%)				
Single	188 (86.6)	141 (87.6)	22 (81.5)	25 (86.2)
Multiple	29 (13.4)	20 (12.4)	5 (18.5)	4 (13.8)
Lymphovascular invasion, n (%)				
Absent	201 (92.6)	150 (93.2)	24 (88.9)	27 (93.1)
Present	16 (7.4)	11 (6.8)	3 (11.1)	2 (6.9)
Contaminate with CIS, n (%)				
Absent	202 (93.1)	152 (94.4)	24 (88.9)	26 (89.7)
Present	15 (6.9)	9 (5.6)	3 (11.1)	3 (10.3)

(*Continued*)

Table 1 (Continued).

	Total=217	No Recur=161	Early Recur=27	Late Recur=29
Renal vein invasion, n (%)				
Absent	214 (98.6)	159 (98.8)	27 (100)	28 (96.6)
Present	3 (1.4)	2 (1.2)	0 (0)	1 (3.4)
Main tumour				
<6.7 mm	206 (94.9)	150 (93.2)	27 (100)	29 (100)
≥6.7 mm	1 1(5.1)	11 (6.8)	0 (0)	0 (0)
Treatment-specific factor				
Preop ureter manipulation, n (%)				
Absent	81 (37.3)	69 (42.9)	3 (11.1)	9 (31)
Present	136 (62.7)	92 (57.1)	24 (88.9)	20 (69)
Surgical approach, n (%)				
Open method	96 (44.2)	75 (46.6)	9 (33.3)	12 (41.4)
Laparoscopic method	106 (48.8)	76 (47.2)	16 (59.3)	14 (48.3)
Robotic assisted method	15 (6.9)	10 (6.2)	2 (7.4)	3 (10.3)
Complication, n (%)				
Absent	215 (99.1)	159 (98.8)	27 (100)	29 (100)
Present	2 (0.9)	2 (1.2)	0 (0)	0 (0)
Surgical margin, n (%)				
Free	215 (99.1)	161 (100)	27 (100)	27 (93.1)
Positive	2 (0.9)	0 (0)	0 (0)	2 (6.9)
Bladder recurrence				
Absent	161 (74.2)	161 (100)	0 (0)	0 (0)
Present	56 (25.8)	0 (0)	27 (100)	29
Prophylactic IVC, n (%)				
No use	206 (94.9)	152 (94.4)	0 (0)	27 (93.1)
Epirubicin	7 (3.2)	5 (3.1)	0 (0)	2 (6.9)
MMC	4 (1.8)	4 (2.5)	0 (0)	0 (0)

cystoscopy and confirmed by pathology. The relapsing high-risk non-muscle-invasive bladder tumour was defined as the 2nd recurrence of bladder tumour with high risk (T1, high-grade, multiple tumours) when it developed after complete resection of the 1st IVR and completion of intravesical chemotherapy (epirubicin or mitomycin C). The cause of death was collected using death certificates. Follow-ups were censored until their last visit or death.

Categorical variables were compared using the chi-square test. Survival analyses were performed using the Kaplan–Meier method and were compared using the log rank test. Variables in which the p value for the univariate analysis was <0.05 were subjected to either multivariate logistic regression or the Cox regression model. All reported p values were single sided with statistical significance considered at $p<0.05$. All statistical analyses were performed using IBM SPSS Statistics 22 software.

Results

Table 1 reveals the clinicopathologic characteristics of 217 patients with primary UTUC treated using standard radical nephroureterectomy in our institution between January 2012 and December 2016. The median age was 70 (34–90) years, and 138 (63.6%) patients were female. The median follow-up period was 42.0 (1.18–83.34) months. Twenty-one (9.7%) patients had a history of end-stage renal disease and were under renal replacement therapy. Open RNU was performed in 96 (44.2%) patients, laparoscopic method in 106 (48.8%) patients, and robotic-assisted method in 15 (6.9%) patients.

