

Development of ureteroscopy-independent scoring systems for predicting muscle invasive upper tract urothelial carcinoma: A multicenter study

Hiroshi Yamane

yamanehiroshi@tottori-u.ac.jp

Tottori University Faculty of Medicine: Tottori Daigaku Igakubu <https://orcid.org/0000-0003-2857-8181>

Shuichi Morizane

Tottori University Hospital: Tottori Daigaku Igakubu Fuzoku Byoin <https://orcid.org/0000-0003-0344-5892>

Sumiyo Toji

Sanin Rosai Hospital: Sanin Rosai Byoin

Katsuya Hikita

Tottori University Faculty of Medicine: Tottori Daigaku Igakubu

Kuniyasu Muraoka

Tottori Prefectural Central Hospital: Tottori Kenritsu Chuo Byoin

Hirofumi Ohno

Japanese Red Cross Society: Nihon Sekijujisha

Tadahiro Isoyama

National Hospital

Koji Ono

Tottori Red Cross Hospital: Tottori Sekijuji Byoin

Takehiro Sejima

City Hospital: Hospital Municipal

Atsushi Takenaka

Tottori University Faculty of Medicine: Tottori Daigaku Igakubu

Research Article

Keywords: Muscle-invasive cancer, radical nephroureterectomy, upper tract urothelial carcinoma, ureteral cancer, renal pelvis cancer

Posted Date: August 12th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10545886/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.
[Read Full License](#)

Abstract

Background

Accurate preoperative staging of upper tract urothelial carcinoma (UTUC) remains challenging. This study aimed to develop site-specific scoring systems for predicting muscle-invasive UTUC without ureteroscopic findings.

Methods

This retrospective multicenter study initially included 386 patients who underwent radical nephroureterectomy for UTUC at Tottori University Hospital and affiliated hospitals between January 2015 and December 2021. Patients with clinically node-positive disease or those who received neoadjuvant chemotherapy were excluded. Preoperative variables included age, sex, body mass index, hydronephrosis, urinary cytology, clinical T stage, tumor size, and multifocality. Univariable and multivariable logistic regression analyses were performed separately for ureteral and renal pelvic tumors to identify the predictors of muscle-invasive disease.

Results

Among 356 eligible patients, 157 (44.1%) had muscle-invasive UTUC. Multivariable analysis identified positive urinary cytology and clinical T stage as independent predictors of muscle-invasive disease in both ureteral and renal pelvic tumors, whereas hydronephrosis was an additional independent predictor in ureteral tumors. Scoring systems incorporating these variables achieved areas under the curve of 0.865 for ureteral cancer and 0.745 for renal pelvic cancer. Optimal cutoff scores based on the Youden index were ≥ 3 for ureteral tumors and ≥ 2 for renal pelvic tumors, with sensitivity rates of 85.4% and 68.0% and specificity rates of 77.4% and 73.6%, respectively.

Conclusion

Site-specific scoring systems based on routinely available preoperative variables accurately predicted muscle-invasive UTUC without requiring ureteroscopic findings. These models may facilitate preoperative risk stratification, although external validation is required.

Introduction

Upper tract urothelial carcinoma (UTUC) is a relatively rare malignancy, accounting for approximately 5%–10% of all urothelial carcinomas, with an annual incidence of 2 per 100,000 population in Western countries [1]. Approximately 60% of patients with UTUC have muscle-invasive disease at diagnosis, compared with 15%–25% of patients with bladder cancer [2]. Muscle-invasive and locally advanced

UTUC are associated with poor oncological outcomes [3, 4]. Radical nephroureterectomy (RNU) with bladder cuff excision is the standard treatment for localized UTUC. However, accumulating evidence suggests that patients with muscle-invasive or locally advanced disease may benefit from neoadjuvant or adjuvant chemotherapy and regional lymph node dissection [5–8]. Therefore, accurate preoperative identification of muscle-invasive UTUC is essential for treatment planning before RNU. Despite its clinical importance, accurate preoperative staging of UTUC remains challenging [9]. A previous study reported a concordance rate of only 51.4% between clinical and pathological staging, with pathological upstaging observed in 24.6% of patients [10]. Several nomograms have been developed to predict muscle-invasive or non-organ-confined disease in UTUC and have demonstrated potential clinical utility [11–13]. However, most incorporate ureteroscopic findings, including tumor morphology and biopsy-derived tumor grade. Although ureteroscopy is an important diagnostic tool, it is not routinely performed before RNU. Current European Association of Urology guidelines strongly recommend diagnostic ureteroscopy only when imaging and urinary cytology are insufficient for diagnosis or risk stratification. Therefore, predictive models incorporating ureteroscopic findings have limited applicability in patients who do not undergo the procedure. A predictive model based exclusively on routinely available preoperative variables therefore has broader clinical applicability for identifying muscle-invasive UTUC.

