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FULL PAPER

Prediction of high-grade ureteral urothelial carcinoma on CT urography

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Objective: To evaluate the correlation between CT urography (CTU) findings and histological grade of ureteral urothelial carcinoma (UUC), and to identify predictors of high-grade UUC.

Methods: CTU images of 73 patients with pathologically proven UUC via nephroureterectomy were independently reviewed by two radiologists for tumour size, tumour location, hydronephrosis grade, periureteral infiltration, presence of enlarged retroperitoneal lymph nodes and tumour enhancement value. Interobserver agreement was assessed with kappa statistics. Histological grade was classified as either low or high according to the WHO 2004 classification system and pathologic T stage was assessed according to the TNM staging system. Binary logistic regression, Spearman correlation analysis and receiver operating characteristic curves were used to evaluate relationships between CTU findings and histological grade.

Results: 58 patients had high-grade UUCs and 15 had low-grade UUCs. Among CTU features, only hydronephrosis grade was significantly correlated with high tumour grade for both readers ($p < 0.001$). Multivariate logistic regression revealed that hydronephrosis of Grade 3 or higher was a significantly independent predictor of high-grade UUC for both readers ($p \leq 0.004$). Interobserver agreement was excellent for hydronephrosis grade ($\kappa = 0.862$). With the cut-off value of hydronephrosis Grade 3, the sensitivity, specificity and area under the curve for predicting high-grade UUC were, respectively, 88%, 79% and 0.830 for reader 1 and 86%, 80% and 0.763 for reader 2.

Conclusion: Hydronephrosis of Grade 3 or higher on CTU may be predictive of high-grade UUC.

Advances in knowledge: Radical surgery should be considered for UUC causing hydronephrosis of Grade 3 or higher on CTU, even in small tumours without periureteral infiltration.

INTRODUCTION

Upper tract urothelial carcinoma (UTUC) is less common than bladder urothelial carcinoma and accounts for 5–10% of all urothelial carcinoma.¹ The incidence of ureteral urothelial carcinoma (UUC) is approximately half that of pyelocaliceal urothelial carcinoma.² UUC has a worse prognosis than pyelocaliceal urothelial carcinoma.^{3,4} Owing to different anatomical considerations and oncological outcomes in UTUC, these different malignant entities must be evaluated independently.⁵

The gold standard treatment for UTUC is radical nephroureterectomy with excision of the bladder cuff, regardless of the tumour location.⁶ Recently, conservative surgery such as endoscopic ablation or segmental ureteral resection, which allows preservation of the upper urinary renal unit, has also

been applied.⁷ However, preoperative histological evaluation through biopsy of the upper urinary tract is difficult, because ureteroscopy is an invasive procedure and usually requires general anaesthesia. Furthermore, the accuracy of ureteroscopic biopsy in predicting tumour stage and grade is limited, and the limitations of endoscopic biopsy must be balanced against the possible advantage of avoiding radical surgery.⁸ Thus, accurate preoperative prediction of tumour grade could be helpful in selecting more appropriate therapeutic options.

CT urography (CTU) is an imaging modality with high diagnostic accuracy in the detection of UTUC and has replaced intravenous excretory urography and ultrasonography as the first-line imaging test for investigating high-risk patients.⁹ Even though several studies have investigated

diffusion-weighted MRI (DW-MRI) as an imaging assessment for predicting tumour grade of UTUC,¹⁰⁻¹³ characteristic CTU findings that can predict tumour grade of UUC have not been identified, to the best of our knowledge.

In this study, we aimed to evaluate the correlation between CTU imaging variables, including tumour size and imaging features, and histological grade of UUC, and to identify CTU imaging features that allow prediction of high-grade UUC, which should be treated by radical surgery.

METHODS AND MATERIALS

Patients

This retrospective single-centre study was approved by the institutional review board and written informed consent was not required. We searched institutional patient information systems to identify all consecutive patients with UUC who had undergone nephroureterectomy between January 2005 and July 2016. A total of 79 consecutive patients who underwent surgery with removal of a surgical specimen for histological analysis were registered. The inclusion criteria for this study were as follows: (i) tumours only located in the ureter, (ii) patients had undergone CTU scan prior to surgery and (iii) histological confirmation of UUC with clear statement of histological grade according to the WHO 2004 classification system. Four patients were excluded because histological grade was not available in the pathological reports, and two patients did not undergo a CTU scan. Ultimately, 73 patients (52 males and 21 females; mean age, 68.92 ± 9.08 years) with 81 UUCs were included in our study. All pathological data were reviewed by a board-certificated pathologist, and all tumours were classified into low-grade and high-grade groups according to the WHO 2004 classification system and pathologic T stage of the tumours was assessed according to the TNM staging system.