The tumours were pelvicalyceal in 129 (59.4%) patients, ureteric in 66 (30.4%), and both pelvicalyceal and ureteric in 22 (10.1%) patients. IVCT was not routinely arranged after surgery, there were only 11 patients who received the installation (epirubicin 7 cases and mitomycin 4 cases).

The tumour stage was <T2 in 119 (54.8%) patients and ≥T2 in 98 (45.2%) patients. Histology with infiltrating type (66.4%) and high-grade tumours (75.6%) were predominant. As for additional pathological finding, lymphovascular invasion (LVI) was seen in 7.4% of patients, concomitant carcinoma in situ (CIS) in 6.9%, renal vein invasion in 1.4%, and surgical margin positive in 2.8% of patients.

IVR after RNU was noted in 56 (25.8%) patients after a median follow-up of 35.2 (1.18–83.34) months. The recurrent bladder tumours were managed with endoscopic resection and intravesical chemoimmunotherapy following the standard protocol. The recurrent bladder tumours showed the following characteristics: 71.4%, 26.8%, and 1.8% of tumours were in Ta, T1, and T2 stages,

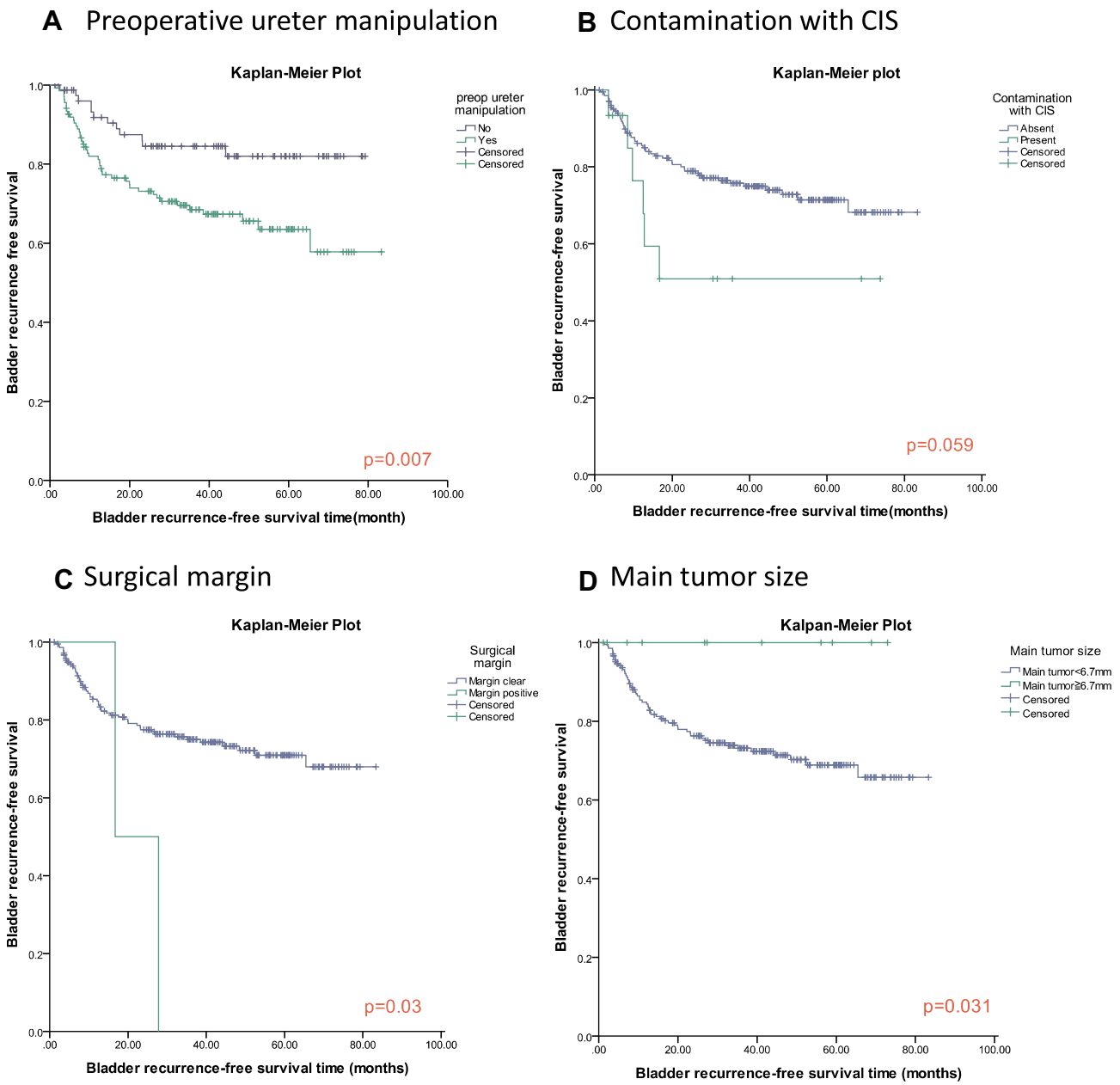

Figure 1 Kaplan–Meier estimates of bladder recurrence free survival: (**A**) preoperative ureter manipulation; (**B**) contamination with CIS; (**C**) surgical margin; (**D**) main tumour size.

