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Assessment of the Diagnostic Value of the UF-5000 Parameter Atyp.C in Upper Tract Urothelial Carcinoma

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Abstract

Background/Aim: Urine cytology is widely used for diagnosing urothelial carcinoma. However, it has limited sensitivity, particularly in upper tract urothelial carcinoma. The UF-5000 automated urine analyzer includes the research parameter Atyp.C, which quantifies cells with a high nuclear-to-cytoplasmic ratio. Although it has been utilized in bladder cancer, its application has not been evaluated in upper tract urothelial carcinoma. This study compared the diagnostic performance of urine cytology versus Atyp.C and assessed the advantage of combining them.

Patients and Methods: This retrospective study included 41 patients with pathologically confirmed upper tract urothelial carcinoma without concomitant bladder cancer, as confirmed via cystoscopy. The sensitivities of urine cytology (Class ≥III), Atyp.C (≥0.1), and their combined use were compared.

Results: Positive findings on urine cytology were detected in 11/41 patients (26.8%) and Atyp.C was observed in 9/41 (22.0%). When either test yielded a positive result, the detection rate increased to 17/41 (41.5%). A paired comparison using McNemar's test demonstrated that the combined cytology-Atyp.C approach detected significantly more upper tract urothelial carcinoma cases than urine cytology alone (6 *vs.* 0 discordant pairs, p=0.041).

Conclusion: The sensitivity of Atyp.C was similar to that of urine cytology. Some patients without hydronephrosis presented with Atyp.C positivity. However, this finding may be overlooked in routine clinical practice. Although its performance is lower than that reported in bladder cancer, Atyp.C is non-invasive and does not require additional procedures. Hence, it can be clinically useful for upper tract urothelial carcinoma diagnosis. Nevertheless, to validate this notion, prospective studies should be conducted.

Keywords: Atyp.C, diagnostic performance, UF-5000, upper tract urothelial carcinoma, urine cytology.

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Introduction

Upper tract urothelial carcinoma (UTUC) accounts for approximately 5%-10% of all urothelial carcinomas (1), and approximately 60% of cases are muscle-invasive at diagnosis (2). The diagnostic workup for suspected UTUC is primarily based on a combination of computed tomography urography (CTU), urine cytology, and ureteroscopic biopsy. CTU is the imaging standard, offering high sensitivity for papillary or mass-forming lesions (3-4). Meanwhile, urine cytology demonstrates high specificity when used as a non-invasive adjunct (5). Ureteroscopy enables the direct visualization and histological confirmation of lesions (6).

Despite these advantages, each method has certain drawbacks. CTU may overlook small or flat lesions and cannot always be performed on patients with renal dysfunction or iodine contrast allergy (4). Urine cytology has variable sensitivity based on sample quality and interpretation (5). Ureteroscopy provides definitive diagnosis. However, it requires instrumentation and is not suitable for all patients. Several studies have reported an increased risk of tumor seeding or intravesical recurrence after biopsy (7).

Among urine-based diagnostic methods, cytology and UroVysion FISH are the most commonly used tests for UTUC (8). When combined with cytology, UroVysion FISH can improve diagnostic sensitivity (9). Nevertheless, both methods have certain limitations. These include inconsistent sensitivity and the need for specialized laboratory processing (10-11). These limitations emphasize the need for a simple, objective, and readily available adjunctive test to help in UTUC detection.

The UF-5000 (Sysmex, Kobe, Japan) is an automated urine analyzer that is widely used in clinical laboratories. In addition to standard urinary parameters, the analyzer provides a research parameter referred to as "Atyp.C," which automatically quantifies cells with a high nuclear-to-cytoplasmic ratio–a cytomorphological feature associated with malignancy. This parameter is established from optical and flow-cytometric data obtained during particle analysis (12).

Recent studies indicate that the Atyp.C value shows a moderate diagnostic accuracy for bladder cancer, with area under the curve values of approximately 0.78-0.83 (13-14). However, its diagnostic performance for UTUC has not been systematically evaluated. Therefore, the current study compared the diagnostic performance of urine cytology and Atyp.C in patients with UTUC. Further, it assessed whether their combined use could improve detection across different clinical settings.