CTU technique

All CTU examinations were performed using various CT scanners from 16-channel to 128-channel MDCT scanners (Somatom Sensation 16, Siemens Healthcare, Brilliance 64, Philips Medical Systems, Best, Netherlands or Somatom Definition Flash 128, Siemens Healthcare Forchheim, Germany). Scanning parameters of the most frequently used CT scanner (Brilliance 64, Philips Medical Systems, Best, Netherlands) were as follows: tube voltage, 120 kVp; effective tube current, 300 mAs; section thickness, 5 mm; pitch and speed, 0.891:1; rotation time, 0.75 s and collimation, 64×0.625 mm for 64-channel MDCT. Before acquisition of contrast-enhanced scans, simple unenhanced scans were obtained, after which 2 ml kg^{-1} non-ionic contrast material containing 300–350 mg ml⁻¹ of iodine

[iopromol (Iomeron 300, Bracco Altana Pharma, Konstanz, Germany), iopamidol (Pamiray 300, Dongkook Pharmaceutical, Seoul, Republic of Korea) or iobitridol (Xenetix 300, Guerbet, Villepinte, France)] was intravenously administered at a rate of 3.0 ml s^{-1} using a standard power injector. For CTU, in addition to the unenhanced scan, two-phase studies were performed with combinations of corticomedullary and excretory phases at our institution. The corticomedullary phase began 30–40 s after contrast administration, and excretory phases began 300 s after contrast administration, respectively.

Image analysis

Two radiologists (DJS and STH with 17 and 3 years of experience, respectively, in interpreting genitourinary images) independently reviewed all CTU images on a picture archiving and communication system workstation (INFINITT PACS, INFINITT Healthcare, Seoul, Republic of Korea). The readers knew all patients had been diagnosed with UUC, but were informed of neither the histological grade nor the findings listed in the initial radiological report. They evaluated the following CTU imaging features: tumour location, tumour size, tumour enhancement value, multiplicity, periureteral infiltration, enlarged retroperitoneal lymph nodes with a short axis of more than 1 cm, and hydronephrosis grade. Tumour location was categorized into three groups (proximal, middle, and distal) according to anatomic ureteral segmentation. Tumour size was determined as the maximal length or diameter of the whole tumour presenting as ureteral soft-tissue mass or enhancing wall thickening on the axial, sagittal, or coronal CTU images. In patients with multiple lesions, the largest one was selected for size measurement. Tumour enhancement value was calculated as the difference between attenuation values in the corticomedullary phase and unenhanced phase. On corticomedullary phase images, the readers drew a circular ROI that included the enhancing solid portion of the tumour, avoiding adjacent mesenteric fat. The ROI was as large as possible to minimize noise. A ROI of the same size was placed in the corresponding location on the unenhanced scan image.

The readers also reported hydronephrosis grade according to the modified version of the Society for Foetal Urology Hydronephrosis Grading System (Table 1).

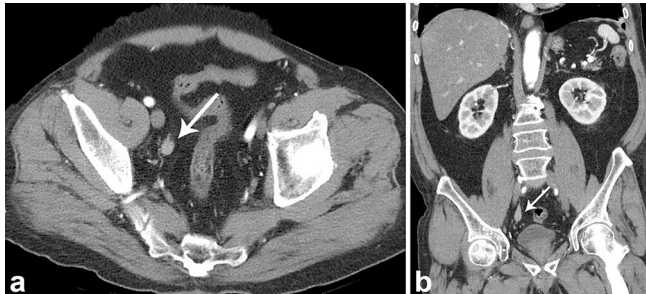
Statistical analysis

Descriptive statistics of means, standard deviations and frequencies were used to describe patient characteristics. Univariate logistic regression modelling, Mann–Whitney *U* tests, and X^2 tests were used to assess the correlation between CTU imaging variables and histological tumour grade. Multiple logistic regression