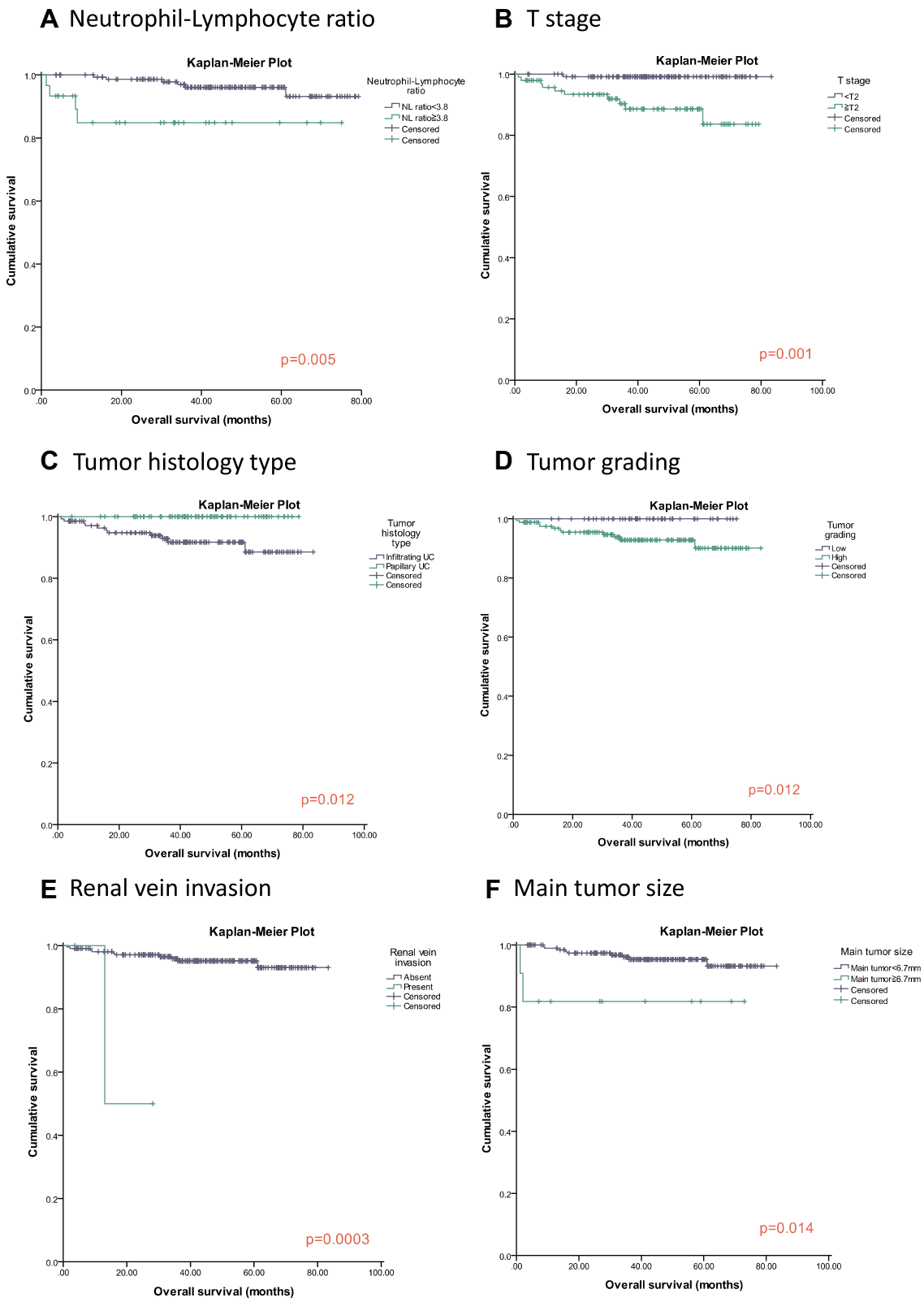

Figure 2 Kaplan–Meier estimates of overall survival: (**A**) neutrophil to lymphocyte ratio; (**B**) T stage; (**C**) tumour histology type; (**D**) tumour grading; (**E**) renal vein invasion; (**F**) main tumour size.

respectively. Refractory bladder tumours were noted in 16 patients (28.6%). One patient underwent radical cystectomy after refractory muscle invasive bladder tumour and contralateral UTUC developed. Two patients had partial cystectomy after multiple endoscopic resection of T1 tumour and intravesical chemotherapy failed.

We analysed the possible risk factors of developing bladder tumours after RNUs. Univariate analysis showed that preoperative ureter manipulation, contamination with carcinoma in situ (CIS), positive surgical margin, and main tumour size >6.7 mm had more bladder recurrences (Figure 1). Preoperative ureter manipulation (HR: 2.42, p=0.009) was an independent predictor for development of bladder tumours. As for overall survival, univariate analysis showed that the neutrophil to lymphocyte ratio (NLR), T stage, tumour histology type, tumour grading, presence of renal vein invasion, and tumour size were significant factors for overall survival (Figure 2). Renal vein invasion (HR: 17.7, p=0.017), pre-operation NLR (HR: 4.793, p=0.021), and main tumour size (HR: 7.912, p=0.015) were independent predictors for overall survival.

Since there were scarce cases who received prophylactic IVCT after RNU (11 of 217 patients) and only 2 of them developed bladder recurrence, we excluded them and performed further analysis. We divided the rest of 54 patients with bladder recurrence after RNU into early recurrence (<10 months) and late recurrence (>10 months) groups based on the timing of bladder recurrence. The overall survival showed no difference between groups. Figure 3 shows that the early recurrence group (<10 months) is associated with shorter time to develop relapsing high-risk non-muscle invasive bladder cancer (p=0.042), which may cause further cystectomy or concurrent chemoradiation therapy. Relapsing high-risk non-muscle invasive bladder cancer was observed in 7 patients. In addition, we examined the risk factors for early recurrence within 10 months after RNU for UTUC using 206 patients who underwent RNU for UTUC and without prophylactic IVCT. Table 2 shows the results of the χ^2 test and the logistic regression model used to analyse the clinicopathological factors related to early recurrence. Preoperative ureter manipulation (HR: 6.27, p=0.005) and tumour located both pelvicalyceally and ureterically (HR: 4.681, p=0.042) were identified as an independent factor associated with early recurrence.