Patients and Methods

Patients and study design. This single-center retrospective observational study included patients diagnosed with UTUC between January 2022 and July 2025. The initial suspicion of UTUC arose from macroscopic or microscopic hematuria or abnormal urine cytology findings that prompted CT urography. All included UTUC cases were histologically confirmed by surgical pathology and/or biopsy (ureteroscopic or CT-guided). In total, 63 patients were initially identified. After excluding 7 patients with missing data on tumor location and 15 patients with concomitant bladder cancer or unknown bladder status at the time of urine testing, 41 patients were found to be eligible for the analysis.

Urine specimens. All index comparisons were performed using voided urine specimens. For each patient, we used urine collected before cystoscopy and confirmed the absence of any visible bladder lesions. Urine cytology and UF-5000 Atyp.C results were paired within 2 months, and the closest available pair per patient was used for the primary analysis. Atyp.C was measured from fresh, unfixed urine using the UF-5000 and processed promptly after collection according to our routine laboratory workflow.

Ethical considerations. The protocol for this research project has been approved by Ethics Committee of Kochi Medical School, and it conforms to the provisions of the Declaration of Helsinki (approval no. 2025-85). The

requirement for written informed consent was waived in accordance with the committee's approval, as this was a retrospective database study, and an opt-out approach was adopted.

Assessment and statistical analysis. Urine cytology was considered positive when classified as Papanicolaou class III or higher. Positive Atyp.C was defined as a UF-5000 measurement of ≥0.1. Sensitivity was defined as the percentage of pathologically confirmed UTUC cases with positive results. The primary endpoints were the sensitivities of urine cytology alone, Atyp.C alone, and their combination. A paired comparison of cytology and Atyp.C was performed using the McNemar's test. A two-sided *p*-value of <0.05 indicated statistically significant differences. EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria), was used to perform all statistical analyses. EZR is a modified version of R commander designed to add statistical functions frequently used in biostatistics (15). The sample size was not based on an *a priori* power calculation, as this was an exploratory retrospective study with a limited number of patients.

Results

Table I shows the characteristics of the patients. This study included 41 patients with pathologically confirmed UTUC. The median age was 72 (interquartile range=68-79) years, and 28 (68.3%) patients were men. Sixteen (39.0%) patients had never smoked, whereas 25 (61.0%) were former or current smokers. Four (9.8%) patients had a previous history of urothelial carcinoma. The renal pelvis (53.7%) was the most common tumor location, followed by the proximal- or mid-ureter (U1-U2, 29.2%) and the distal ureter (U3, 17.1%).

In total, 17 (41.5%) patients presented with hydronephrosis. In terms of pathological T classification, Ta/Tis was observed in 8 (19.5%) patients, T1 in 7 (17.1%), ≥T2 in 20 (48.8%), and Tx in 6 (14.6%).

Table I. *Patient characteristics (n=41).*

Characteristics	*n* (%)
Sex, no (%)	
Male	28 (68.3)
Female	13 (31.7)
Age, median (IQR)	72 (68-79)
Smoking, no (%)	
Never	16 (39.0)
Former	14 (34.2)
Current	11 (26.8)
History of bladder cancer/UTUC, no (%)	
Absent	37 (90.2)
Present	4 (9.8)
Tumor location, no (%)	
Pelvis	22 (53.7)
U1	6 (14.6)
U2	6 (14.6)
U3	7 (17.1)
Hydronephrosis, no (%)	
Absent	24 (58.5)
Present	17 (41.5)
T classification, no (%)	
Ta, Tis	8 (19.5)
T1	7 (17.1)
T2	4 (9.8)
T3	11 (26.8)
T4	5 (12.2)
Tx	6 (14.6)
NM classification, no (%)	
N0M0	33 (80.5)
Others	8 (19.5)
Histological subtype, no (%)	
Pure urothelial carcinoma	37 (90.2)
Variant/unknown	4 (9.8)
Urine cytology class, no (%)	
I	1 (2.4)
II	29 (70.7)
III	9 (22.0)
IV, V	2 (4.9)
Atyp.C value, no (%)	
0	32 (78.0)
>0.1	9 (22.0)
Urine RBC, no (%)	
0-4	14 (34.1)
5-19	6 (14.6)
20-49	5 (12.2)
50-99	3 (7.3)
>100	13 (31.7)
Urine WBC, no (%)	
0-4	17 (41.4)
5-19	20 (48.8)
20-49	2 (4.9)
50-99	2 (4.9)
>100	0 (0.0)

IQR, Interquartile range; RBC, red blood cells; UTUC, upper tract urothelial carcinoma; WBC, white blood cells.

