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Research Article

SURVIVAL OUTCOMES AND PROGNOSTIC FACTORS OF SMALL CELL CARCINOMA OF THE KIDNEY AND UPPER URINARY TRACT: A SEER DATABASE ANALYSIS

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ABSTRACT

Objective: Small cell carcinomas of the kidney (SCCK) and the upper urinary tract (SCC UUT) are exceedingly rare and aggressive malignancies. This study aimed to compare survival outcomes of these two conditions using a large population-based database.

Materials and Methods: Data from the Surveillance, Epidemiology, and End Results (SEER) database (2000–2022) were analysed. Patients with histologically confirmed SCCK (n = 41) and SCC UUT (n = 54) were included. Clinicopathological variables and treatment modalities were evaluated. Cancer-specific survival (CSS) was estimated using the Kaplan–Meier method and Cox proportional hazards models were employed to identify independent prognostic factors.

Results: The study cohort consisted of 95 patients. Patients with SCCK exhibited significantly higher rates of distant metastasis than the UUT group (58.5% vs. 40.7%, p = 0.029). The median CSS was 9 months for the UUT group and 6 months for the kidney group (p = 0.068). Multivariate analysis in the kidney group identified surgical intervention (HR: 0.18, p<0.001) and radiotherapy (HR: 0.35, p=0.020) as factors significantly associated with improved survival. Conversely, in the UUT group, distant stage and liver metastasis (HR: 3.94, p = 0.007) were significant predictors of poor prognosis. In the SCCK, lung metastasis was associated with poorer survival outcomes.

Conclusion: SCCK and SCC UUT are characterised by early mortality and aggressive clinical courses. Survival in UUT tumours is largely determined by tumour stage and visceral metastasis. Surgical resection and radiotherapy were associated with prolonged survival in patients with kidney tumours. These findings suggest that site-specific, multimodal treatment strategies involving local control and systemic therapy may be beneficial.

Keywords: Small cell carcinoma, Kidney neoplasms, Upper urinary tract, SEER database, Survival analysis, Nephrectomy.

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INTRODUCTION

Small cell carcinoma (SCC) is a highly aggressive malignancy that most commonly occurs in the lungs, though it can also arise in various other organs (1). Historically, it was thought that SCC originated exclusively from neuroendocrine cells (2). However, recent literature has largely debunked this concept, demonstrating that SCC can develop in almost any organ as a form of de-differentiation or lineage plasticity from conventional carcinomas arising in those respective organs (3). Lineage plasticity is a well-documented phenomenon in prostate and urothelial carcinomas, which are often driven by convergent genomic events such as the loss of TP53 and RB1 (4). SCCs arising from these organs may develop from multipotent stem cells or the typical epithelium of the organ (5, 6). These rare non-pulmonary tumours account for between 2.5% and 5.0% of all SCCs (5). The most common sites for these malignancies are the gastrointestinal and genitourinary (GU) systems.

Within the GU system, while the bladder and prostate are the most common primary sites, involvement of upper urinary tract regions such as the kidney, renal pelvis, and ureter is extremely rare (1, 7). Importantly, classifying tumours in this specific anatomical region presents unique challenges. The histogenesis of primary SCC of the kidney (SCCK) is debated; while true primary SCCK exists, it can be difficult to differentiate from SCC of the renal pelvis that has deeply invaded the renal parenchyma (8, 9). Despite this diagnostic complexity, large population-level databases such as the Surveillance, Epidemiology, and End Results (SEER) categorise these entities based on their primary clinical presentation. It is essential to acknowledge this potential diagnostic overlap; however, evaluating them as coded provides critical real-world insights into how tumours presenting primarily as renal masses behave differently from those confined to the upper urinary tract (UUT).

SCCK and SCC UUT typically exhibit an aggressive clinical course and are frequently diagnosed at an advanced stage (10). Current knowledge regarding these rare malignancies relies largely on small retrospective series and case reports (11, 12). While another large-scale study has conducted survival analyses for bladder and prostate SCC (7), there remains a significant gap in the literature regarding upper urinary tract tumours. Therefore, gaining a deeper understanding of the pathogenesis, prognosis, and management of SCCK and SCC UUT is a critical clinical necessity in combating this aggressive disease.

The objective of this exploratory study was to comparatively analyse the demographic characteristics, tumour features, and survival outcomes of patients with rare SCCK and SCC UUT using the SEER database of the National Cancer Institute (NCI). Furthermore, the study evaluated the potential associations of surgical intervention and adjuvant therapies with survival in these two distinct anatomical sites within the same system.

MATERIALS AND METHODS

This retrospective cohort study utilised data from the SEER Research Data, 17 Registries, November 2024 Submission (2000–2022), which covers approximately 26.5% of the U.S. population. The dataset is de-identified and publicly accessible. The study protocol was approved by the Uşak University Clinical Research Ethics Committee (ethics no: 993-993-12, date: 17.12.2025). The study was conducted in full accordance with the ethical standards of the Declaration of Helsinki and respected the privacy rights of all human subjects.