Furthermore, to the best of our knowledge, only a few studies have developed site-specific prediction models that separately evaluate ureteral and renal pelvic tumors. This study identified preoperative predictors of muscle-invasive UTUC and developed separate scoring systems for ureteral and renal pelvic tumors using routinely available preoperative variables without incorporating ureteroscopic findings.

Methods

Study design and patients

This retrospective multicenter study included 386 consecutive patients who underwent RNU for UTUC at Tottori University Hospital and affiliated hospitals between January 2015 and December 2021. Patients with clinically node-positive (cN+) disease or those who received neoadjuvant chemotherapy (NAC) were excluded. Of the 386 eligible patients, 22 had cN+ disease and 12 received NAC, with 4 patients meeting both exclusion criteria. After exclusion of 30 patients, 356 were included in the final analysis.

The study cohort partially overlapped with that of a previous study evaluating pathological upstaging [10]. The previous study excluded patients with cT4 disease and examined discordance between clinical and pathological staging, whereas the present study included patients with cT4 disease and focused on predicting pathological muscle-invasive disease and developing site-specific scoring systems.

Study variables

Preoperative variables included age at surgery, sex, body mass index (BMI), Eastern Cooperative Oncology Group performance status (ECOG-PS), smoking status, history of bladder cancer, clinical T (cT) stage, tumor laterality, tumor location (ureteral or renal pelvic), tumor size, multifocality, and hydronephrosis. Tumor size and multifocality were assessed based on computed tomography imaging. Tumors involving multiple anatomical sites were classified according to the predominant lesion identified on imaging. Urine cytology results were obtained from either voided urine or selective upper urinary tract specimens, with the higher-grade result used for analysis when both were available.

Cytological findings were classified according to the Papanicolaou classification, and a category of 4 or higher was considered positive. Pathological evaluation of the resected specimen was performed by an experienced pathologist. cT stage was assigned by urologists based on computed tomography urography findings. Suspected invasion of the muscular layer was classified as cT2. Meanwhile, suspected periureteral fat invasion in ureteral tumors or renal parenchymal/parapelvic fat invasion in renal pelvic tumors was classified as cT3.

Statistical analysis

Patient characteristics were compared between muscle-invasive and non-muscle-invasive disease using the Mann-Whitney U test for continuous variables and the χ -square test for categorical variables.

Univariate and multivariable logistic regression analyses were performed separately for ureteral and renal pelvic tumors to identify predictors of muscle-invasive disease. Predictive scoring systems were developed based on the multivariable logistic regression models. Integer-based scores were derived by dividing each regression coefficient by the smallest non-zero coefficient in the corresponding model and rounding the resulting values to the nearest integer. Model discrimination was assessed using receiver operating characteristic (ROC) curve analysis and the areas under the curve (AUCs). Internal validation was performed using 200 bootstrap resamples to obtain optimism-corrected performance estimates. The optimal cutoff score was determined using the Youden index. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy were calculated for each cutoff value. Statistical analyses were performed using IBM SPSS Statistics for Windows version 29.0 (IBM Corp., Armonk, NY, USA) and R version 4.6.1 (R Foundation for Statistical Computing, Vienna, Austria) within RStudio (Posit Software, Boston, MA, USA). All statistical tests were two-sided, and statistical significance was defined as a p value of < 0.05 .

Results

Patient characteristics

A total of 356 patients were included in the analysis (Table 1). The median age was 75 years, and 243 patients (68.3%) were men. Pathological muscle-invasive disease ($\geq$ pT2) was identified in 157 patients (44.1%). Clinically, 293 patients (82.3%) had cT stage ≤ 2 disease, whereas 63 (17.7%) had stage ≥ 3

disease. Tumors were located in the renal pelvis in 181 patients (50.8%) and in the ureter in 175 (49.2%). Multifocal tumors were present in 103 patients (28.9%), whereas 253 (71.1%) had solitary tumors. The median tumor size was 21.0 mm, hydronephrosis was present in 184 patients (51.7%), and urinary cytology was positive in 193 patients (54.2%). Diagnostic ureteroscopy was performed in 214 patients (60.1%).