According to clinical stage, 33 (80.5%) patients exhibited N0M0. Urothelial carcinoma was the primary histological diagnosis in 37 (90.2%) patients, with 4 (9.8%) presenting with variant or unclassified histology. Eleven (26.8%) patients had positive urine cytology (class ≥III), and nine (22.0%) patients exhibited Atyp.C positivity (≥0.1). Microscopic hematuria (0-4 red blood cells/HPF) was absent in 14 (34.1%) patients, and 17 (41.4%) patients had a normal white blood cell count (WBC) (0-4 WBCs/HPF).

Table II depicts the characteristics of the patients according to urine cytology and Atyp.C status. The overall positivity when either test had a positive result reached 41.5%.

The baseline characteristics, including age, sex, smoking status, previous history of urothelial carcinoma, and tumor location, did not significantly differ between the cytology-positive and cytology-negative groups (p>0.05). Similarly, no significant association was observed between Atyp.C positivity and any clinical or pathological variable (p>0.05). In terms of tumor location, the positivity rates of either test were 40.9% for renal pelvic tumors, 25.0% for proximal- to mid-ureteral (U1-U2) tumors, and 71.4% for distal ureteral (U3) tumors. In patients without hydronephrosis, the positivity rates were 33.3% for cytology, 20.8% for Atyp.C, and 45.8% for the combination of both. Meanwhile, the corresponding values in those with hydronephrosis were 17.6%, 23.5%, and 35.3%, respectively. According to T classification, the positivity rates for either test were 40.0% in Ta/Tis/T1 tumors, 40.0% in T2-T3 tumors, and 45.5% in T4/Tx tumors. No significant trends were observed across N/M classification, histological subtype, or urine red blood cell/WBC counts (p>0.05).Overall, the diagnostic performance of urine cytology and Atyp.C was comparable, and the diagnostic performance of the combined procedures yielded the highest detection rate across all subgroups.

Table III presents the results of a paired comparison using McNemar's test. The combined cytology-Atyp.C approach demonstrated significantly higher positivity than urine cytology alone (6 *vs.* 0 discordant pairs, p=0.041). This finding indicates that combining urine cytology with Atyp.C enabled the detection of UTUC cases missed by urine cytology alone.

Discussion

This study evaluated the diagnostic performance of Atyp.C, a research parameter derived from the UF-5000 automated urine particle analyzer, in patients with UTUC. Although voided urine cytology continues to be a widely used non-invasive test, its sensitivity for UTUC is limited. Atyp.C reflects the proportion of cells with a high nuclear-to-cytoplasmic ratio, and previous studies have shown that it may be a useful quantitative adjunct in bladder cancer. However, its clinical relevance in UTUC has not been investigated previously. The current study compared Atyp.C with conventional urine cytology and examined the potential benefit of combining the two tests. Recent work has also explored artificial intelligence-assisted interpretation to improve upper urinary tract cytology, aiming to enhance reproducibility and diagnostic performance beyond conventional morphology alone (16).

In this cohort, the sensitivities of Atyp.C and urine cytology were comparable (22.0% and 26.8%, respectively). Neither modality alone achieved satisfactory sensitivity. However, notably, the combined use of cytology and Atyp.C significantly improved the diagnostic yield. A paired comparison using McNemar's test demonstrated that the combination detected six additional cases missed by cytology alone, resulting in a statistically significant improvement in positivity (p=0.041). This finding indicates that Atyp.C and cytology identify partially overlapping but distinct exfoliated tumor cell populations and that their combined use improves diagnostic performance for UTUC. In line with this concept, recent UF-5000-based approaches in bladder cancer have proposed integrating multiple urine parameters, including inflammatory indices, to enhance detection performance (17).