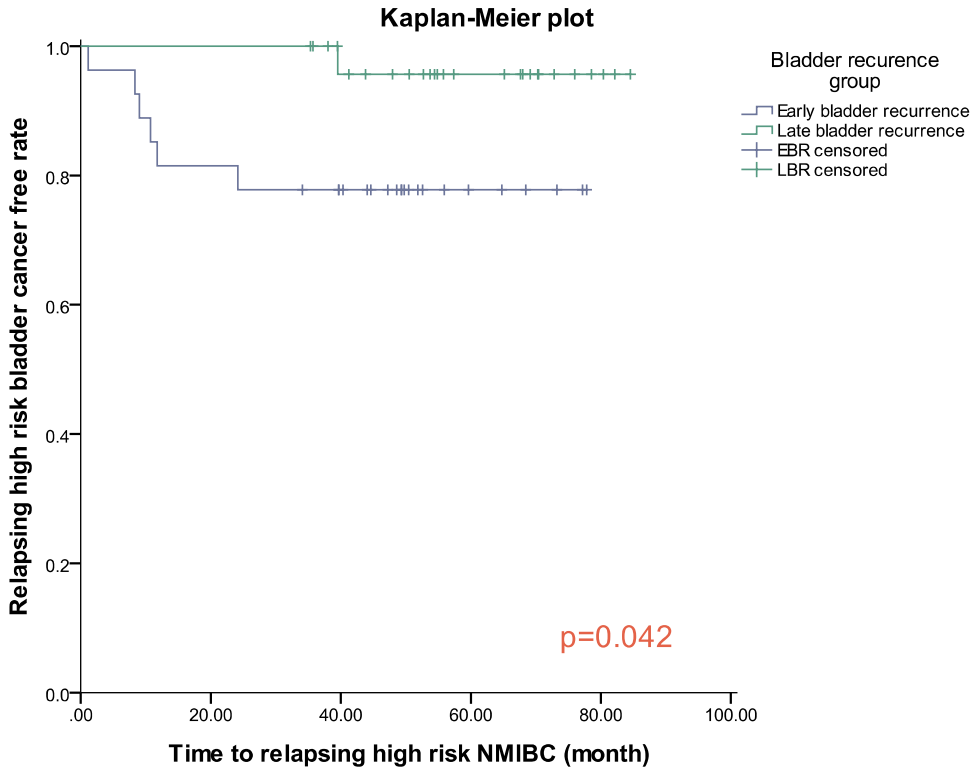

Figure 3 Relationship between early recurrence group (<10 months) and risk of developing relapsing high-risk non-muscle invasive bladder cancer: early recurrence group (<10 months) is associated with shorter time to develop relapsing high-risk non-muscle invasive bladder cancer (p=0.042).

Table 2 Results of the Univariate and Multivariate Analyses of the Clinicopathologic Factors of Early Recurrence Group (Without Prophylactic Intravesical Chemotherapy)

	Early Recur=27	Other=179	Univariate Analysis, *p*	Multivariate Analysis	
				HR (95% CI)	*p*
Patient-specific factor					
Age, yr (%)			0.693		
<60	6 (22.2)	34			
>60	21 (77.8)	145			
Gender, n (%)			0.383		
Male	12 (44.4)	64			
Female	15 (55.6)	115			
ESRD, n (%)			0.608		
No	25 (92.6)	160			
Yes	2 (7.4)	19			
Hydronephrosis, n (%)			0.847		
Absent	10 (37.0)	69			
Present	17 (63.0)	108			
Neutrophil to lymphocyte ratio, n (%)			0.866		
<3.8	23 (85.1)	155			
≥3.8	4 (14.9)	24			
Platelet to lymphocyte ratio, n (%)			0.232		
<133	21 (77.8)	122			
>133	6 (22.2)	57			
Tumour-specific factor					
Location, n (%)			0.031		0.042
Kidney	11 (40.7)	113		1	
Ureter	10 (37.0)	51		1.346 (0.523–3.466)	
Kidney and ureter	6 (22.2)	15		4.681 (1.401–15.643)	
T stage, n (%)			0.267		
<T2	12 (44.4)	100			
≥T2	15 (55.6)	79			
Histology type, n (%)			0.939		
Infiltrating	18 (66.7)	118			
Papillary	9 (33.3)	61			
Grading, n (%)			0.54		
Low	8 (29.6)	43			
High	19 (70.4)	135			
Tumour focality, n (%)			0.371		
Single	22 (81.5)	157			
Multiple	5 (18.5)	22			
Lymphovascular invasion, n (%)			0.486		
Absent	24 (88.9)	166			
Present	3 (11.1)	13			

(*Continued*)

Table 2 (Continued).

