ISSN: 3066-8123
Review Article
Science Set Journal of Cancer Research

Evaluating Upper Tract Urothelial Malignancies with Computed Tomography Urography in Hematuria Patients: A Retrospective Study

Bjane, O., Elouadih, A., Ibrahim, M., Kbiro, A., Moataz, A., Dakir, M., Debbagh, A., and Aboutaieb, R

Urology department, Ibn rochd hospital, faculty of medicine and pharmacy, Hassan II university, Casablanca, Morocco.

***Corresponding author:** Bjane O, Urology department, Ibn rochd hospital, faculty of medicine and pharmacy, Hassan II university, Casablanca, Morocco.

Submitted: 24 December 2024 **Accepted:** 30 December 2024 **Published:** 06 January 2025

https://doi.org/10.63620/MKSSJCR.2024.1015

Citation: *Bjane, O., Elouadih, A., Ibrahim, M., Kbiro, A., Moataz, A., Dakir, M., Debbagh, A., & Aboutaieb, R. (2025). Evaluating Upper Tract Urothelial Malignancies with Computed Tomography Urography in Hematuria Patients: A Retrospective Study. Sci Set J of Cancer Res, 4(1), 01-06.*

Abstract

Objective: *To assess the age-stratified prevalence of upper tract urothelial malignancies identified through computed tomography urography in a large cohort of patients referred for the initial evaluation of hematuria.*

Materials and Methods: *A total of 961 consecutive adults, all without a prior history of urothelial cancer, underwent initial computed tomography urography for gross hematuria (n = 563), microscopic hematuria (n = 839), or unspecified hematuria (n = 9) at a single institution, the urology department of CHU Casablanca, between February 2020 and February 2024. Imaging findings indicative of urothelial lesions were cross-referenced with clinical data, including cystoscopy, cytology, and surgical pathology reports. Patients who were later diagnosed with urothelial cancer despite a normal initial radiographic evaluation were identified and analyzed. Factors such as age, gender, smoking history, as well as the location and type of malignancy, were examined.*

Results: *Upper tract urothelial cancer was diagnosed in 5 patients (0.48%), with a mean age of 68.4 years. All 5 patients were presented with gross hematuria and had a history of smoking, either current or former. One case involved a patient under the age of 50 who was diagnosed with upper tract urothelial cancer following computed tomography urography. Additionally, no cases of upper tract cancer were identified in patients referred for microscopic hematuria, regardless of their age.*

Conclusion: *Detection of upper tract urothelial cancer through computed tomography urography is extremely uncommon in patients with hematuria, especially in those categorized as lower risk (e.g., younger age, microscopic hematuria) at tertiary referral centers. Further research into risk-stratified imaging strategies for hematuria workup is essential to reduce unnecessary costs and radiation exposure.*

Keywords: Computed Tomography Urography, Hematuria, Upper Tract Urothelial Malignancy, Urology, Risk Stratification, Diagnostic Imaging, CHU Casablanca

Introduction

Hematuria is an exceedingly common clinical finding with a diverse spectrum of etiologies. Malignancies of the kidney and urinary tract are the entities of greatest clinical concern, but benign etiologies including prostatic enlargement, urinary tract infections, urinary calculi, intrinsic renal disease, and trauma may also present with hematuria [1]. Bladder cancer is the fourth most common malignancy in adults, responsible for 90%-95% of urothelial carcinomas (UC). Upper tract urothelial carcinoma (UTUC) is a relatively rare entity that accounts for approximately 5%- 10% of all UCs [2].

UTUC is more frequently invasive at the time of diagnosis compared with bladder cancer (60% vs 15%-25%, respectively), and 70%-80% of patients diagnosed with UTUC present with either gross hematuria (GH) or microscopic hematuria (MH) [3].

UTUC is 3 times more common in men and occurs more commonly in older patients, with a peak incidence in the seventh and eighth decades of life [3].

Multiphasic computed tomography urography (CTU), which includes non-contrast, nephrographic, and excretory phases, is regarded as the most precise imaging technique for detecting upper tract urothelial carcinoma (UTUC). It has become the gold standard for radiographic assessment of hematuria [4]. The American Urological Association (AUA) advises using CTU for the radiographic evaluation of asymptomatic microscopic hematuria (AMH), while the European Association of Urology strongly endorses CTU in their guidelines for diagnosing suspected upper tract urothelial carcinoma (UTUC). However, previous studies have demonstrated that UTUC is identified in less than 1% of patients undergoing CTU for AMH. This suggests that most patients may face potential risks from the procedure without significant benefit [5, 6].