Previous studies in bladder cancer have demonstrated that voided urine cytology achieves moderate sensitivity,

Table II. *Patient characteristics according to Urine cytology and/or Atyp.C.*

	Total, n (%)	Urine cytology class ≤ II, *n* (%)	Urine cytology ≧ class III	*p*-Value	Atyp.C = 0, *n* (%)	Atyp.C ≧0.1, *n* (%)	*p*-Value	Both negative (cytology ≦ II and Atyp.C = 0)	Either positive (cytology ≧ III or Atyp.C ≧0.1)	*p*-Value
	n=41 (100.0)	*n*=30 (73.1)	*n*=11 (26.8)		*n*=32 (78.0)	*n*=9 (22.0)		*n*=24 (58.5)	*n*=17 (41.5)	
Sex, no (%)				0.073			0.429			0.098
Male	28 (100.0)	23 (82.1)	5 (17.9)		23 (82.1)	5 (17.9)		19 (67.9)	9 (32.1)	
Female	13 (100.0)	7 (53.8)	6 (46.2)		9 (69.2)	4 (30.8)		5 (38.5)	8 (61.5)	
Age, median (IQR)	72 (68-79)	72 (68-79.75)	72 (69.5-76)	0.848	72.5 (70-78.25)	68 (67-81.0)	0.813	74.5 (70-80.25)	72 (67-78)	0.327
Smoking, no (%)				0.074			0.276			0.518
Never	16 (100.0)	9 (56.3)	7 (43.8)		11 (68.8)	5 (31.3)		8 (50.0)	8 (50.0)	
Former/Current	25 (100.0)	21 (84.0)	4 (16.0)		21 (84.0)	4 (16.0)		16 (64.0)	9 (36.0)	
History of bladder cancer/UTUC, no (%)				0.288			1.000			1.000
Absent	37 (100.0)	28 (75.7)	9 (24.3)		29 (78.4)	8 (21.6)		22 (59.5)	15 (40.5)	
Present	4 (100.0)	2 (50.0)	2 (50.0)		3 (75.0)	1 (25.0)		2 (50.0)	2 (50.0)	
Tumor location lowest site, no (%)				0.500			0.459			0.165
Pelvis	22 (100.0)	16 (72.7)	6 (27.3)		18 (81.8)	4 (18.2)		13 (59.1)	9 (40.9)	
U1 + U2	12 (100.0)	10 (83.3)	2 (16.7)		10 (83.3)	2 (16.7)		9 (75.0)	3 (25.0)	
U3	7 (100.0)	4 (57.1)	3 (42.9)		4 (57.1)	3 (42.9)		2 (28.6)	5 (71.4)	
Hydronephrosis, no (%)				0.309			1.000			0.539
Absent	24 (100.0)	16 (66.7)	8 (33.3)		19 (79.2)	5 (20.8)		13 (54.2)	11 (45.8)	
Present	17 (100.0)	14 (82.4)	3 (17.6)		13 (76.5)	4 (23.5)		11 (64.7)	6 (35.3)	
T classification				0.712			0.701			1.000
Ta, Tis, T1	15 (100.0)	12 (80.0)	3 (20.0)		11 (73.3)	4 (26.7)		9 (60.0)	6 (40.0)	
T2, T3, T4, Tx	26 (100.0)	18 (69.2)	8 (30.8)		21 (80.8)	5 (19.2)		14 (53.8)	11 (42.3)	
NM classification				1.000			1.000			1.000
N0M0	33 (100.0)	24 (72.7)	9 (27.3)		26 (78.8)	7 (21.2)		19 (57.6)	14 (42.4)	
Others	8 (100.0)	6 (75.0)	2 (25.0)		6 (75.0)	2 (25.0)		5 (62.5)	3 (37.5)	
Histological subtype				0.559			1.000			0.629
Pure urothelial carcinoma	37 (100.0)	26 (70.3)	11 (29.7)		29 (78.4)	8 (21.6)		21 (56.8)	16 (43.2)	
Variant/Unknown	4 (100.0)	4 (100.0)	0 (0.0)		3 (75.0)	1 (25.0)		3 (75.0)	1 (25.0)	
Urine RBC				1.000			0.692			0.742
0-4	14 (100.0)	10 (71.4)	4 (28.6)		12 (85.7)	2 (14.3)		9 (64.3)	5 (35.7)	
>5	27 (100.0)	20 (74.1)	7 (25.9)		20 (74.1)	7 (25.9)		15 (55.6)	12 (44.4)	
Urine WBC				0.476			0.711			1.000
0-4	17 (100.0)	11 (64.7)	6 (35.3)		14 (82.4)	3 (17.6)		10 (58.8)	7 (41.2)	
>5	24 (100.0)	19 (79.2)	5 (20.8)		18 (75.0)	6 (25.0)		14 (58.3)	10 (41.7)	

