Original Article

The accuracy of computed tomography in the diagnosis of upper urinary tract urothelial carcinoma in correlation with the final histopathology: A retrospective study in 275 patients at a Tertiary Urology Institute

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Abstract

Introduction: Because the reports in the literature of radiologic investigations for upper tract urothelial cancer (UTUC) are limited by the number of patients, and included patients with different pathologies, we aimed to study the overall accuracy of computed tomography (CT) in the diagnosis of UTUC and their accuracy on predicting tumor location.

Methods: A retrospective review from 1990 to 2017 included patients who were treated for UTUC. Unenhanced CT scan was obtained first using Multi-Detector Computed Tomography (MDCT, Philips Medical Systems), then nonionic contrast medium, containing 350 mg iodine /ml was injected at 4 mL/s. Analysis was performed using SPSS®.

Results: Of 275 patients, complete data on CT was available on 270 (98%) patients. CT reported only two false positive and six false negative results and the overall accuracy was 96-97%. In comparison to the final pathological reports, CT /CTU detected 85% of the tumor location of in the renal pelvic and 50% of the calyceal tumors. In ureteric tumors, they detected distal (66/71 = 93%) more than proximal ureteric tumors (60%).

Conclusion: In our cohort, CT/ CTU has a high overall accuracy (97%) in diagnosing UTUC, capability to well visualize tumors of distal ureter and renal pelvis, but could miss calyceal tumors. The matter to rely only on CT without ureteroscopic biopsy in the diagnosis of UTUC especially if radical surgery is planned needs further prospective studies.

Keywords: Carcinoma transitional cell, computed tomography, upper tract urothelial carcinoma, upper urothelial cancer

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INTRODUCTION

Multi-centricity and recurrence are key features of upper tract urothelial carcinoma (UTUC) with inherited differences from renal cell carcinoma. Hence, the role

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of diagnostic imaging in UTUC extends from the visualization of the entire execratory system at the time of the diagnosis to early detection of tumor recurrence during the follow-up. Subsequently, the necessity of having radiologic diagnostic tools for UTUC with higher accuracy certainly decreases the need for retrograde urography and ureteroscopy (URS).[1]

The reports in the literature on the accuracy of computed tomography (CT) on the diagnosis of UTUC are limited by the number of patients.[1,2] They have studied the accuracy in patients with diverse etiology, such as hematuria,[3] different renal pathology,[1] and enrolled patients with upper and lower urothelial tumors.[4] Others used retrograde urography and ureteroscopy as a referral and comparison[5] − not the histopathology, which is the gold standard. In addition, there is only one report on the accuracy of CT on predicting tumor location on small number of patients.[6]

In our comprehensive analysis, we are reporting the accuracy of contrast-enhanced CT on a large series of patients at a tertiary referral Urology institute.

MATERIALS AND METHODS

After institutional review board approval, we retrospectively reviewed our ongoing database of patients who were surgically treated for UTUC from 1990 to 2017.

The preoperative evaluation included complete medical history, physical examination, and standard routine laboratory, as well as radiological investigations such as abdominal ultrasonography and intravenous urography (IVU).

Patients were instructed not to eat or drink for 3 h before examination. The examination was obtained using four rows MDCT scanner (high-speed advantage CT scanner) and 64-multislice helical CT scanner (Brilliance, Philips Medical System, Best, the Netherlands). Unenhanced CT scan was obtained. 120 ml of nonionic contrast medium, containing 320 mg iodine/mL, was injected as a single bolus at a flow rate of 4 mL/s. The multiphasic CT study included a noncontrast scan of the upper abdomen from the level of diaphragm to the iliac crest, corticomedullary (CM) phase after 25 s from the injection of contrast for the kidney, then, 50-s after CM phase, we obtained nephrographic phase. Excretory phase scan was done 10 min from contrast injection.

In our institute, the initial CT is usually reported by a specialist (4–5 years of experience), and verified and authorized by an associated consultant (over 8 years of experience). All the CT reports of the study population were reviewed again by a single consultant level.

We had performed cystoscopy, retrograde ureteropyelography and/or diagnostic ureteroscopy in a separate session and any concurrent bladder tumors were resected. Samples for upper tract (UT) cytologic examination were obtained by ureteric catheterization and flushing with 3–5 ml of the saline solution before contrast administration for retrograde pyelography. In addition, UT tumors were biopsied whenever it is feasible. Biopsies were obtained by URS, cup biopsy was performed in all patients using 3F cold cup biopsy forceps. The specimen was fixed in formalin and sent for pathological examination. Multiple samplings were taken, and the results were drown from the most representative ones. Standard management was radical nephroureterectomy, accomplished through open approach in the majority of the patients. Laparoscopy and nephron-sparing (open ureterectomy) which were performed in appropriately selected patients.