Kidney, renal pelvis, and ureter cancers were identified using ICD-10 codes C64.9, C65.9, and C66.9, respectively. Patients were included if they had a histologically confirmed diagnosis of malignant SCC based on ICD-O-3 morphology codes 8041/3–8045/3, and only individuals with a single primary tumour were eligible. Exclusion criteria consisted of survival time less than one month and the absence of positive histological confirmation. A total of 95 patients met the inclusion criteria, with 54 cases originating from the UUT and 41 from the kidney. Because the SEER program began collecting organ-specific metastatic information only after 2010, data on bone, brain, liver, and lung metastases were available for 29 kidney cases and 46 UUT cases diagnosed in or after that year. Consequently, specific metastasis data (bone, brain, liver, lung) were missing for 29.2% (12/41) of the kidney cohort and 14.8% (8/54) of the UUT cohort due to their diagnosis year falling before 2010. In the kidney cohort, 49 patients were initially identified, but 8 were excluded due to survival <1 month, resulting in a final sample of 41. In the UUT cohort, 59 patients were initially identified and 5 were excluded for survival <1 month, yielding 54 final cases; among these, 17 tumours originated in the renal pelvis and 37 in the ureter.

Baseline variables included age at diagnosis (categorised as <70 or ⩾70 years), sex, race/ethnicity (Non-Hispanic White (NHW), Non-Hispanic Asian/Pacific Islander (NHAPI), Non-Black Hispanic (NBH), Hispanic, and Non-Hispanic American Indian/Alaska Native (NHAIA)),

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marital status, residence type, and median household income. Tumour-related variables included anatomical site (kidney vs. renal pelvis vs. ureter), laterality, and stage based on the SEER Summary Stage system (localised, regional, distant, or unknown). Treatment variables consisted of cancer-directed surgery, chemotherapy, and radiotherapy. Survival variables consisted of cancer-specific mortality, other-cause mortality, and survival months.

Statistical analysis

Descriptive statistics were used to summarise the baseline characteristics of the cohort. Categorical variables were compared between the kidney and UUT groups using the Chi-square or Fisher's exact test, while continuous variables were summarised as medians with interquartile ranges. Cancer-specific survival (CSS) was estimated using the Kaplan–Meier method, and differences between subgroups such as stage, sex, and treatment modalities were evaluated with the Log-rank test. Median CSS with 95% confidence intervals was calculated for all relevant subgroups. Univariate and multivariate Cox proportional hazards regression models were performed to identify predictors of CSS, and variables with $p < 0.20$ in univariate analysis were entered into the multivariate model. Hazard ratios (HR) with 95% confidence intervals were reported. All analyses were conducted using IBM SPSS Statistics version 31.0 (IBM Corp., Armonk, NY, USA), and two-sided p-values <0.05 were considered statistically significant.

RESULTS

Patient Population and Demographic Characteristics

The study cohort consisted of 95 patients with small cell carcinoma, stratified into the UUT group (n=54, 56.8%) and the Kidney group (n=41, 43.2%). No statistically significant differences were observed between the two groups regarding age, sex, marital status, residence type, or median household income ($p>0.05$). In the overall study population, the majority of patients were aged 70 years or older (UUT: 74.1%, Kidney: 68.3%), and the sex distribution was balanced in both groups (UUT: 50% Male, Kidney: 48.8% Male). However, a significant difference was noted in racial/ethnic distribution (p=0.027); the proportion of Hispanic patients was higher in the Kidney group (12.2%) compared to the UUT group (0%). However, given the small number of patients in these specific racial and ethnic subcategories, this statistical difference is probably due to the small sample size rather than representing a true epidemiological variance. The main characteristics of the study population are shown in Table 1.

Tumour Characteristics and Staging

There was no significant difference between the groups regarding tumour laterality (p=0.763). Conversely, a statistically significant difference was detected between the UUT and Kidney groups in terms of tumour stage at diagnosis (p=0.029). While 58.5% of patients in the Kidney group were diagnosed at the distant metastatic stage, this rate was 40.7% in the UUT group. Furthermore, the rate of regional involvement was higher in the UUT group (38.9%) compared to the Kidney group (19.5%). Regarding metastatic sites, the Kidney group exhibited a significantly higher metastatic burden compared to the UUT group. Specifically, the rates of liver (41.4% vs 19.6%, p=0.040), bone (37.9% vs 17.4%, p=0.046), and brain metastases (13.8% vs 0%, p=0.010) were significantly higher in patients with SCCK.