UTUC, Upper tract urothelial carcinoma; UC, urothelial carcinoma; RBC, red blood cells; WBC, white blood cells; IQR, interquartile range. Categorical variables were compared using Fisher's exact test, and continuous variables using the Mann-Whitney *U* test. A two-sided *p*-Value <0.05 was considered statistically significant.

typically ranging from 35% to 70% (18), depending on tumor grade and specimen quality. Atyp.C has also been reported as a useful adjunct marker, with published data showing its sensitivity and specificity to be approximately 59% and 82%, respectively, in bladder cancer (6). These findings indicate that, in the lower urinary tract, exfoliated tumor cells can be captured relatively efficiently during voiding.

In contrast, the diagnostic performance of voided urine cytology for UTUC is generally low. A previous study has reported sensitivities of 30%-50% (1), highlighting

Table III. *McNemar's test comparing urine cytology alone with the combined cytology–Atyp.C (n=41).*

	Either positive	Both negative	Total
Urine cytology ≥ class III	11	0	11
Urine cytology ≤ class II	6	24	30
Total	17	24	41

the inherent difficulty of detecting upper tract lesions using voided urine specimens. The current study's findings are consistent with these observations, demonstrating a cytology sensitivity of 26.8% and an Atyp.C sensitivity of 22.0% for UTUC. The lower sensitivities observed in this study may be partly attributable to exclusion of patients with visible bladder lesions on cystoscopy, which eliminated cases in which concurrent bladder tumors could have increased the likelihood of detecting exfoliated malignant cells. Collectively, these findings suggest that UTUC is intrinsically more challenging to detect than bladder cancer using urine-based tests. This discrepancy likely results from fundamental differences in urine dynamics and cell recovery between the upper and lower urinary tracts.

Several physiological mechanisms may contribute to the reduced sensitivity of urine-based testing for UTUC. Urine in the renal pelvis and ureter is generally more diluted than that in the bladder. Based on previous studies, aquaporin-mediated water reabsorption, particularly via aquaporin-2 in the bladder epithelium (19, 20), plays a role in urine concentration. Thus, the number of exfoliated tumor cells suspended in the urine may differ between the upper and lower tracts. In the bladder, exfoliated tumor cells may remain suspended for longer periods. Meanwhile, in the upper tract, cells are shed only transiently as urine passes over the lesion. Further, upper tract tumor cells may undergo partial degeneration or lysis during their passage to the bladder, thereby further reducing cytological detectability. These biological factors collectively emphasize the inherent diagnostic challenges of UTUC when relying on voided urine specimens.

The combination of cytology and Atyp.C did not achieve sufficient sensitivity to function as a standalone diagnostic tool. Nevertheless, the finding that either test was positive in >40% of cases indicates potential utility as an early alert indicator. In particular, this may be relevant in non-specialist or community settings. Compact analyzers such as the UF-1500, which has analytical performance comparable to that of the UF-5000 (21, 22), could facilitate the incorporation of Atyp.C-based screening in primary care or general outpatient clinics. Such an approach may help identify patients who require timely referral for further urological assessment. In addition, among patients without hydronephrosis–who often do not undergo upper tract evaluation–either test yielded positive results in 45.8% of cases. For urologists, this is clinically significant, as UTUC without hydronephrosis and without concomitant bladder tumors can be easily overlooked but may still be amenable to early endoscopic management, including kidney-sparing laser ablation (23-25). Notably, low-risk UTUC has been reported among candidates for kidney-sparing management, underscoring the clinical importance of timely identification even in patients without classic high-risk features (26). Thus, even modest positivity in cytology or Atyp.C could be a valuable trigger for further investigation. Notably, the incorporation of Atyp.C does not require additional testing procedures or added costs when routine urine sediment analysis is already being performed. This cost-neutral improvement in diagnostic sensitivity may support broader clinical implementation.