For tumor grading, the most conventional 3-tiered World Health Organization grading system was used to determine the pathologic grade by different pathologists.[7] The tumor was staged according to the 2010 tumour-node-metastasis classification. The tumor location was divided into three groups: Pelvicalyceal, ureteral, or both (pelvicalyceal and ureteric). A few patients were operated on in view of radiologically confirmed UTUC with negative pathological findings on biopsy.

Frequency and percentage were used for nominal and categorical variables. Sensitivity and specificity were initially calculated by correlating the results of different radiological modalities with the final histopathological criteria, but because the number of true negative cases was small (only one case) that could bias the results of specificity, the overall accuracy was used more frequently than sensitivity or specificity using the standard equations (true positive + true negative/total population). The analysis was performed using commercial computer software (IBM® SPSS®) version 21.

RESULTS

Out of 275 total patients who were initially diagnosed with UTUC, the study included 239 men (87%), and the tumor was left-sided in 167 cases (56%). The mean age of the study population was 59 ± 11 years (range, 26–85 years). The median follow-up period was 32 months (range,

Table 1: Patients' and tumors' characteristics (*n*=275)

Characteristics	Value (%)*
Gender	
Male	239 (87)
Female	36 (13)
Presentation	
Hematuria	151 (55)
Flank pain	24 (9)
Hematuria and flank pain	74 (27)
Incidentally-discovered	12 (4)
Others	14 (5)
History of previous bladder tumor	46 (17)
Concomitant bladder tumor	71 (26)
Side	
Right	108 (44)
Left	167 (56)
Surgical approach	
Open	240 (87)
Laparoscopy	24 (9)
Nephron-sparing	11 (4)
Site of the tumor	
Kidney (pelvi-calyceal)	112 (41)
Ureter	112 (41)
Kidney and ureter	51 (18)
Tumor grade	
No malignancies	3 (1)
Grade I TCC	14 (5)
Grade II TCC	165 (60)
Grade III TCC	93 (34)
Tumor stage	
No malignancies	3 (1)
T1	176 (64)
T2	36 (13)
T3	59 (21)
T4	1 (1)
Final pathology	
TCC	267 (97)
Non-TCC	5 (2)
No malignancies	3 (1)
Lymph node pathology	
N (−)	264 (96)
N (+)	11 (4)
The final size in cm, median (range)	
Renal pelvis tumors	
Length	3 (2-8)
Width	4 (3-10)
Ureteric tumors	
Length	4 (1-6)
Width	2 (0.5-3)

*Decimals were removed for simplification. TCC: Transitional cell carcinoma

Table 2: The overall accuracy of computed tomography in the diagnosis of upper tract urothelial carcinoma

Enhanced CT results	Final pathology		Total number
	Cancer	Benign	
Positive (%)	261 (TP)	2 (FP)	263
Negative (%)	6 (FN)	1 (TN)	7
Total number (%)	267 (99)	3 (1)	270 (100)

Overall accuracy=TP+TN/TP+TN+FP+FN=261+1/261+1 + 6+2 = 262/270=96%.
CT: Computed tomography, TP: True positive, FP: False positive, FN: False negative, TN: True negative

18–180 months). The basic patients' and pathologic tumor characteristics are listed in Table 1.

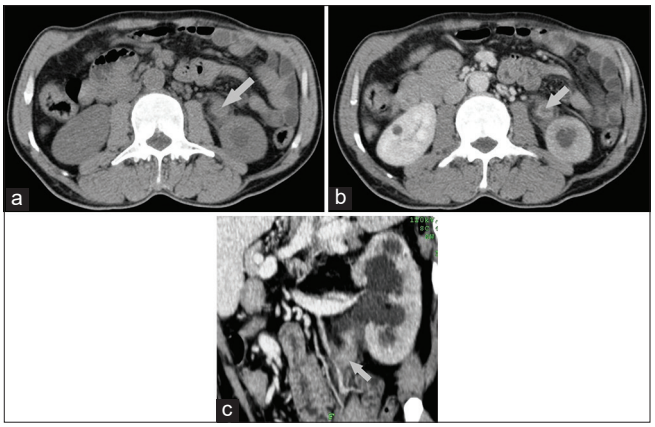

Figure 1: (a) Axial non contrast computed tomography: a well defined relatively hyperdense lesion at the left upper lumbar ureter with proximal hydronephrosis (arrow). (b) Contrast enhanced axial computed tomography scan: nephrographic phase: mild postcontrast enhancement of the intra-ureteric lesion (arrow). (c) Coronal reconstructed image of the intra-ureteric enhancing soft tissue mass (arrow). Histopathological findings revealed: Grade III papillary transitional cell carcinoma