This study aims to assess the prevalence of upper tract urothelial carcinoma (UTUC) across different age groups, as diagnosed by CTU conducted for the initial evaluation of microscopic, gross, or unspecified hematuria at a tertiary referral center.

Materials and Methods

After obtaining Institutional Review Board approval, a search for Current Procedural Terminology (CPT) codes was conducted to identify all CTU examinations performed at a single institution, the urology department of CHU Casablanca, from February 2020 to February 2024. The records of 1544 consecutive adult patients referred for CTU were retrospectively reviewed. Of these, 1036 patients were referred for screening CTU as part of the evaluation for incident gross, microscopic, or unspecified hematuria during the four-year period.

Patients with a prior history of urothelial carcinoma (UC), renal malignancy, prostate cancer, or hematuria due to trauma were excluded (n = 75). However, patients with known or suspected histories of kidney stones or benign prostatic hyperplasia were included as long as their indication for CTU was incident hematuria. Inclusion criteria were applied regardless of the timing of cystoscopy in relation to CTU or the cystoscopic findings. Ultimately, 961 patients met the criteria for the final analysis (Fig. 1).

Multiple authors reviewed the medical records of each patient to correlate imaging findings suggestive of urothelial lesions with clinical information. This included clinic notes, problem lists, cystoscopy and ureteroscopy operative reports, upper and lower tract cytology, and surgical pathology reports, such as ureteral biopsies, nephroureterectomy specimens, and ureteral specimens. The goal was to identify patients diagnosed with urothelial carcinoma (UC) following a normal CTU.

Data analyzed included age, gender, smoking history, and other patient factors, as well as the location and type of malignancy (bladder, upper tract, or kidney). All imaging studies were interpreted by radiologists specializing in abdominal imaging.

Results

A total of 961 patients (n = 491 male, n = 470 female) were included in the analysis. All participants had no history of urothelial malignancy, prostate cancer, renal malignancy, or trauma-related hematuria. They underwent CTU for the following indications: gross hematuria (n = 563), microscopic hematuria (n = 389), or unspecified hematuria (n = 9) (Table 1, Fig. 1).

Urothelial carcinoma of the upper tract (UTUC) was identified in 5 patients (0.48%), with a mean age of 68.4 years (range: 50-78). All patients were presented with gross hematuria and had a history of current or former smoking.

Four of these cases were pathologically confirmed through endoscopic biopsy, two in the renal pelvis and two in the ureter matching the abnormal findings seen on CTU. These four patients subsequently underwent nephroureterectomy, with final pathology confirming the initial CTU and biopsy results. The fifth patient, diagnosed at age 78, chose palliative care due to multiple comorbidities after consulting with urologists about the clear imaging findings. Cytology performed during cystoscopy for three of the five patients with UTUC findings on CTU returned negative results. Only one patient underwent a renal ultrasound (RUS) after the CTU, which confirmed hydronephrosis and a tumor in the renal pelvis. Notably (Table 2).

At our institution, there were no cases of upper tract urothelial carcinoma (UTUC) diagnosed in patients with negative CT urographies (CTUs). However, five patients were eventually diagnosed with non-invasive bladder urothelial carcinoma (UC) specifically, three with low-grade papillary lesions and two with high-grade papillary lesions, with no cases of carcinoma in situ. All lesions were detected during cystoscopy performed immediately after the CTU. Notably, urine cytology was negative for all five patients at the time of the cystoscopy. A retrospective review of the CTUs by an abdominal radiologist identified two true misses, while the other four lesions were classified as radio-occult.