Table 1
Patient characteristics

Variables	Overall
	n = 356
Age (year)	75 (69–82)
Sex	243 (68.3)
Male	113 (31.7)
Female	
BMI (kg/m2)	22.7 (20.9–25.1)
Smoking history	176 (49.4)
Absent	180 (50.6)
Present	
ECOG-PS	235 (66.0)
0	98 (27.5)
1	23 (6.5)
≥2	
Clinical T stage	30 (8.4)
cTa	11 (3.1)
cTis	106 (29.8)
cT1	146 (41.0)
cT2	60 (16.9)
cT3	3 (0.8)
cT4	
Tumor location	181 (50.8)
Renal pelvis	175 (49.2)
Ureter	
Multifocality	253 (71.1)
Single	103 (28.9)
Data are expressed as n (%) or median (interquartile range).	
BMI, Body mass index; ECOG-PS, Eastern Cooperative Oncology Group performance status	

Variables	Overall
	n = 356
Multiple	
Tumor side	165 (46.3)
Right	191 (53.7)
Left	
Hydronephrosis	172 (48.3)
Absent	184 (51.7)
Present	
Maximum tumor diameter (mm)	21.0 (12.2–33.0)
Urine cytology	163 (45.8)
Negative	193 (54.2)
Positive	
Diagnostic ureteroscopy	142 (39.9)
No	214 (60.1)
Yes	
Pathological T stage	9 (2.5)
pT0	106 (29.8)
pTa	28 (7.9)
pTis	56 (15.7)
pT1	44 (12.4)
pT2	105 (29.5)
pT3	8 (2.2)
pT4	
Pathological N stage	147 (41.3)
pNx	188 (52.8)
pN0	13 (3.7)
pN1	8 (2.2)
Data are expressed as n (%) or median (interquartile range).	
BMI, Body mass index; ECOG-PS, Eastern Cooperative Oncology Group performance status	

Variables	Overall
	n = 356
pN2	
Data are expressed as n (%) or median (interquartile range).	
BMI, Body mass index; ECOG-PS, Eastern Cooperative Oncology Group performance status	

Univariable and multivariable analyses of factors associated with muscle-invasive disease

Comparison of clinicopathological characteristics between patients with muscle-invasive and non-muscle-invasive disease showed that hydronephrosis ($p < 0.001$), maximum tumor diameter ($p = 0.018$), positive urine cytology ($p < 0.001$), and cT stage ($p < 0.001$) were significantly associated with muscle-invasive disease (Table 2).

Table 2

Comparison of patient characteristics between muscle-invasive and non-muscle-invasive upper tract urothelial carcinoma

Variables	Non-muscle invasive n = 199	Muscle invasive n = 157	p-value
Age (year)	75 (69–81)	75 (70-82.5)	0.337
Sex	143 (71.9)	100 (63.7)	0.109
Male	56 (28.1)	57 (36.3)	
Female			
BMI (kg/m2)	22.7 (20.8–25.1)	22.6 (21.1–25.0)	0.809
Smoking history	104 (52.3)	76 (48.4)	0.522
Absent	95 (47.7)	81 (51.6)	
Present			
ECOG-PS	131 (65.8)	104 (66.2)	1.000
0	68 (34.2)	53 (33.8)	
≥1			
Clinical T stage	26 (13.1)	4 (2.5)	< 0.001
cTa	10 (5.0)	1 (0.6)	
cTis	85 (42.7)	21 (13.4)	
cT1	65 (32.7)	81 (51.6)	
cT2	13 (6.5)	47 (29.9)	
cT3	0 (0)	3 (1.9)	
cT4			
Tumor location	106 (53.3)	75 (47.8)	0.337
Renal pelvis	93 (46.7)	82 (52.2)	
Ureter			
Multifocality	148 (74.4)	105 (66.9)	0.128
Single	51 (25.6)	52 (33.1)	
Multiple			
Data are expressed as n (%) or median (interquartile range).			
BMI, Body mass index; ECOG-PS, Eastern Cooperative Oncology Group performance status			

Variables	Non-muscle invasive n = 199	Muscle invasive n = 157	p-value
Tumor side	90 (45.2)	75 (47.8)	0.669
Right	109 (54.8)	82 (52.2)	
Left			
Hydronephrosis	118 (59.3)	54 (34.4)	< 0.001
Absent	81 (40.7)	103 (65.6)	
Present			
Maximum tumor diameter (mm)	20.0 (10.0–32.0)	23.0 (15.0–33.2)	0.018
Urine cytology	110 (55.3)	53 (33.8)	< 0.001
Negative	89 (44.7)	104 (66.2)	
Positive			
Data are expressed as n (%) or median (interquartile range).			
BMI, Body mass index; ECOG-PS, Eastern Cooperative Oncology Group performance status			