Ultrasonography was done for the majority of patients 265 (96%), and the most common findings were different degrees of hydronephrosis 132 (48%). IVU was done in 100 patients (36%) and the most common findings were filling defects 34 cases.

For CT Urography (CTU) protocol, hematuria and incidentally-discovered masses on US were the most common indication for imaging.

Complete data on CT was available on 270 (98%) patients, the sensitivity was 97% and the overall accuracy was 96%–97%, as shown in Table 2. Cross-tabulation between CT and pathological locations for renal urothelial tumors showed that CT detected (42/49 = 85%) of the renal pelvic and (12/20 = 60%) of calyceal tumors, Table 3. In ureteric tumors, CT was more effective in detecting distal ureteric tumors (84/90 = 93%) than proximal ones (16/27 = 60%), Table 4 and Figure 1a-c.

Eight cases were radiologically diagnosed with renal parenchymal tumors which were managed by radical nephrectomy. A second surgery for ureterectomy and bladder cuff excision was performed when the pathology confirmed urothelial cancer. Two of them were squamous cell carcinoma of the renal pelvis on the final diagnosis.

Additionally, six cases couldn't be diagnosed with imaging and reported to have transitional cell carcinoma (TCC) on final histopathology reports (false negative); 2 pelvicalyceal, and 4 ureteric tumors. Three cases had cytology and URS

Table 3: Correlation between the results of computed tomography and final histopathology in pelvicalyceal tumor locations

CT findings	Free	Final pathology findings - pelvicalyceal tumors			
		Calyceal (1 or more calyx)	RP	RP+calyceal	Total *n*
Free		2	1		3
Calyceal (1 or more calyx)		12	7	1	20
RP	1	3	42	3	49
RP+calyceal	2	3	33	32	70
Total *n*	3	20	83	36	142

RP: Renal pelvis, CT: Computed tomography

Table 4: Correlation between the results of computed tomography and final histopathology in ureteral tumor locations

CT findings	Free	Proximal	Distal	Multicentric	Total *n*
Free		1	3		4
Proximal	1	16	4	6	27
Distal		1	84	5	90
Multicentric	2	1	7	13	23
Total *n*	3	19	98	24	144

CT: Computed tomography

biopsy that showed TCC, and the remaining 3 cases were operated based on significant hydronephrosis and lost renal parenchyma.

Ureteroscopic biopsy was done for 124 patients (42%) that yielded a total of 135 biopsies (94 ureteric and 41 pelvicalyceal tumors). Sixteen total negative biopsies were reported, with an overall diagnostic accuracy of 87%**.** For 94 ureteric biopsies, one was a true negative, leaving 6 of false-negative biopsies with diagnostic accuracy of 93%.

DISCUSSION

CTU is the dominant imaging modality for upper urinary tract cancer. It has the best diagnostic performance characteristics, is widely available, and essentially serves as an all-in-one test capable of covering nearly the entire range of relevant imaging tasks detection, staging, and follow-up.[8]

Our research is a comprehensive analysis, not only report the accuracy of the CT in diagnosing UTUC, but also reported their accuracy in detecting tumor location. The reference to all the radiologic data was the final histopathological diagnosis, which is the gold standard, unlike studies which compared the radiologic data to retrograde pyelography and ureteroscopy.[5]

IVU is relatively inexpensive, technically feasible, widely available and has low radiation exposure risk. In our series, it gave filling defects in only 34% with nonspecific findings in the other patients. Because of these limitations, CT has become the first choice for noninvasive imaging modality in diagnosing upper urinary tract TCC.[9]