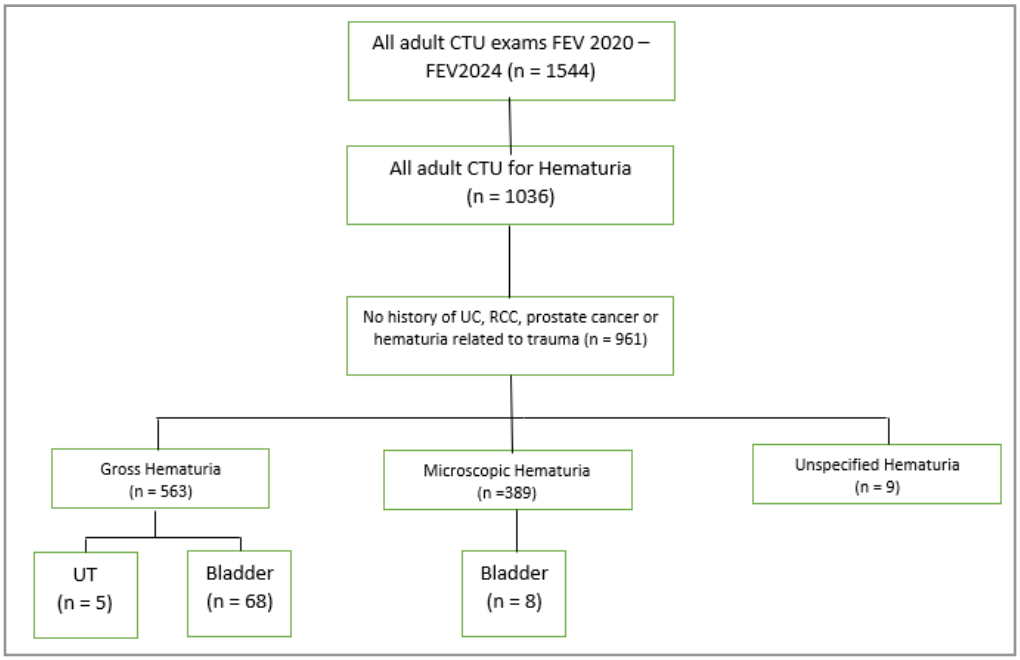

Figure 1: Inclusion Criteria and CTU-Detected Malignancies by Type of Hematuria.

CTU: Computed Tomography Urography

Table 1: Distribution of computed tomography urography studies by age and hematuria type

Age Range (y)	All Patients (%)	Male (%) / Female (%)	Gross Hematuria (%)	Microscopic Hematuria (%)	Unspecified Hematuria (%)
≤40	112 (11)	62 (53)/50 (45)	62 (54)	47 (41)	3 (3)
41-50	208 (22)	93 (46)/115 (54)	105 (51)	101 (48)	2 (1)
51-60	262 (27)	153 (58)/109 (42)	135 (52)	125 (47)	1 (1)
61-70	219 (23)	140 (63)/79 (37)	144 (64)	74 (33)	2 (1)
≥71	160 (17)	97 (61)/63 (39)	117 (72)	42 (27)	1 (1)
Mean age (y)	57.4	Male : 51.9/ female: 48.1	61.3	53.6	47.5
Total	961	491 (51) / 470 (49)	563	389	9

Table 2: malignancies detected by age, location, and hematuria type

Age Range (y)	Location	Malignancies Detected in Patients Referred for Gross Hematuria (%)	Malignancies Detected in Patients Referred for Microscopic Hematuria (%)	Total Malignancies (%)
≤40 (n = 144)	Upper tract	0	0	0
	Bladder	0	0	0
41-50 (n = 198)	Upper tract	1 (0.1)	0	1 (0.1)
	Bladder	3 (0.3)	0	3 (0.3)
51-60 (n = 248)	Upper tract	1 (0.1)	0	1 (0.1)
	Bladder	28 (2.9)	4 (0.4)	32 (3.3)
61-70 (n = 218)	Upper tract	2 (0.2)	0	2 (0.2)
	Bladder	20 (2.1)	3 (0.3)	23 (2.3)
≥71 (n = 153)	Upper tract	1 (0.1)	0	1 (0.1)
	Bladder	17 (1.7)	1	18 (1.8)
Total (n = 961)	Upper tract	5 (0.5)	0	5 (0.5)
	Bladder	68 (7)	8 (0.8)	76 (7.9)
	All	73(7.5)	8 (0.8)	81 (8.4)

Bladder cancer was identified in 76 patients (7.9%) via CTU, including 68 (7%) with a history of gross hematuria (GH) and 8 (0.8%) with a history of microscopic hematuria (MH) (Table 2). All 76 cases were confirmed through cystoscopy. Additionally, renal cell carcinoma was diagnosed in 17 patients, all of whom had GH, and was detected through a combination of the non-contrast and nephrographic phases of the CTU. Of the 81 urothelial malignancies detected (76 bladder cancers and 5 UTUCs), 71.6% (n = 58) were found in men and 28.3% (n = 23) in women. Additionally, 69 of the 81 patients (85.1%) with urothelial malignancies had a history of smoking, including 84.2% (n = 64) of those with bladder cancer and 100% (n = 5) of those with UTUC.