Study limitations. First, its single-center retrospective design might have introduced selection and information bias. The statistical power, particularly in the subgroup analyses stratified by tumor location and hydronephrosis status, was further limited by the relatively small sample size. Second, patients with visible bladder tumors were excluded based on cystoscopic findings. However, the presence of occult flat lesions–such as carcinoma *in situ*–cannot be completely ruled out. Such undetected bladder lesions could potentially influence urinary cytological or Atyp.C results. Third, differences in sample processing, urine stability, and timing of collection were unavoidable in this retrospective setting, and these factors might have

affected test results, especially considering the fragility of exfoliated upper tract tumor cells. Fourth, Atyp.C is a research-use parameter, and its analytical characteristics–such as reproducibility, optimal cutoff determination, and inter-device comparability–were not formally validated in this cohort. Finally, this study only included patients with confirmed UTUC. Therefore, specificity and predictive values could not be assessed, and the findings could not be generalized to screening populations or patients without suspected upper tract disease.

These limitations should be considered when interpreting the results. Nevertheless, prospective multicenter studies with standardized urine-handling methods should be performed to further validate the clinical utility of Atyp.C in the diagnosis of UTUC.

Conclusion

To the best of our knowledge, this study first evaluated the UF-5000 research parameter Atyp.C in UTUC. The sensitivity of Atyp.C was comparable to that of urine cytology, and their combined use had a better sensitivity. Nonetheless, their overall diagnostic performance remained limited. Importantly, Atyp.C may play a supportive role in diagnostically challenging groups, such as those with lower ureteral tumors and those with mild hematuria without hydronephrosis. Further prospective multicenter studies should be carried out to validate its clinical utility and optimal application.

Conflicts of Interest

KI received honoraria for lectures from Sysmex. However, this had no influence on the research results or interpretations.

Authors' Contributions

RS and SF were responsible for conceptualization, data curation, investigation, and manuscript preparation, including writing the original draft and revising the manuscript. AP, SY, HO, and KI contributed to manuscript review and editing. KS, SM, ST, and CK were involved in data curation and investigation. SS, EY, and KA contributed to data curation. ST, DT, TN, TS, HF, NS, and SA supervised the study. All Authors reviewed and approved the final manuscript.

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Artificial Intelligence (AI) Disclosure

During the preparation of this manuscript, a large language model (ChatGPT, OpenAI) was used solely for language editing and stylistic improvements in select paragraphs. No sections involving the generation, analysis, or interpretation of research data were produced by generative AI. All scientific content was created and verified by the authors. Furthermore, no figures or visual data were generated or modified using generative AI or machine learning-based image enhancement tools.

References

1 Soria F, Shariat SF, Lerner SP, Fritsche H, Rink M, Kassouf W, Spiess PE, Lotan Y, Ye D, Fernández MI, Kikuchi E, Chade DC, Babjuk M, Grollman AP, Thalmann GN: Epidemiology, diagnosis, preoperative evaluation and prognostic assessment of upper-tract urothelial carcinoma (UTUC). World J Urol 35(3): 379-387, 2017. DOI: 10.1007/s00345-016-1928-x

2 Herout R, Baunacke M, Flegar L, Borkowetz A, Reicherz A, Koch R, Kraywinkel K, Thomas C, Groeben C, Huber J: Upper tract urothelial carcinoma in Germany: epidemiological data and surgical treatment trends in a total population analysis from 2006 to 2019. World J Urol 41(1): 127-133, 2023. DOI: 10.1007/s00345-022-04219-5