CT, along with the introduction of multi-detector technology and CTU, have emerged as advanced tools for the evaluation of the urinary tract.[1,10,11] CTU allows a detailed anatomic depiction of the urinary tract, delineation of the peripheral calyces, collecting system and gives a better anatomic visualization for the ureter.[12] On unenhanced CT scans, TCC may occasionally show fine encrusted calcifications. During the excretory phase, early urothelial cancers are typically seen on CT as small filling defects, a mass lesion, or circumferential wall thickening in the urothelial wall. In the ureters, only circumferential thickening of the ureter may be seen. CT permits the assessment of nodal and distant metastases.[13]

A clear tumor on CTU in combination with high-grade UTUC in urine cytology identifies high-risk UTUC, and in some cases, indirect staging can be obtained. Bladder urine cytology has limited sensitivity, and in most cases, ureterorenoscopy (URS) with *in situ* samples for cytology and histopathology are mandatory for an exact diagnosis.[14]

In our review, CT/CTU was done for 270 patients. It produced only 2 false-positive and 6 false-negative results with an overall accuracy of 97%. Our results are similar to the published data (96%–99%);[1,3,9] however, our data are more solid because it accounts for a larger number of patients.

With the emergence of conservative management for UTUC, delineation of the entire urinary execratory system is essential not only in deciding for nephron-sparing surgeries. But also in the follow-up. CT reformatted images provide this advantage over IVU.[10] However, the major drawbacks of CTU are high cost, radiation risk, the need for contrast injection and its associated side effects, and the need for expertise. Furthermore, some still consider URS to be essential in the follow-up for patients with conservative management.[15]

Although MR Urography has a less established and less reliable diagnostic image quality relative to CTU in the evaluation of urinary tract, it is the appropriate choice when CT report is inconclusive or when the administration

of ionized contrast is contraindicated.[16] In magnetic resonance imaging T1W images, urothelial tumors are often isointense to the renal parenchyma and bladder muscle. In T2W images, UTUC is hyperintense to the wall of the collecting system, ureteral muscle, and urinary bladder detrusor muscle.[16]

In our cohort, CT/CTU had a high overall accuracy in diagnosing UTUC, which reaches 97%, highly specific with low false positive. A negative result on CT does not mean no UTUC, especially in susceptible patients, and more investigative tools have to be used like cytology, retrograde pyelography, and URS biopsy. CT visualizes ureteral better than pelvicalyceal tumors, distal than proximal ureteral tumors and could miss calyceal tumors.

In a prospective study, Grahn *et al*.[17] observed that multiphase CTU, including a cotticomedullay phase, offered 85% sensitivity in detecting UTUC, which dropped to 58% when a nonoptimized CT was performed. When comparing sensitivity and specificity of ureterorenoscopy (URS) and multiphase CT in UTUC, Grahn *et al*. found evidence that multiphase CTU might even provide higher sensitivity than endoscopy, although the specificity was significantly higher for URS.[17]

Our results come in agreement with Potretzke *et al*.[18] who suggested that URS can be omitted as a part of the diagnostic work up in appropriately selected patients. URS did not alter the surgical plan, particularly when radical surgeries were decided based on cross-sectional imaging.

Among six patients with false-negative results by cross-sectional imaging, four of them had ureteral tumors; Wang *et al*. found that ureteric tumor location is among the independent factors of tumor undetectability by CT.[4] The ureter is a thin tube with continuous peristalsis, the issue that may hide its full visualization by the contrast media. Furthermore, presences of CIS and/or small lesions also were found as contributing factors for missed lesions by CT.[4,11] In our study, CT detected ureteric tumor locations better than pelvicalyceal tumors and higher in distal ureteral tumors (93%) versus (60%) for proximal ones.

It may happen that CT does not distinguish between urothelial and parenchyma tumors. In eight patients in our series (2 of them with squamous cell carcinoma of the renal pelvis) were diagnosed first as parenchymal tumors, which then proved to be urothelial TCC on the final histopathology.

One of the limitations of our study was using different versions of CT of different quality. UTUC is not a common disease and to get a solid data, a considerable number of patients have to be included in a study. To achieve that, we had to the extent the study period in a retrospective design study. Despite this limitation, our study has a considerably larger number of patients at one of the leading Urology institutes that makes it a comprehensive and convenient review to both radiologists and urologists.

CONCLUSION

In our cohort, CT/CTU has a high overall accuracy (97%) in diagnosing UTUC, capability to well visualize tumors of the distal ureter and renal pelvis, but could miss calyceal tumors. The matter to rely only on CT without ureteroscopic biopsy in the diagnosis of UTUC, especially if radical surgery is planned, needs further prospective studies.

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Conflicts of interest
There are no conflicts of interest.

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