

Diagnostic Value of Urine Cytology in Pharmacologically Forced Diuresis for Diagnosis and Follow-Up of Upper Tract Urothelial Carcinoma: An Observational Cohort Study

Christopher Soliman², Marc A. Furrer^{1,2}, Niranjana Sathianathan², Nicola Giudici¹, Jennifer Blarer¹, George N. Thalmann¹, Roland Seiler¹

1. Department of Urology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland

2. Department of Urology, The University of Melbourne, Royal Melbourne Hospital, Parkville, Victoria, Australia

#C85

OBJECTIVES

- Diagnosis of **upper-tract urothelial-cancer (UTUC)** is challenging and based on mainly invasive-procedures.
- We performed **urine-cytology analysis** of a **pharmacologically forced-diuresis (UCFD)** for the evaluation of upper tract urothelial carcinoma (UTUC) as a **diagnostic-tool** and **follow-up method**.
- This study aims to evaluate the value of UCFD for **both** purposes.

METHODS

- To evaluate the **diagnostic-value** of UCFD, a first consecutive-cohort (**n=72 patients**) from 2009-2019 with confirmed primary-UTUC treated with radical cystectomy (RC) was enrolled. Patients with UTUC who underwent endoscopic treatments as well as patients with past history of RC were excluded. UCFD was performed in tumour-naive patients in case of radiological suspect of UTUC to support diagnostic workup. In 25/72 (35%) patients UCFD was preoperatively performed.
- To evaluate UCFD as a **follow-up procedure**, a second cohort (**n=1250**) of patients from 2000 to 2020 that underwent RC in a curative intent due to UC was selected. **High-grade UC-cells in UCFD were considered positive**. Imaging of the UUT was performed by CT Scan, MRI or intravenous pyelography at 6, 12, 18 and 24 months. In addition, UCFD was performed as follow-up control to detect recurrence in the UUT. It was performed at 6 months and yearly thereafter in case of tumour location close to or in the ureter, multifocal carcinoma in situ, lymph node metastasis at the time of RC or on demand in case of suspicious imaging.
- UCFD was performed by collecting urine after a **forced diuresis** induced by **oral furosemide 40mg** and an **oral fluid overload**.

Clinicopathological characteristics of the first and second cohorts

Patient data	First Cohort (n=25)	Second cohort (n=689)
Age (median, range) at surgery (years)	66 (81 - 44)	68 (30-89)
Female/male (n)	8/17	201/488
Follow-up (median, range) [months]	24.5	37.5 (0.3 – 212)
Diagnostic data		
Pelvic-calyceal/ureter location (n)	15/7	-
Multifocality (n)	3	-
Hydronephrosis (n)	14	131
Selective cytology (n)	20	-
high-grade/atypia, suspicious, low-grade/negative	7/9/4	-
URS Biopsy (n)	12	-
Synchronous UTUC (n)	-	5
Metachronous UTUC prior to RC (n)	-	36

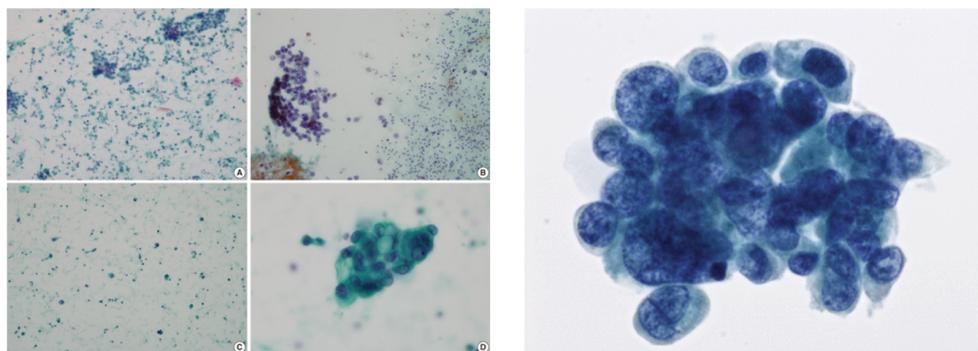
Surgical data		
≤pT2/>pT2 (n)	12/13	510/179
High-grade/Low-grade	-	625/64
Concomitant Cis (n)	8	280
pN0/pN+ (n)	20/5	528/161
Median lymph nodes removed (median, IQR)	-	33 (24-43)
Positive surgical margin (n)	1	19
Chemotherapy		
Neoadjuvant/adjuvant (n)	0/1	118/70
Recurrence		
Extra-vesical/vesical (n)	7/15	-
UTUC/local/distant (n)	-	46/92/177
Outcomes		
3yr-OS (%)	71	68
3yr-CSS (%)	82	90
5yr-OS (%)	-	56
5yr-CSS (%)	-	76

RESULTS

	UCFD positive (n=2)	UCFD negative (n=23)	p-value
Preoperative			
Hydronephrosis (n)	0 (0%)	13 (56%)	0.22
Smoking history positive (n)	2 (100%)	5 (22%)	0.07
Pelvic-calyceal/ureter location (n)	2 (100%) / 0 (0%)	13 (56%) / 7 (30%)	0.50 / 1.00
Local cytology positive (n)	2 (100%)	5 (22%)	0.07
Preoperative eGFR >75ml/min/1.73m ²	2 (100%)	6 (26%)	0.09
Variant histology	1 (sarcomatoid) (50%)	0 (0%)	0.08
Postoperative			
pN+	1 (50%)	4 (17%)	0.36
Bladder recurrence	2 (100%)	13 (56%)	0.50

First cohort, 25/72 (35%) patients had UCFD preoperatively performed. **17/25 (57%)** had **muscle-invasive** UTUC and most UTUC were **high-grade (23/25 vs. 2/25 patients)**. ~33% of patients had concomitant carcinoma-in-situ. Sensitivity of UCFD in patients with invasive, high-grade, low-grade and concomitant CIS was **8%, 9%, 0% and 14%**, respectively.

Second cohort, UCFD was performed as follow-up for **upper urinary tract (UUT)** in **689/1250 (55%)** patients. A total of **1431 UCFD** were analysed, **49/1431 (2.23.4%)** were positive. UCFD was positive in **30/689 (4.3%)** of patients. UUT recurrence was present in **21/30 (70%)** cases, urethral recurrence was present in **8/30 (26.7%)** cases and **1 of 30 patients (3.3%)** had a false-positive UCFD. Overall, **46/1250 (3.7%)** of patients had radiological proven recurrence in the UUT during follow-up. In **35/46 (76%)** patients UCFD was analysed prior to curative or palliative treatment and was positive in **21/35 (60%)** patients. In this cohort, as follow-up tool, UCFD showed a sensitivity, specificity and positive predictive value of **60%, 99% and 70%**, respectively.



Left: Voided urine cytology of HG UC. Right: HG UC (high mag).

CONCLUSION

- As a **diagnostic tool**, sensitivity is slightly **better** in patients with **invasive-UTUC** and **concomitant carcinoma-in-situ**.
- For **follow-up**, **positive UCFD** was **diagnostic** and could reveal **cancer-recurrence in the urethra** in cases with orthotopic bladder-substitute.
- Although UCFD may add some diagnostic value, the need for more reliable biomarkers for follow-up and diagnosis of UTUC remains.