In the subgroup analysis of ureteral tumors, multivariable logistic regression analysis identified positive urine cytology (odds ratio (OR), 2.735; 95% confidence interval (CI), 1.237–6.048; $p = 0.013$), hydronephrosis (OR, 3.294; 95% CI, 1.324–8.197; $p = 0.010$), and cT stage as independent predictors of muscle-invasive disease. Compared with cT ≤ 1 disease, cT2 (OR, 9.413; 95% CI, 3.950–22.436; $p < 0.001$) and cT ≥ 3 (OR, 71.974; 95% CI, 8.090–640.299; $p < 0.001$) were associated with significantly higher odds of muscle-invasive disease (Table 3a). In renal pelvic tumors, multivariable logistic regression analysis identified positive urine cytology (OR, 2.390; 95% CI, 1.178–4.850; $p = 0.016$) and cT stage as independent predictors of muscle-invasive disease. Compared with $\leq$ cT1, cT2 (OR, 3.213; 95% CI, 1.402–7.366; $p = 0.006$) and cT ≥ 3 (OR, 13.084; 95% CI, 4.787–35.763; $p < 0.001$) were associated with significantly higher odds of muscle-invasive disease (Table 3b).

Table 3
a. Univariate and multivariate analysis of muscle-invasive ureteral tumors

Variables	Univariate		Multivariate	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age (year)	1.016 (0.980–1.052)	0.396		
Sex Female vs Male	2.173 (1.134–4.167)	0.019		
Maximum tumor diameter, ≥ 20 mm	1.244 (0.670–2.202)	0.523		
Urine cytology, Positive vs Negative	3.506 (1.880–6.541)	< 0.001	2.735 (1.237–6.048)	0.013
Hydronephrosis, Present vs Absent	6.465 (2.974–14.057)	< 0.001	3.294 (1.324–8.197)	0.010
cT stage	-	< 0.001	-	< 0.001
$\leq$ cT1	11.367 (5.095–25.360)	< 0.001	9.413 (3.950–22.436)	< 0.001
cT2		< 0.001		< 0.001
$\geq$ cT3	105.400 (12.594–882.068)		71.974 (8.090–640.299)	
OR, odds ratio				

Table 3
b. Univariate and multivariate analysis of muscle-invasive renal pelvis tumors

Variables	Univariate		Multivariate	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age (year)	1.012 (0.980–1.044)	0.475		
Sex Female vs Male	0.997 (0.529–1.878)	0.991		
Maximum tumor diameter, $\geq 20\text{mm}$	2.152 (1.104–4.193)	0.024	0.823 (0.363–1.868)	0.641
Urine cytology, Positive vs Negative	1.786 (0.967–3.297)	0.064	2.390 (1.178–4.850)	0.016
Hydronephrosis, Present vs Absent	1.629 (0.877–3.026)	0.122		
cT stage	-	< 0.001	-	< 0.001
$\leq \text{cT1}$	2.739 (1.294–5.800)	< 0.001	3.213 (1.402–7.366)	0.006
cT2		< 0.001		< 0.001
$\geq \text{cT3}$	10.141 (4.286–23.994)		13.084 (4.787–35.763)	

Development of a scoring system for predicting muscle-invasive cancer

Based on the multivariable logistic regression models, separate risk scoring systems were developed for ureteral and renal pelvic tumors. For ureteral tumors, 1 point each was assigned for positive urinary cytology and hydronephrosis, whereas cT stage was scored as 0, 2, and 4 points for $\text{cT} \leq 1$, cT2, and $\text{cT} \geq 3$, respectively. For renal pelvic tumors, 1 point was assigned for positive urinary cytology, whereas cT stage was scored as 0, 1, and 3 points for $\text{cT} \leq 1$, cT2, and $\text{cT} \geq 3$, respectively (Table 4). The observed probabilities of pathological muscle-invasive disease increased with higher total scores. In ureteral tumors, the probabilities were 5.3%, 14.6%, 20.8%, 60.6%, 82.5%, 100%, and 91.7% for scores of 0, 1, 2, 3, 4, 5, and 6, respectively. In renal pelvic tumors, the corresponding probabilities were 17.9%, 25.7%, 52.9%, 60.0%, and 84.0% for scores of 0, 1, 2, 3, and 4, respectively (Table 5). ROC curve analysis demonstrated