Table 1. Modified version of the Society for Fetal Urology Hydronephrosis Grading System

Grade	0	1	2	3	4
Ureter and pelvocalyceal system	No dilatation	Local dilatation of the ureter	Ureteral and renal pelvis dilatation	Ureteral and renal pelvis dilatation plus calices dilatation	Further dilatation of ureter, pelvis and calices
Renal parenchymal thickness	Normal	Normal	Normal	Normal	Thin

Figure 1. A 74-year-old male with a low-grade tumour in the right distal ureter. Axial (a) and coronal (b) contrast-enhanced CT images demonstrate a soft tissue tumour (arrow) in the right distal ureter without hydronephrosis in the right kidney. The tumour was 16 mm in length and was pathologically proven to be low-grade urothelial carcinoma after radical nephroureterectomy.



analysis using a backward selection method was performed to identify significantly independent CTU imaging variables that could predict high-grade tumours. Spearman correlation analysis was used to assess the correlation between tumour size and hydronephrosis grade. X^2 test and linear-by-linear association were used to investigate the correlation of hydronephrosis grade and peritumoural infiltration with pathologic T stage. A receiver operating characteristic (ROC) curve was constructed to identify the cut-off value of effective factors that provided the best diagnostic accuracy. Interobserver agreement was calculated using kappa statistics for nominal values, including hydronephrosis grade, peritumoural infiltration, multiplicity and presence of enlarged retroperitoneal lymph nodes. Intraclass correlation was calculated for continuous values including tumour size and contrast enhancement value. The scores were used to define agreement as follows: 0.41–0.60 denoted moderate agreement; 0.61–0.80, good agreement and greater than 0.81, excellent agreement.

Statistical analysis was done using IBM SPSS Statistics version 22.0 for Windows (IBM Corp., Armonk, NY). A p value of less than 0.05 was considered statistically significant.

RESULTS

Images of the 73 patients with 81 UUCs were reviewed. The lesions were unilateral in all cases. 15 patients (20.5%) had low-grade UUCs (Figure 1) and 58 patients (79.5%) had high-grade UUCs (Figure 2). 22 (27.1%) lesions were located in the proximal ureter, 14 (17.2%) in the middle ureter, and 45 (55.5%) in the distal ureter. Eight (5.8%) patients had multiple lesions in the ipsilateral ureter. Clinicopathological characteristics of the patients are summarized in Table 2.

CTU imaging variables (tumour size, multiplicity, peritumoural infiltration, hydronephrosis grade, contrast enhancement value, presence of enlarged retroperitoneal lymph nodes) with respect to histological grade of UUCs are summarized in Table 3. The readers had excellent agreement for the other CT variables ($\kappa = 0.862$ for hydronephrosis grade, intraclass correlation = 0.829 for tumour size, intraclass correlation = 0.892 for contrast

Figure 2. A 80-year-old male with high-grade tumour in the right middle ureter. Axial (a) and coronal (b) contrast-enhanced CT images demonstrate a soft tissue tumour (arrow) in the right middle ureter. Coronal CT images (b and c) show the dilated right upper ureter (arrow head) and Grade 4 hydronephrosis (arrow head) in the right kidney, respectively. The tumour was 7 mm in length and was pathologically proven to be high-grade urothelial carcinoma after radical nephroureterectomy.



enhancement value). In addition, there were good or moderate interobserver agreements for the other subjective assessments ($\kappa = 0.748$ for multiplicity, $\kappa = 0.546$ for periureteral infiltration). Tumour size was significantly larger in the high-grade group than in the low-grade group according to reader 1 ($p = 0.028$). Hydronephrosis grade was significantly higher in the high-grade group than in the low-grade group ($p < 0.001$ for both readers). There was no significant difference in multiplicity, peritumoural infiltration, contrast enhancement value, or presence of enlarged retroperitoneal lymph nodes between the two groups.

Univariate logistic regression analysis revealed that hydronephrosis of Grade 3 or higher was significantly associated with high-grade tumour for both readers, and tumour size was significantly associated with high-grade tumour for reader 1. Multivariate logistic regression analysis using a backward selection method demonstrated that only hydronephrosis of Grade 3 or higher was a significant independent predictor of high-grade tumour for both readers (Table 4). Other CTU imaging variables, including tumour size, were omitted as independent variables in multivariate logistic regression analysis. In addition, there was no significant correlation between tumour size

Table 2. Clinicopathological characteristics of enrolled patients

Characteristic	Data
Age (years) ^a	68 ± 9 (43–86)
Sex ^b	
Male	52 (71.2)
Female	21 (28.8)
Histologic grade of UTUC ^b	
High grade	58 (79.5)
Low grade	15 (20.5)

^aData are presented as mean (range) values.