3 Cowan NC, Turney BW, Taylor NJ, McCarthy CL, Crew JP: Multidetector computed tomography urography for diagnosing upper urinary tract urothelial tumour. BJU Int 99(6): 1363-1370, 2007. DOI: 10.1111/j.1464-410X.2007.06766.x
4 Janisch F, Shariat SF, Baltzer P, Fajkovic H, Kimura S, Iwata T, Korn P, Yang L, Glybochko PV, Rink M, Abufaraj M: Diagnostic performance of multidetector computed tomographic (MDCTU) in upper tract urothelial carcinoma (UTUC): a systematic review and meta-analysis. World J Urol 38(5): 1165-1175, 2020. DOI: 10.1007/s00345-019-02875-8
5 Messer J, Shariat SF, Brien JC, Herman MP, Ng CK, Scherr DS, Scoll B, Uzzo RG, Wille M, Eggener SE, Steinberg G, Terrell JD, Lucas SM, Lotan Y, Boorjian SA, Raman JD: Urinary cytology has a poor performance for predicting invasive or high-grade upper-tract urothelial carcinoma. BJU Int 108(5): 701-705, 2011. DOI: 10.1111/j.1464-410X.2010.09899.x
6 Subiela JD, Territo A, Mercadé A, Balañà J, Aumatell J, Calderon J, Gallioli A, González-Padilla DA, Gaya JM, Palou J, Breda A: 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, 2020. DOI: 10.1016/j.ejso.2020.06.024
7 Sharma V, Miest TS, Juvet TS, Toussi A, Packiam V, Chamie K, Matin SF, Boorjian SA, Thompson RH, Frank I, Tollefson MK, Potretzke AM: 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, 2021. DOI: 10.1097/JU.0000000000001834
8 Białek Ł, Bilski K, Dobruch J, Krajewski W, Szydełko T, Kryst P, Poletajew S: Non-invasive biomarkers in the diagnosis of upper urinary tract urothelial carcinoma-a systematic review. Cancers (Basel) 14(6): 1520, 2022. DOI: 10.3390/cancers14061520
9 Pycha S, Trenti E, Mian C, Schwienbacher C, Hanspeter E, Palermo M, Pycha A, Danuser H, D'Elia C: Diagnostic value of Xpert® BC Detection, Bladder Epicheck®, Urovysion® FISH and cytology in the detection of upper urinary tract urothelial carcinoma. World J Urol 41(5): 1323-1328, 2023. DOI: 10.1007/s00345-023-04350-x
10 Jin H, Lin T, Hao J, Qiu S, Xu H, Yu R, Sun S, Zhang P, Liu Z, Yang L, Liu L, Han P, Wei Q: A comprehensive comparison of fluorescence in situ hybridization and cytology for the detection of upper urinary tract urothelial carcinoma: A systematic review and meta-analysis. Medicine (Baltimore) 97(52): e13859, 2018. DOI: 10.1097/MD.0000000000013859
11 Aalami AH, Aalami F: Diagnostic performance of fluorescence in situ hybridization (FISH) in upper tract urothelial carcinoma (UTUC): a systematic review and meta-analysis. Int J Clin Oncol 27(10): 1605-1615, 2022. DOI: 10.1007/s10147-022-02216-7
12 Previtali G, Ravasio R, Seghezzi M, Buoro S, Alessio MG: Performance evaluation of the new fully automated urine particle analyser UF-5000 compared to the reference method of the Fuchs-Rosenthal chamber. Clin Chim Acta 472: 123-130, 2017. DOI: 10.1016/j.cca.2017.07.028
13 Zhang T, Zhu J, Li Z, Zhao Y, Li Y, Li J, He Q, Geng Y, Lu W, Zhang L, Li Z: The UF-5000 Atyp.C parameter is an independent risk factor for bladder cancer. Sci Rep 14(1): 12659, 2024. DOI: 10.1038/s41598-024-63572-0
14 Aydin O: Atypical cells parameter in Sysmex UN automated urine analyzer: feedback from the field. Diagn Pathol 16(1): 9, 2021. DOI: 10.1186/s13000-021-01068-5
15 Kanda Y: Investigation of the freely available easy-to-use software 'EZR' for medical statistics. Bone Marrow Transplant 48(3): 452-458, 2013. DOI: 10.1038/bmt.2012.244
16 Chang KY, Yang CS, Lai JY, Lin SJ, Li JR, Liu TJ, Yang WL, Lin MY, Yeh CH, Hsu SW, Chen CJ: An artificial intelligence-assisted diagnostic system improves upper urine tract cytology diagnosis. In Vivo 38(6): 3016-3021, 2024. DOI: 10.21873/invivo.13785
17 Okada K, Naito Y, Irie S, Nakamoto C, Kuboyama K, Tarumizu T, Ikeda M, Takuma Y, Makino R, Kawahara A, Kawano H: Novel UF-5000-based detection, integrating inflammatory parameters, for urothelial carcinoma of the urinary bladder. Anticancer Res 45(8): 3531-3541, 2025. DOI: 10.21873/anticanres.17714
18 van Rhijn BW, van der Poel HG, van der Kwast TH: Urine markers for bladder cancer surveillance: a systematic review. Eur Urol 47(6): 736-748, 2005. DOI: 10.1016/j.eururo.2005.03.014
19 Morizawa Y, Torimoto K, Hori S, Gotoh D, Nakai Y, Miyake M, Hirayama A, Tanaka N, Fujimoto K: Aquaporin-2 plays an important role in water transportation through the bladder wall in rats. Neurourol Urodyn 37(8): 2434-2440, 2018. DOI: 10.1002/nau.23715
20 Morizawa Y, Torimoto K, Hori S, Gotoh D, Nakai Y, Miyake M, Tanaka N, Hirayama A, Fujimoto K: Sodium plays an important role in the absorption of intravesical fluid. Low Urin Tract Symptoms 13(1): 177-182, 2021. DOI: 10.1111/luts.12319
21 Hoshi M, Nagashima K, Sakurai M, Inoue Y, Terashima M, Fujita T, Ito H: Consistency analysis of the UF-1500 and UF-5000 automated urine particle analyzers. Clin Lab 70(05/2024), 2024. DOI: 10.7754/Clin.Lab.2023.230940
22 Previtali G, Seghezzi M, Marozzi R, Fortino M, Agnolet G, Barretta M, Bizzoni C, Bolla V, Bolzoni G, Cesani A, Diambrini M, Esposito SA, Giuliani G, Picciau A, Alessio MG: Performance verification of the new UF-1500 urine particle analyser: a new opportunity for small and medium laboratories. Pract Lab Med 46: e00481, 2025. DOI: 10.1016/j.plabm.2025.e00481
23 Ditonno F, Veccia A, Bignante G, Wu Z, Wang L, Abdollah F, Stephens A, Simone G, Tuderti G, Lee R, Eun DD, Correa AF, De Cobelli O, Ferro M, Porpiglia F, Amparore D, Checcucci E, Tufano A, Contieri R, Perdonà S, Bhanvadia R, Margulis V, Brönimann S, Singla N, Porter J, Ghodoussipour S, Minervini A, Mari A, Lambertini L, Ghoreifi A, Nativ OF, Gonzalgo ML, Sidhom D, Sundaram CP, Ben-David R, Eraky A, Mehrazin R,