apparent AUCs of 0.865 for ureteral tumors and 0.745 for renal pelvic tumors. Following internal validation using 200 bootstrap resamples, the optimism-corrected AUCs were 0.863 and 0.747, respectively (Fig. 1a **and b**). The diagnostic performance of each scoring system was evaluated using multiple cutoff scores. For ureteral tumors, a cutoff score of ≥ 3 yielded the best overall performance, with a sensitivity of 85.4%, a specificity of 77.4%, a PPV of 76.9%, an NPV of 85.7%, and an accuracy of 81.1%. For renal pelvic tumors, the optimal cutoff score was ≥ 2 , yielding a sensitivity of 68.0%, a specificity of 73.6%, a PPV of 64.6%, an NPV of 76.5%, and an accuracy of 71.3%. The Youden index was also calculated for each cutoff score. For ureteral tumors, the Youden index values were 18.2, 48.5, 62.8, 52.4, 18.6, and 12.3 for cutoff scores of ≥ 1 , ≥ 2 , ≥ 3 , ≥ 4 , ≥ 5 , and 6, respectively. For renal pelvic tumors, the corresponding values were 15.0, 41.6, 32.7, and 24.2 for cutoff scores of ≥ 1 , ≥ 2 , ≥ 3 , and 4, respectively (Table 6).

Table 4
Risk scoring system for predicting muscle-invasive upper tract urothelial carcinoma

		Urereral tumor	Renal pelvis tumor
Urine cytology	Negative	0	0
	Positive	1	1
Hydronephrosis	Absent	0	-
	Present	1	-
cT stage	$\leq$ cT1	0	0
	cT2	2	1
	$\geq$ cT3	4	3

Table 5
Relationship between the total score and the
prevalence of muscle-invasive upper tract urothelial
carcinoma

Ureteral tumor	
Total score	Patients with $\geq$ pT2 disease, % (n/N)
0	5.3 (1/19)
1	14.6 (6/41)
2	20.8 (5/24)
3	60.6 (20/33)
4	82.5 (33/40)
5	100 (6/6)
6	91.7 (11/12)
Renal pelvis tumor	
Total score	Patients with $\geq$ pT2 disease, % (n/N)
0	17.9 (5/28)
1	25.7 (19/74)
2	52.9 (18/34)
3	60.0 (12/20)
4	84.0 (21/25)

Table 6

Cut-off values and diagnostic performance of risk scoring systems for predicting muscle-invasive upper tract urothelial carcinoma

Ureteral tumor		Sensitivity, %	Specificity, %	PPV, %	NPV, %	Accuracy, %	Youden index, %
Total score	≥ 1	98.8	19.4	51.9	94.7	56.6	18.2
	≥ 2	91.5	57.0	65.2	88.3	73.1	48.5
	≥ 3	85.4	77.4	76.9	85.7	81.1	62.8
	≥ 4	61.0	91.4	86.2	72.6	77.1	52.4
	≥ 5	20.7	97.9	94.4	58.6	62.3	18.6
	6	13.4	98.9	91.7	56.4	58.9	12.3

Renal pelvis tumor		Sensitivity, %	Specificity, %	PPV, %	NPV, %	Accuracy, %	Youden index, %
Total score	≥ 1	93.3	21.7	45.8	82.1	51.4	15.0
	≥ 2	68.0	73.6	64.6	76.5	71.3	41.6
	≥ 3	44.0	88.7	73.3	69.1	70.2	32.7
	4	28.0	96.2	84.0	65.4	68.0	24.2
NPV, negative predictive value; PPV, positive predictive value							

Discussion

This study identified positive urinary cytology, cT stage, and hydronephrosis as independent predictors of muscle-invasive UTUC in ureteral tumors, whereas positive urinary cytology and cT stage independently predicted muscle-invasive disease in renal pelvis tumors. Site-specific scoring systems incorporating these variables demonstrated excellent discrimination for ureteral tumors and moderate discrimination for renal pelvic tumors.

Previous studies have identified positive urinary cytology, hydronephrosis, and ureteroscopic findings as predictors of pathological stage in UTUC and have developed nomograms for predicting muscle-invasive or locally advanced UTUC. Brien et al. reported that high-grade ureteroscopic biopsy findings, hydronephrosis, and positive urinary cytology were independently associated with muscle-invasive

UTUC, with a positive predictive value of 89% when all three factors were present [14]. Favaretto et al. found that radiographic evidence of local invasion and high-grade ureteroscopic biopsy were independent predictors of muscle-invasive or non-organ-confined UTUC, with an estimated probability of 82% when both factors were present [15]. Yoshida et al. developed a nomogram for predicting locally advanced UTUC without incorporating ureteroscopic findings [16]. The model included the neutrophil-to-lymphocyte ratio, chronic kidney disease, hydronephrosis, radiographic evidence of tumor invasion, and tumor location, and achieved an AUC of 0.77.