^bData are presented as number (percentage) of patients.

Table 3. Clinical characteristics of the enrolled patients according to histological grade

	Grade			<i>p</i> value
	High grade (<i>n</i> = 58) ^a	Low grade (<i>n</i> = 15) ^a	Total (<i>n</i> = 73)	
Reader 1				
Tumour size (mm)	39.7 (10–140)	23.3 (1–41)		0.028 ^b
Hydronephrosis grade				<0.001 ^c
4	22 (37.9)	1 (6.7)	23	
3	27 (46.6)	2 (13.3)	29	
2	6 (10.3)	5 (33.3)	11	
1	2 (3.4)	2 (13.3)	4	
0	1 (1.7)	5 (33.3)	6	
Enhancement value	56.4 (2–120)	51.2 (6–92)		0.508
Peritumoural infiltration				0.07 ^c
Present	17 (29.3)	1 (6.7)	18	
Absent	41 (70.7)	14 (93.3)	55	
Multiplicity				0.55 ^c
Present	7 (12.1)	1 (6.7)	8	
Absent	51 (87.9)	14 (93.3)	65	
Enlarged retroperitoneal lymph nodes				0.611 ^c
Present	11 (19.0)	2 (13.3)	13	
Absent	47 (81.0)	13 (86.7)	57	
Reader 2				
Tumour size(mm)	43.10 (11–140) 34.50	30.14 (15–58) 27.50		0.234 ^b
Hydronephrosis grade				<0.001 ^c
4	22 (37.9)	1 (6.7)	23	
3	27 (46.6)	4 (26.7)	31	
2	4 (7.0)	2 (13.3)	6	
1	4 (7.0)	2 (13.3)	6	
0	1 (1.7)	6 (40.0)	7	
Enhancement value	55.5 (2–121)	58.9 (19–101)		0.793
Peritumoural infiltration				0.127 ^c
Present	8 (13.8)	0 (0.0)	8	
Absent	50 (86.2)	15 (100.0)	65	
Multiplicity				0.239 ^c
Present	5 (8.6)	0 (0.0)	5	
Absent	53 (91.4)	15 (100.0)	68	
Enlarged retroperitoneal lymph nodes				0.611 ^c
Present	11 (19.0)	2 (13.3)	13	
Absent	47 (81.0)	13 (86.7)	57	
Pathologic T stage				
T _a	4 (6.9)	6 (40.0)	10	<0.001 ^c
T ₁	14 (24.1)	8 (53.3)	22	

(Continued)

Table 3. (Continued)

	Grade			<i>p</i> value
	High grade (<i>n</i> = 58) ^a	Low grade (<i>n</i> = 15) ^a	Total (<i>n</i> = 73)	
T2	11 (19.0)	0 (0.0)	11	
T3	29 (50.0)	1 (6.7)	30	

^aData are presented as number (percentage) of patients.

^bMann-Whitney *U* test.

^cPearson's χ^2 test.

and hydronephrosis grade according to Spearman correlation analysis.

Pathologic T stage did not significantly correlate with peritumoral infiltration and hydronephrosis grade, respectively (Table 5).

ROC curve analysis showed that the best cut-off point of hydronephrosis grade was 2.5 for the prediction of high-grade tumour. The area under the curve (AUC) using the final model was 0.856 for reader 1 and 0.813 for reader 2 (Figure 3). For clinical application in practice, the optimal cut-off grade of hydronephrosis was set at Grade 3, which corresponded to a prediction of high-grade

Table 4. Results of the multivariate logistic regression analysis with backward selection of independent variables predictive of high-grade tumours