Among the 961 patients in our sample undergoing CTU for hematuria, 25.4% (n = 245) were diagnosed with urinary calculi, all of which were detected during the non-contrast phase of the CTU examination. The average age of patients with urinary calculi was 56.6 years, whereas the average age of patients diagnosed with urothelial malignancies was 64.8 years. Prostatic enlargement (greater than 5.0 cm on axial images) was observed in 126 patients. A total of 322 patients had previously undergone 351 related radiological studies within two years of the index CTU, all of which were negative for malignancy. Of these, 283 patients had abdominal cross-sectional imaging (279 with computed tomography and 4 with magnetic resonance imaging), and 304 patients underwent abdominal or renal ultrasound.

Out of the 279 CT scans, 114 were conducted to evaluate hematuria, including 67 cases where hematuria occurred alongside renal colic. Additionally, 45 CT scans were performed specifically for renal colic. Of the 304 ultrasound exams, 135 were carried out to assess hematuria. In 11 patients who had prior negative imaging, bladder tumors were subsequently detected on CT urography (CTU). The average time between the prior imaging and the CTU scan was 60 days, with a range from 0 to 360 days. No patients with prior imaging had upper tract lesions suggestive of malignancy identified on CTU.

Discussion

Our study demonstrates that UTUC is identified in a very small proportion of patients undergoing hematuria screening with CTU. Among a large cohort of patients referred for both microscopic hematuria (MH) and gross hematuria (GH), only one case of UTUC was found in patients under the age of 50. Additionally, no upper tract lesions were detected in patients referred for MH, regardless of age or smoking history. Furthermore, malignant renal tumors were identified in only 0,2% of patients during the combined non-contrast and nephrographic phases.

All bladder tumors detected by CTU were also visible during cystoscopy evaluation. These findings indicate that a significant number of patients without UC undergo multiphasic CTU, exposing them to potential risks such as increased radiation exposure, a higher chance of radiation-induced malignancy, possible side effects from iodinated contrast, incidental findings, and unnecessary costs [4, 7].

Two previous studies have examined the detection rates of patients undergoing CTU for hematuria, finding similarly low rates of UTUC [5. 6]. Gray Sears and colleagues prospectively evaluated 115 patients (60 men, 55 women, mean age 50.4) referred for AMH with CTU and intravenous urography (IVU). In this cohort, only 1 patient (0.9%) was diagnosed with UTUC. Consistent with our study's findings, the most common result was urinary calculi (n = 245, 25.4%), followed by benign prostatic hypertrophy in 126 patients (13.1%). Two renal tumors (1.7%) and 1 bladder tumor (0.9%) were also detected. No cause for hematuria was found in 77 of the 115 patients (67.0%). The mean age of patients diagnosed with malignancy was not provided. However, for patients with any positive CTU findings, the mean age was 53 years for men and 57 years for women [5].

Lang and colleagues conducted a multi-institutional study involving 600 patients (393 men and 207 women, with a combined mean age of 48.2) who underwent contrast-enhanced tomography urography (CTU) for the evaluation of abnormal microhematuria (AMH), after previous negative hematuria workups. These prior investigations may have included urinalysis, urine culture, urine cytology, cystoscopy, abdominal radiography, intravenous pyelogram, or renal ultrasound (RUS). Among this low-risk cohort, upper tract urothelial carcinoma (UTUC) was identified in only 3 patients (0.5%). The ages of these 3 patients with UTUC were not provided [6].

The current study differs from previous reports in several keyways. Firstly, our cohort was not limited to patients with abnormal microhematuria (AMH), nor was it restricted to those who had previously undergone a negative hematuria evaluation. As a result, this represents a higher-risk population. Second, we included age as a factor in our analysis, offering additional insights into the diagnostic utility of CTU across different populations. Third, we conducted a chart review to assess the false-negative rate in patients diagnosed with urothelial carcinoma (UC) after a negative CTU, finding a false-negative rate of 12.1%. Finally, we examined the additional investigations performed as part of the hematuria evaluation to assess whether CTU provided any supplementary diagnostic value.