	Early Recur=27	Other=179	Univariate Analysis, *p*	Multivariate Analysis	
				HR (95% CI)	*p*
Contaminate with CIS, n (%)			0.411		
Absent	24 (88.9)	167			
Present	3 (11.1)	12			
Renal vein invasion, n (%)			0.498		
Absent	27 (100)	176			
Present	0 (0)	3			
Main tumour, n (%)			0.208		
<6.7 mm	27 (100)	169			
≥6.7 mm	0 (0)	10			
Treatment-specific factor					
Preop ureter manipulation, n (%)			0.002		0.005
Absent	3 (11.1)	75		1	
Present	24 (88.9)	104		6.27 (1.722–22.826)	
Surgical approach, n (%)			0.523		
Open method	9 (33.3)	80			
Laparoscopic method	16 (59.3)	86			
Robotic assisted method	2 (7.4)	13			
Complication, n (%)			0.697		
Absent	27 (100)	178			
Present	0 (0)	1			
Surgical margin, n (%)			0.581		
Free	27 (100)	177			
Positive	0 (0)	2			

Late recurrence was observed in 27 patients. The factors related to late recurrence were investigated in 145 patients who were confirmed to be recurrence free 10 months after RNU. Table 3 shows the results of the univariate and multivariate analyses of the clinicopathologic factors contributing to the late recurrence. An end-stage renal disease (ESRD) history and surgical margin positive have more late bladder recurrence; however, the results were not significant.

Discussion

We demonstrated a relatively large number of patients with UTUC who received RNU at a single institute in Taiwan. A previous study showed that the peak of IVR was detected in the early period (<2.5 years) after surgery, and the IVR hazard decreased afterwards.[8] In our study, 25.8% patients presented with bladder recurrence with a median time to IVR 10 months after a median follow-up of 35.2 (1.18–83.34) months, which concurs with the results of a previous meta-analysis which showed 29% IVR in a median time to IVR of 22.2 (6.7–56.5) months.[4]

Several studies have been published to identify patients at a higher risk of IVR after RNU. However, limited studies have discussed about the impact of the timing of intravesical bladder recurrence in UTUC. In our study, early recurrence (within 10 months) was significantly associated with relapsing high-risk non-muscle invasive bladder cancer (p=0.042), which may contribute further to muscle invasive bladder cancer and poor oncological outcomes. Previous studies showed that IVR did not have an impact on recurrent free survival (RFS) and cancer-specific survival (CSS).[9,10] Kim et al[9] demonstrated that patients with muscle invasive bladder cancer (MIBC) had significantly worse CSS than those without MIBC. Therefore, further study should emphasize risk analysis of patients with bladder recurrence with MIBC and high-risk non-MIBC (NMIBC).

Table 3 Results of the Univariate and Multivariate Analyses of the Clinicopathologic Factors of Late Recurrence Group (Without Prophylactic Intravesical Chemotherapy)