Site-specific scoring systems were developed using hydronephrosis, positive urinary cytology, and cT stage for ureteral tumors, and positive urinary cytology and cT stage for renal pelvic tumors. Increasing total scores were associated with a higher probability of pathological muscle-invasive disease. In ureteral tumors, the probability of $\geq$ pT2 disease increased from 20.8% at a score of 2 to 60.6% at a score of 3. In renal pelvic tumors, the corresponding probability increased from 25.7% at a score of 1 to 52.9% at a score of 2. The optimal cutoff values, determined using the Youden index, were ≥ 3 for ureteral tumors and ≥ 2 for renal pelvic tumors, yielding accuracy rates of 81.1% and 71.3%, respectively. Although scoring system for ureteral tumors demonstrated performance comparable to that of previously reported nomograms, discrimination for renal pelvic tumors was more modest. This finding may reflect the limited predictive performance of models that do not incorporate ureteroscopic findings.

Diagnostic ureteroscopy enables direct visualization of the upper urinary tract, enabling assessment of tumor morphology, location, and size, as well as histological confirmation and grading through targeted biopsy. Tumor grade determined by ureteroscopic biopsy, together with clinical and radiological findings, plays an important role in risk stratification and treatment selection between kidney-sparing treatment and RNU [17]. However, the diagnostic accuracy of ureteroscopic biopsy for tumor staging and grading remains limited. Mori et al. reported a concordance rate of only 34.5% between ureteroscopic biopsy-based clinical staging and pathological staging following RNU. Moreover, 41.7% of patients clinically diagnosed with $\leq$ cT1 disease were upstaged to muscle-invasive disease on final pathological examination [9]. A meta-analysis reported concordance rates between ureteroscopic biopsy and final surgical pathology of 97% for high-grade tumors but only 66% for low-grade tumors [18]. In addition, several studies have suggested that diagnostic ureteroscopy may increase the risk of subsequent intravesical recurrence [19, 20]. Although diagnostic ureteroscopy remains a valuable tool for the evaluation of UTUC, its limitations may restrict its routine use in all patients. Therefore, a risk prediction model based on routinely available preoperative variables without ureteroscopic findings may therefore provide a practical approach to preoperative risk stratification.

The present study performed site-specific analyses by evaluating ureteral and renal pelvic tumors separately and developed distinct scoring systems for each tumor location. Although both are classified as UTUC, ureteral and renal pelvic tumors differ in their anatomical, pathological, and molecular characteristics [21, 22]. Nevertheless, comparable oncological outcomes have been reported, and current clinical practice generally manages them as a single disease entity [23]. Consequently, few studies have evaluated predictors of muscle-invasive disease separately according to tumor location.

Hydronephrosis may reflect not only the depth of tumor invasion but also the tumor location. These findings support the value of site-specific analyses and the development of separate scoring systems for ureteral and renal pelvic tumors.

This study has some limitations. First, its retrospective design and inclusion of only patients who underwent RNU may have introduced selection bias. Second, the multicenter design may have resulted in interinstitutional variability in the assessment of cT stage and urinary cytology. Third, as the scoring systems were derived from the present cohort, external validation in an independent cohort is required to confirm their generalizability and predictive performance.

In conclusion, separate scoring systems were developed to predict muscle-invasive disease in ureteral and renal pelvic tumors using routinely available preoperative variables without ureteroscopy findings. The scoring systems demonstrated good discrimination for ureteral tumors and moderate discrimination for renal pelvic tumors. These models may facilitate preoperative risk stratification; however, external validation is required before they can be used to inform decisions regarding NAC or lymph node dissection.

Declarations

Ethics approval

This study was approved by the Ethics Committee of Tottori University, Japan (approval number: 23A124). The need for informed consent was waived owing to the retrospective nature of the study.

Competing interests

The authors have no relevant financial or non-financial interests to disclose.

Funding

No funding was received for conducting this study

Consent to participate

The ethics committee waived the requirement for informed consent owing to the retrospective study design.

Consent to publish

Not applicable

Data availability statement

The datasets utilized and/or analyzed in this study can be obtained from the corresponding author upon reasonable request.

Acknowledgment

The authors would like to thank all patients and clinical staff who contributed to this study.