Devlin and colleagues recently published a smaller series of 247 patients from a hematuria clinic who underwent CTU following renal ultrasound (RUS) and urologic evaluation. Of these patients, 234 (95%) had gross hematuria (GH), and 240 (97.2%) were considered high risk based on age, presence of GH, and smoking history. Nine cases of upper tract urothelial carcinoma (UTUC) (3.6%) were diagnosed among 17 patients with CTU findings suggestive of UTUC, resulting in a false-negative rate of 47.0%.

Similar to our study, all UTUC cases were diagnosed in patients with GH. However, unlike our study, these patients underwent RUS and formal urologic evaluation before the decision for CTU, with CTU selection based on a higher pretest probability of malignancy. Hydronephrosis was observed on RUS in 8 of the 9 UTUC cases (88.9%), whereas it was present without UTUC in 6 of the 14 patients (42.9%). The mean age of patients diagnosed with UTUC was 70.2 years (range: 56-85). Interestingly, urine cytology was positive in only 1 of the 9 cases (11.1%), in contrast to our findings, where cytology was negative in 3 of the 5 patients diagnosed with UTUC who underwent this examina-

tion. Renal tumors were identified in only 0.8% of this cohort. However, this study did not include data on the 839 patients seen at the hematuria clinic who did not undergo CTU but were later found to have urothelial carcinoma (UC) [7, 8]. It would have been valuable to compare the false-negative rate of this approach with the rate observed in our study.

Although only 5 cases of upper tract urothelial carcinoma (UTUC) were identified over the 4-year period examined, it is important to note that this figure does not represent the total number of UTUC cases diagnosed or treated at our institution during that time. Instead, it reflects the number of patients presenting with hematuria who underwent screening CT urography (CTU), which led to a new diagnosis of UTUC. The majority of UTUC patients treated at our institution were referred with a pre-existing diagnosis from external workups and were intentionally excluded from this cohort. It is possible that some patients with negative CTU and cystoscopy results later developed urothelial carcinoma (UC) that was not captured in our dataset. Additionally, we rely on the image requisitions from the referring clinicians to indicate whether a patient had hematuria. Therefore, some patients who presented with hematuria may have been excluded from our cohort if the referring clinician listed a secondary symptom, such as "flank pain," as the reason for the CTU.

The results of our study should not discourage the appropriate evaluation of clinically significant hematuria in high-risk patients. Strategies that minimize radiation exposure should be considered, particularly for lower-risk groups defined in our study (younger than 55, with only a history of microhematuria). While magnetic resonance urography is a viable alternative to CTU, offering the advantage of avoiding radiation and ionic contrast, its higher costs and longer completion time make it a less optimal screening modality for the average patient undergoing evaluation for new hematuria.

One approach, supported by the European Society of Urogenital Radiology CTU Working Group, advocates for a risk-stratified strategy. This involves reserving CTU as the first-line test for high-risk patients, while prioritizing RUS for those in low- and intermediate-risk categories [9]. The guideline emphasizes the importance of assessing the pretest probability of malignancy to determine whether CTU is necessary. The Canadian Urological Association recommends RUS as the preferred initial imaging technique, with CTU and IVU reserved for cases where clinically indicated [10].

The AUA guidelines for AMH suggest that cystoscopy may be deferred in certain patients under the age of 35 at the clinician's discretion; however, they do not explicitly recommend forgoing imaging in younger patients. While the AUA recognizes that RUS and IVU are commonly used in clinical practice and may serve as suboptimal alternatives, they emphasize that the optimal imaging strategy should be determined by the evaluating physician, taking into account the clinical context [1].

A comprehensive evaluation using CTU, cystoscopy, and cytology is strongly recommended for patients at higher risk of urologic malignancy. This includes individuals with risk factors such as gross hematuria (GH), advanced age, smoking history, environmental exposures, and familial or genetic predispositions. Notably, patients with a significant smoking history have a 3.1- to 7.2-fold increased risk of developing upper tract urothelial carcinoma (UTUC) [11]. Additionally, patients with hereditary non-polyposis colorectal cancer (HNPCC) have an approximate 6% lifetime risk of developing upper tract urothelial carcinoma (UTUC) and tend to present at a younger age, with a mean onset between 56 and 62 years [12].

The risk-benefit profile of performing CTU varies in these patients and should be carefully considered when selecting the appropriate imaging modality for hematuria screening. It is important to note that patients with hereditary non-polyposis colorectal cancer were not included in our cohort. However, the remarkably low number of malignancies identified on CTU alone in younger patients and those with a medical history of hematuria (MH) in our study suggests that a reassessment of the cost-benefit balance for initial CTU in lower-risk groups may be necessary.