	Late Group=27	Other=137	Univariate Analysis, *p*	Multivariate Analysis	
				HR (95% CI)	*p*
Patient-specific factor					
Age, yr (%)			0.697		
<60	6	26			
>60	21	111			
Gender, n (%)			0.072		
Male	14	46			
Female	13	91			
ESRD, n (%)			0.011		0.101
No	20	125			
Yes	7	12		2.604 (0.829–8.184)	
Hydronephrosis, n (%)			0.28		
Absent	8	55			
Present	19	80			
Neutrophil to lymphocyte ratio, n (%)			0.278		
<3.8	22	126			
≥3.8	4	11			
Platelet to lymphocyte ratio, n (%)			0.272		
<133	21	95			
>133	6	42			
Tumour-specific factor					
Location, n (%)			0.249		
Kidney	20	79			
Ureter	6	44			
Kidney and ureter	1	14			
T stage, n (%)					
<T2					
≥T2					
Histology type, n (%)			0.354		
Infiltrating	15	89			
Papillary	12	48			
Grading, n (%)			0.953		
Low	7	36			
High	20	101			
Tumour focality, n (%)			0.815		
Single	23	119			
Multiple	4	18			
Lymphovascular invasion, n (%)			0.504		
Absent	25	131			
Present	2	6			

(*Continued*)

Table 3 (Continued).

	Late Group=27	Other=137	Univariate Analysis, *p*	Multivariate Analysis	
				HR (95% CI)	*p*
Contaminate with CIS, n (%)			0.16		
Absent	24	131			
Present	3	6			
Renal vein invasion, n (%)			0.198		
Absent	26	136			
Present	1	1			
Main tumour			0.23		
<6.7 mm	27	130			
≥6.7 mm	0	7			
Treatment-specific factor					
Preop ureter manipulation, n (%)			0.423		
Absent	9	57			
Present	18	80			
Surgical approach, n (%)			0.771		
Open method	11	62			
Laparoscopic method	13	65			
Robotic assisted method	3	10			
Complication, n (%)			0.656		
Absent	27	136			
Present	0	1			
Surgical margin, n (%)			0.001		0.999
Free	25	137			
Positive	2	0			

The NLR, an indicator of the presence of systemic inflammation, has been identified as a biomarker for predicting the poor prognosis and recurrence in cancer patients.[11,12] A previous study showed that high NLR significantly increased the risk for CSS, RFS, and overall survival (OS);[13] these results were consistent with our results.

In our study, the male to female ratio of UTUC was 1:1.75, showing a female-predominant result but did not show significant difference during analysis. Similarly, the Taiwan Cancer Registry Annual Report in 2016 also revealed that the crude incidence rate was higher in females. However, this ratio was different from the ratio of 2:1 in other Western countries. Huang et al had a culturally based explanation for this observation: in Taiwan, most postpartum females receive special nourishment and herbal medicine supplements daily for at least 1 month after each pregnancy. Therefore, our females have a higher risk of exposure to a potent carcinogen in some herbal medicine, aristolochic acid, which is well-known to cause UTUC.[15]

Patients who underwent diagnostic URS were at a higher risk of IVR after RNU when they had undergone URS before RNU but did not have a negative impact on CSS, OS, RFS, or MFS.[14] In our study, preoperative ureter manipulation was an independent factor for bladder recurrence. Unlike previous studies, we included patients who underwent ureter stenting, and the result showed that it was independent for bladder recurrence but not related to OS. This implies the need for prophylactic intravesical chemotherapy after nephroureterectomy as diagnostic URS has an important role in the diagnosis and treatment of UTUC.

The prognostic role of operation method has been debated in the literature. Pooled data showed significantly increased risk of IVR in patients treated with laparoscopic RNU.[4] In our study, most of the patients underwent laparoscopic RNU (48.8%), and the surgical approach was not associated with bladder recurrence or OS in our study.

The present study has several limitations. First, this is a retrospective study representing single-centre data. Second, patients who received non-surgical treatment were excluded from the analysis. Finally, lack of information on local recurrence and distant metastasis may reduce the strength of the findings. Therefore, further studies are necessary.

Conclusions

Bladder recurrence (25.8% in 3 years) was common in UTUC after RNU, and early bladder recurrence (within 10 months) was associated with more relapsing high-risk NMIBC. Preoperative ureter manipulation was identified as an independent factor associated with early recurrence. These patients may need more intensive monitoring to undergo prophylactic intravesical chemotherapy after nephroureterectomy.

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Disclosure

The authors report no conflicts of interest in this work.

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