Yoshida T, Kinoshita H, Dehghanmanshadi A, Rais-Bahrami S, Meagher MF, Puri D, Derweesh IH, Moghaddam FS, Djaladat H, Bertolo R, Autorino R, Antonelli A: Radical nephroureterectomy vs kidney sparing surgery for upper tract urothelial carcinoma in solitary kidney patients: a multi-institutional analysis of the ROBUUST 2.0 registry. World J Urol 43(1): 534, 2025. DOI: 10.1007/s00345-025-05882-0

24 Yoshida T, Murota T, Matsuzaki T, Nakao K, Ohe C, Matsuda T, Kinoshita H: Photodynamic diagnosis-guided dual laser ablation for upper urinary tract carcinoma: preoperative preparation, surgical technique, and clinical outcomes. Eur Urol Open Sci 28: 17-25, 2021. DOI: 10.1016/j.euros.2021.03.009

25 Miyake M, Yoshida T, Nishimura N, Oda Y, Shimizu T, Nakahama T, Hori S, Morizawa Y, Gotoh D, Nakai Y, Anai S, Torimoto K, Fujii T, Tanaka N, Fujimoto K: A prospective, single-arm trial of fluorescent ureteroscopy-assisted thulium-holmium:YAG dual laser ablation for upper urinary tract cancer: Study protocol of the FLUAM trial. Contemp Clin Trials Commun 26: 100902, 2022. DOI: 10.1016/j.conctc.2022.100902

26 Matsumoto S, Waseda Y, Kobayashi M, Nakamura Y, Ishikawa Y, Fukushima H, Fukuda S, Tanaka H, Yoshida S, Fujii Y: Incidence of low-risk upper tract urothelial carcinoma in candidates for kidney-sparing surgery. Anticancer Res 45(10): 4333-4341, 2025. DOI: 10.21873/anticanres.17783