	Univariate logistic		Multivariate logistic with variable selection	
	OR ^a	<i>p</i> value	OR ^a	<i>p</i> value
Reader 1				
Tumour size (mm)	1.050 (1.006–1.096)	0.025		
Grade of hydronephrosis				
4	110 (5.83–2074.45)	0.002	72 (3.67–1411.89)	0.005
3	67.50 (5.09–893.63)	0.001	48 (3.48–661.60)	0.004
2	6 (0.51–69.75)	0.152	6 (0.47–75.34)	0.165
1	5 (0.27–91.51)	0.278	8 (0.31–206.37)	0.21
0	0.16	0.097		
Enhancement value	1.01 (0.98–1.03)	0.536		
Peritumoural infiltration	5.81 (0.71–47.69)	0.102		
Multiplicity	1.92 (0.22–16.95)	0.557		
Enlarged retroperitoneal lymph nodes	1.47 (0.29–7.53)	0.646		
Reader 2				
Tumour size (mm)	1.027 (0.99–1.06)	0.146		
Grade of hydronephrosis				
4	126 (6.82–2328.09)	0.001	68 (3.46–1336.27)	0.005
3	40.5 (3.81–430.28)	0.002	24 (2.11–273.59)	0.009
2	12 (0.80–180.97)	0.073	16 (0.72–354.80)	0.08
1	12 (0.780–180.97)	0.073	16 (0.72–354.80)	0.08
0		0.01		
Enhancement value	0.99 (0.97–1.02)	0.718		
Peritumoural infiltration	5.22 (0.24–113.30)	0.293		
Multiplicity	3.25 (0.12–81.44)	0.4737		
Enlarged retroperitoneal lymph nodes	1.47 (0.29–7.53)	0.646		

^aValues in parentheses are 95% confidence intervals.

Table 5. Pathologic T stage correlation with periureteral infiltration and hydronephrosis grade

Reader 1		Hydronephrosis grade (n)				Total	p value
Pathologic T stage	Peritumoral infiltration		0	1, 2	3, 4		0.194 ^a , 0.308 ^b
	Present	Absent					
Ta-T1	5 (15.6)	27 (84.4)	4 (12.5)	9 (28.1)	19 (59.4)	32 (100.0)	
T2	4 (36.3)	7 (63.7)	0 (0.0)	4 (36.4)	7 (63.7)	11 (100.0)	
T3-4	9 (30.0)	21 (70.0)	2 (6.7)	2 (6.7)	26 (86.7)	30 (100.0)	
Total	18 (24.7)	55 (75.3)	6 (8.2)	15 (20.6)	52 (71.2)	73 (100.0)	

Reader 2		Hydronephrosis grade (n)				Total	p value
Pathologic T Stage	Peritumoral infiltration		0	1, 2	3, 4		0.403 ^a , 0.173 ^b
	Present	Absent					
Ta-T1	1 (3.1)	31 (96.9)	5 (15.6)	7 (21.9)	20 (62.5)	32 (100.0)	
T2	1 (9.0)	10 (91.0)	0 (0.0)	3 (27.3)	8 (72.7)	11 (100.0)	
T3-4	6 (20.0)	24 (80.0)	2 (6.7)	2 (6.7)	26 (86.7)	30 (100.0)	
Total	8 (11.0)	65 (89.0)	7 (9.7)	12 (16.6)	54 (73.7)	73 (100.0)	

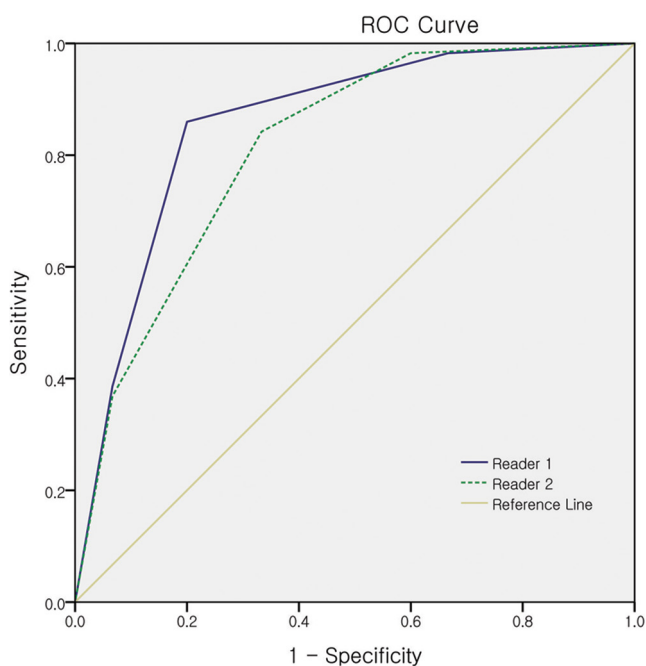
Data in parentheses are percentages.