Using RUS (Renal Ultrasound) as the initial radiographic imaging modality for low-risk patients, with follow-up cross-sectional imaging if suspicious findings are detected or in conjunction with cystoscopic or cytological results, may offer a favorable cost-benefit profile and warrants further exploration [4, 9]. Additionally, alternative cross-sectional imaging options, such as low-dose renal colic or non-contrast CT, could be considered to minimize radiation exposure in low-risk patients.

The results of our study indicate that only one case of UTUC was detected by CTU in patients under 50 years of age, whereas in the study by Clayton W. Commander, no cases were identified by CTU in patients under 55 years of age or with MH, regardless of age [8]. These findings highlight the need to explore alternative, lower-radiation imaging techniques for the initial evaluation of hematuria in specific patient populations.

References

1. Davis, R., Jones, J. S., Barocas, D. A., Castle, E. P., Lang, E. K., Leveillee, R. J., ... & Weitzel, W. (2012). Diagnosis, evaluation and follow-up of asymptomatic microhematuria (AMH) in adulte : AUA guideline. The Journal of urology, 188(6S), 2473-2481.
2. Siegel, R. L., Miller, K. D., & Jemal, A. (2018). Cancer statistics, 2018. CA : a cancer journal for clinicians, 68(1), 7-30.
3. Rouprêt, M., Babjuk, M., Compérat, E., Zigeuner, R., Sylvester, R. J., Burger, M., ... & Shariat, S. F. (2015). European association of urology guidelines on upper urinary tract urothelial cell carcinoma: 2015 update. European urology, 68(5), 868-879.
4. Chlapoutakis, K., Theocharopoulos, N., Yarmenitis, S., & Damilakis, J. (2010). Performance of computed tomographic urography in diagnosis of upper urinary tract urothelial carcinoma, in patients presenting with hematuria: systematic review and meta-analysis. European journal of radiology, 73(2), 334-338.
5. Gray Sears, C. L., Ward, J. F., Sears, S. T., Puckett, M. F., Kane, C. J., & Amling, C. L. (2002). Prospective comparison of computerized tomography and excretory urography in the initial evaluation of asymptomatic microhematuria. The Journal of urology, 168(6), 2457-2460.

6. Lang, E. K., Thomas, R., Davis, R., Myers, L., Sabel, A., Macchia, R., ... & Helbich, T. (2004). Multiphasic helical computerized tomography for the assessment of microscopic hematuria:: a prospective study. The Journal of urology, 171(1), 237-243.
7. Devlin, C. M., Hull, G., Coupland, A., Gill, K., & Browning, A. (2015). CT urography as the first line investigation for haematuria: is it truly indicated? A single centre analysis of the use of CT urography in the haematuria clinic. Journal of Clinical Urology, 8(6), 390-395.
8. Commander, C. W., Johnson, D. C., Raynor, M. C., Burke, L. M., Hacker, K. E., Hoag, B., ... & Lee, E. R. (2017). Detection of upper tract urothelial malignancies by computed tomography urography in patients referred for hematuria at a large tertiary referral center. Urology, 102, 31-37.
9. Van Der Molen, A. J., Cowan, N. C., Mueller-Lisse, U. G., Nolte-Ernsting, C. C., Takahashi, S., Cohan, R. H., & CT Urography Working Group of the European Society of Urogenital Radiology (ESUR). (2008). CT urography: definition, indications and techniques. A guideline for clinical practice. European radiology, 18, 4-17.
10. Wollin, T., Laroche, B., & Psooy, K. (2009). Canadian guidelines for the management of asymptomatic microscopic hematuria in adults. Canadian Urological Association Journal, 3(1), 77.
11. McLaughlin, J. K., Silverman, D. T., Hsing, A. W., Ross, R. K., Schoenberg, J. B., Yu, M. C., ... & Fraumeni Jr, J. F. (1992). Cigarette smoking and cancers of the renal pelvis and ureter. Cancer research, 52(2), 254-257.
12. Crockett, D. G., Wagner, D. G., Holmäng, S., Johansson, S. L., & Lynch, H. T. (2011). Upper urinary tract carcinoma in Lynch syndrome cases. The Journal of urology, 185(5), 1627-1630.