References

1. Rouprêt M, Babjuk M, Compérat E et al (2018) European Association of Urology guidelines on upper urinary tract urothelial carcinoma: 2017 update. *Eur Urol* 73(1):111–122.
<https://doi.org/10.1016/j.eururo.2017.07.036>
2. Margulis V, Shariat SF, Matin SF et al (2009) Outcomes of radical nephroureterectomy: a series from the Upper Tract Urothelial Carcinoma Collaboration. *Cancer* 115(6):1224–1233.
<https://doi.org/10.1002/cncr.24135>
3. van Doeveren T, van der Mark M, van Leeuwen PJ, Boormans JL, Aben KKH (2021) Rising incidence rates and unaltered survival rates for primary upper urinary tract urothelial carcinoma: a Dutch population-based study from 1993 to 2017. *BJU Int* 128(3):343–351.
<https://doi.org/10.1111/bju.15389>
4. Chen TS, Chen YT, Wang HJ et al (2022) The prognostic impact of tumor location in pT3N0M0 upper urinary tract urothelial carcinoma: a retrospective cohort study. *Front Oncol* 12:850874.
<https://doi.org/10.3389/fonc.2022.850874>
5. Birtle A, Johnson M, Chester J et al (2020) Adjuvant chemotherapy in upper tract urothelial carcinoma (the POUT trial): a phase 3, open-label, randomised controlled trial. *Lancet* 395(10232):1268–1277. [https://doi.org/10.1016/S0140-6736\(20\)30415-3](https://doi.org/10.1016/S0140-6736(20)30415-3)
6. Meng X, Chao B, Vijay V et al (2019) High response rates to neoadjuvant chemotherapy in high-grade upper tract urothelial carcinoma. *Urology* 129:146–152.
<https://doi.org/10.1016/j.urology.2019.01.058>
7. Dominguez-Escrig JL, Peyronnet B, Seisen T et al (2019) Potential benefit of lymph node dissection during radical nephroureterectomy for upper tract urothelial carcinoma: a systematic review by the European Association of Urology Guidelines Panel on Non-muscle-invasive Bladder Cancer. *Eur Urol Focus* 5(2):224–241. <https://doi.org/10.1016/j.euf.2017.09.015>
8. Yumioka T, Morizane S, Muraoka K et al (2024) The benefits of adjuvant chemotherapy for upper tract urothelial carcinoma require at least three cycles. *Yonago Acta Med* 67(3):183–190.
<https://doi.org/10.33160/yam.2024.08.001>
9. Mori K, Katayama S, Laukhtina E et al (2022) Discordance between clinical and pathological staging and grading in upper tract urothelial carcinoma. *Clin Genitourin Cancer* 20(1).
<https://doi.org/10.1016/j.clgc.2021.10.002>. 95.e1–95.e6
10. Yamane H, Morizane S, Takenaka A et al (2025) Risk scoring system for evaluating pathological upstaging after radical nephroureterectomy for upper tract urothelial carcinoma: a multicenter study in Japan. *Int J Urol* 32(5):502–507. <https://doi.org/10.1111/iju.15681>

11. Venkat S, Khan AI, Lewicki PJ, Borregales L, Scherr DS (2022) Novel nomograms to predict muscle invasion and lymph node metastasis in upper tract urothelial carcinoma. *Urol Oncol* 40(3):108e11–108e17. <https://doi.org/10.1016/j.urolonc.2021.11.027>
12. Petros FG, Qiao W, Singla N et al (2019) Preoperative multiplex nomogram for prediction of high-risk nonorgan-confined upper-tract urothelial carcinoma. *Urol Oncol* 37(4):292e1–292e9. <https://doi.org/10.1016/j.urolonc.2018.12.002>
13. Margulis V, Youssef RF, Karakiewicz PI et al (2010) Preoperative multivariable prognostic model for prediction of nonorgan-confined urothelial carcinoma of the upper urinary tract. *J Urol* 184(2):453–458. <https://doi.org/10.1016/j.juro.2010.03.142>
14. Brien JC, Shariat SF, Herman MP et al (2010) Preoperative hydronephrosis, ureteroscopic biopsy grade and urinary cytology can improve prediction of advanced upper tract urothelial carcinoma. *J Urol* 184(1):69–73. <https://doi.org/10.1016/j.juro.2010.03.030>
15. Favaretto RL, Shariat SF, Savage C et al (2012) Combining imaging and ureteroscopy variables in a preoperative multivariable model for prediction of muscle-invasive and non-organ-confined disease in patients with upper tract urothelial carcinoma. *BJU Int* 109(1):77–82. <https://doi.org/10.1111/j.1464-410X.2011.10288.x>
16. Yoshida T, Kobayashi T, Kawaura T et al (2020) Development and external validation of a preoperative nomogram for predicting pathological locally advanced disease of clinically localized upper urinary tract carcinoma. *Cancer Med* 9(11):3733–3741. <https://doi.org/10.1002/cam4.2988>
17. Clements T, Messer JC, Terrell JD et al (2012) High-grade ureteroscopic biopsy is associated with advanced pathology of upper-tract urothelial carcinoma tumors at definitive surgical resection. *J Endourol* 26(4):398–402. <https://doi.org/10.1089/end.2011.0426>
18. Subiela JD, Territo A, Mercadé A et al (2020) Diagnostic accuracy of ureteroscopic biopsy in predicting stage and grade at final pathology in upper tract urothelial carcinoma: systematic review and meta-analysis. *Eur J Surg Oncol* 46(11):1989–1997. <https://doi.org/10.1016/j.ejso.2020.06.024>
19. Sharma V, Miest TS, Juvet TS et al (2021) The impact of upper tract urothelial carcinoma diagnostic modality on intravesical recurrence after radical nephroureterectomy: a single-institution series and updated meta-analysis. *J Urol* 206(3):558–567. <https://doi.org/10.1097/JU.0000000000001834>
20. Marchioni M, Primiceri G, Cindolo L et al (2017) 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* 120(3):313–319. <https://doi.org/10.1111/bju.13935>
21. Fang D, He S, Xiong G et al (2018) Comparison of clinicopathologic characteristics, epigenetic biomarkers and prognosis between renal pelvic and ureteral tumors in upper tract urothelial carcinoma. *BMC Urol* 18(1):22. <https://doi.org/10.1186/s12894-018-0334-7>
22. Qiwei C, Jiajun S, Cheng L et al (2023) Comparison between renal pelvic and ureteral tumors in muscle-invasive upper tract urothelial carcinoma. *Cancer Sci* 114(3):984–994. <https://doi.org/10.1111/cas.15634>