^ap value from the χ^2 test for correlation of peritumoural infiltration with pathologic T stage.

^bp value from the χ^2 test for correlation of hydronephrosis grade with pathologic T stage.

UUC with an AUC of 0.830 and sensitivity and specificity of 88 and 79%, respectively, for reader 1, and AUC of 0.763 and sensitivity and specificity of 86 and 80%, respectively, for reader 2 (Figure 4).

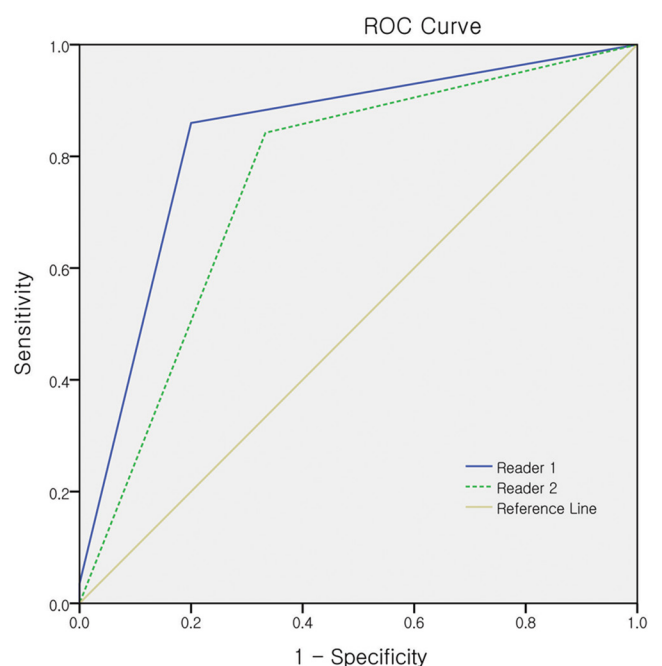
Figure 3. Receiver operating characteristic curve for predicting high tumour grade, with the best hydronephrosis grade cut-off point being 2.5. The AUC was 0.856 for reader 1, and 0.813 for reader 2, respectively. The diagonal line represents an AUC of 0.50. AUC, area under the curve.



DISCUSSION

As with most other malignancies, the most accurate independent predictors of prognostic outcome in UUC are tumour stage and grade.¹⁴ However, preoperative tumour staging is

Figure 4. Receiver operating characteristic curve for predicting high-grade tumour at a cut-off point of Grade 3 hydronephrosis. The AUC was 0.833 for reader 1, and 0.754 for reader 2, respectively. The diagonal line represents an AUC of 0.50. AUC, area under the curve.



difficult in UUC because the accuracy of imaging and endoscopic biopsy for T categorization remains unsatisfactory. It is not possible to differentiate a T1 lesion from T2 UUC on CTU, and it is also difficult to obtain representative muscularis tissue with ureteroscopic biopsy. Even though T3 lesions can be characterized by periureteral infiltration, current imaging modalities cannot reliably identify microscopic invasion. Periureteral infiltration, which represents the invasiveness of UUC on CT, can cause overstaging due to additional inflammatory changes, while understaging can occur due to microscopic invasion.¹⁵ In our study, there was no significant correlation between periureteral infiltration on CT and tumour grade. In addition, periureteral infiltration on CT did not significantly correlate with pathological T stage.

In clinical practice, tumour grade is a crucial factor in determining whether radical surgery or endoscopic conservative treatment is optimal for UUC, because accurate tumour staging is only available postoperatively based on the pathological evaluation of radical nephroureterectomy specimens. Ureteroscopic evaluation and biopsy definitively set up the diagnosis of UUC and provide fundamental information for risk stratification and clinical management. Several studies have reported that biopsy tumour grade accurately predicts surgical tumour grade in 78–91.6% of patients.^{16–18} Contrary to these reports, it has been shown that ureteroscopic biopsy performance is inadequate in predicting final pathological grade.^{19,20} Tumour grade is misinterpreted in more than one third of patients with conservatively managed UTUC,¹⁹ and 15% of high-grade tumours are underestimated as low-grade urothelial carcinoma.²⁰

DW-MRI has shown potential as a biomarker in oncological imaging practice, and apparent diffusion coefficient (ADC) values obtained from DW-MRI may help predict tumour invasiveness and metastatic potential of UTUC.²¹ Some researchers report that high-grade UTUCs have significantly lower ADC values than low-grade tumours.^{10,11} More recently, however, others have found no significant correlation between ADC value and histological grade of UTUC.^{12,13} Furthermore, different imaging sequences, parameters, and MRI scanners can cause inconsistency in ADC measurement. Thus, our study aimed to determine whether CTU imaging features reproducible in routine practice could preoperatively predict the histological grade of UUC.

There have been a number of studies demonstrating an association between hydronephrosis and advanced clinicopathological features and poor oncologic outcomes in UTUC.^{22–27} Pyelocaliceal urothelial carcinomas usually do not result in urinary tract obstruction except in tumours involving the ureteropelvic junction. In contrast, UUCs are more likely to have hydronephrosis compared to pyelocaliceal urothelial carcinomas.⁴ A few studies that focused on UUC alone also reported a predictive role of hydronephrosis in advanced pathological features.^{5,28} Cho et al found that 86% of patients with hydronephrosis of Grade 3 or 4 had an invasive tumour of T2 stage or greater.²⁸ However, their research was based on various imaging assessments using CT, excretory urography,

and renal ultrasonography. In our study, there was no significant correlation between hydronephrosis grade and pathological T stage. Luo et al reported that hydronephrosis of Grade 2 or higher was associated with non-organ-confined disease,⁵ although their imaging review was not performed either in consensus or independently, and the specificity was limited to 37.3%. Chung et al assumed that hydronephrosis may cause outward expansion and longitudinal thinning of the already narrow ureter or renal pelvis wall, which may facilitate the seeding of cancer cells to regional or distant organs.²² Even so, the mechanism of the development of hydronephrosis and its relationship with tumour invasiveness is not fully understood.⁵ To the best of our knowledge, however, our study is the first evaluation of the association between hydronephrosis grade and tumour grade in pure UUC, and adequate diagnostic performance (sensitivity and specificity over 79%) was obtained at a cut-off point of hydronephrosis Grade 3 in the prediction of high-grade tumours.

Cho et al reported that the tumour diameter of UUC correlated with pathological T stage and 80% of patients with a tumour diameter of 1.5 cm or greater had invasive UUC.²⁸ In their study, however, tumour diameter was measured on axial CT images and was classified as less than 1.5 cm, greater than or equal to 1.5 cm but less than 2.5 cm, and 2.5 cm or greater. In our study, in which the largest tumour size was measured on multireconstructed images, tumour size did not independently predict tumour grade. In addition, our study showed no significant association between tumour size and hydronephrosis grade.

At the time of diagnosis, patients with UTUC and a contralateral normal kidney can be classified as having low-risk UTUC or high-risk UTUC.²⁹ Preoperative clinical factors associated with low-risk UTUC include low-grade ureteroscopic biopsy, low-grade cytology, tumour size <1 cm, no invasive features on cross-sectional imaging, unifocal disease, and the availability of feasible close follow-up.²⁹ According to the current European guidelines on UTUC,⁷ diagnostic ureteroscopy with biopsy should be performed in the preoperative assessment of UTUC. On the other hand, the routine use of ureteroscopy is not advocated for the confirmation of UTUC.³⁰ Based on the results of our study, the need for ureteroscopy and biopsy may be obviated in patients with UUC causing hydronephrosis of Grade 3 or higher.

The current study has limitations. First, the study population was relatively small due to the rarity of UUC, and because the study was conducted retrospectively at a single institution, the possibility of selection bias should be considered. Prospective multicentre studies with larger sample size are needed to validate our results. Second, the direct imaging-pathological correlation was not obtained in tumour size assessed on CTU. Consequently, tumour size could have been overestimated if there was concomitant inflammation.

In conclusion, high-grade hydronephrosis on preoperative CTU was significantly associated with high-grade UUC. The

results of the current study may help develop algorithms for risk stratification of patients with pure UUC. Radical surgical treatment should be considered in patients with

UUC causing hydronephrosis of Grade 3 or higher regardless of tumour size and absence of peritumoural infiltration on CTU.

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