23. Raman JD, Ng CK, Scherr DS et al (2010) Impact of tumor location on prognosis for patients with upper tract urothelial carcinoma managed by radical nephroureterectomy. *Eur Urol* 57(6):1072–1079. <https://doi.org/10.1016/j.eururo.2009.07.002>

Figures

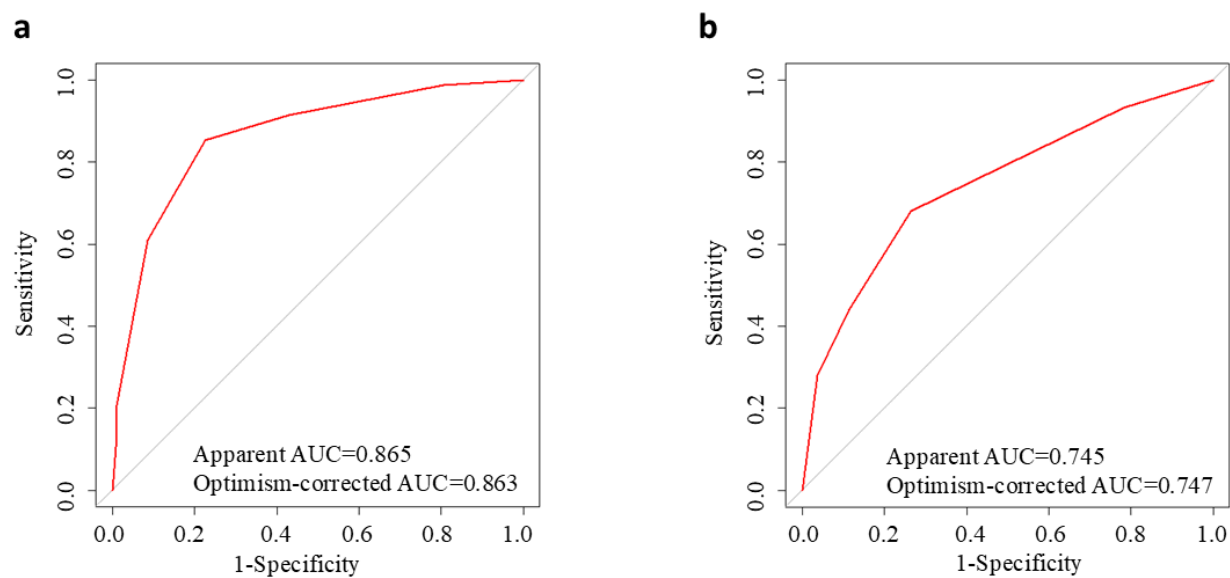


Figure 1
ROC curve of risk scoring system (a) ureteral cancer, (b) renal pelvis cancer

AUC, area under the curve; ROC, receiver operating characteristic