Treatment Approaches

Regarding treatment modalities, a highly significant statistical difference was found between the two groups in terms of surgical intervention rates (p=0.001). Surgical intervention was performed on 64.8% of patients in the UUT group, whereas this rate remained at 31.7% in the Kidney group. No significant differences were observed between the groups regarding the administration of chemotherapy (p=0.906) and radiotherapy (p=0.238). Approximately half of the patients in both groups received chemotherapy (UUT: 50%, Kidney: 48.8%).

Survival Analysis

Although cancer-specific death rates were high in both groups (UUT: 70.4%, Kidney: 80.5%), no statistically significant difference was observed between them (p=0.460). The median CSS was calculated as 9.00 months (IQR: 15.25) in the UUT group and 6.00 months (IQR: 8.00) in the Kidney group; this difference was borderline statistically significant (p=0.068).

Overall Survival (OS): The median survival estimate for the entire cohort was 10 months (95% CI: 6.24–13.75) for the UUT group and 6 months (95% CI: 4.69–7.30) for the Kidney group. Median survival estimates for the study population are shown in Table 2.

Impact of Surgery: The median survival time was markedly higher in patients who underwent surgical treatment compared to those who did not. Specifically in the Kidney group, median survival increased from 3 months in non-surgical patients to 11 months in those who

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Table 1. Baseline Characteristics of the Study Population

Variable	UUT group (n=54)	Kidney group (n=41)	p- value
Age, n (%)			0.536
<70 years	14 (25.9)	13 (31.7)	
≥70 years	40 (74.1)	28 (68.3)	
Sex, n (%)			0.906
Female	27 (50)	21 (51.2)	
Male	27 (50)	20 (48.8)	
Race/Ethnicity, n (%)			**0.027**
NHW	46 (85.2)	30 (73.2)	
NHAPI	6 (11.1)	3 (7.3)	
NBH	2 (3.7)	2 (4.9)	
Hispanic	0 (0)	5 (12.2)	
NHAIA	0 (0)	1 (2.4)	
Marital status, n (%)			0.854
Married	30 (55.6)	22 (53.7)	
Unmarried	24 (44.4)	19 (46.3)	
Residence type, n (%)			0.537
Metropolitan	47 (87)	38 (92.7)	
Non-metropolitan	7 (13)	3 (7.3)	
Median household income, n (%)			0.385
<70,000 dollars	19 (35.2)	11 (26.8)	
≥70,000 dollars	35 (64.8)	30 (73.2)	
Laterality, n (%)			0.763
Left	19 (35.2)	17 (41.5)	
Right	33 (61.1)	22 (53.7)	
Unknown	2 (3.7)	2 (4.9)	
Stage, n (%)			**0.029**
Localised	6 (11.1)	1 (2.4)	
Regional	21 (38.9)	8 (19.5)	
Distant	22 (40.7)	24 (58.5)	
Unknown	5 (9.3)	8 (19.5)	
Site of metastasis, n (%)			
Bone	8/46 (17.4)	11/29 (37.9)	**0.046**
Brain	0/46 (0)	4/29 (13.8)	**0.01**
Liver	9/46 (19.6)	12/29 (41.4)	**0.04**
Lung	2/46 (4.3)	3/29 (10.3)	0.318
Surgery, n (%)			**0.001**
No	19 (35.2)	28 (68.3)	
Yes	35 (64.8)	13 (31.7)	
Chemotherapy, n (%)			0.906
No/unknown	27 (50)	21 (51.2)	
Yes	27 (50)	20 (48.8)	
Radiotherapy, n (%)			0.238
No/unknown	46 (85.2)	31 (75.6)	
Yes	8 (14.8)	10 (24.4)	
Cancer-specific death, n (%)			0.460
No	16 (29.6)	8 (19.5)	
Yes	38 (70.4)	33 (80.5)	
Other-cause death, n (%)			0.460
No	51 (94.4)	37 (90.2)	
Yes	3 (5.6)	4 (9.8)	
Cancer-specific survival (months), median (IQR)	9.00 (15.25)	6.00 (8.00)	0.068

Note: Data are given as number (n), percentage, and median (IQR: Interquartile Range). $p < 0.05$ is statistically significant. UTT: Upper Urinary Tract, NHW: Non-Hispanic White, NHAPI: Non-Hispanic Asian/Pacific Islander, NBH: Non-Black Hispanic, NHAIA: Non-Hispanic American Indian/Alaska Native, Unmarried: single, divorced, widowed, separated, unknown

underwent surgery. Similarly, in the UUT group, median survival was 12 months for surgical patients and 9 months for non-surgical patients.

Survival by Stage: In UUT patients with localised/regional disease, median survival was 15 months, whereas it was 9 months in patients with distant metastasis. In the Kidney group, median survival remained constant at 6 months regardless of stage. Median survival estimates further highlighted the poor prognosis associated with visceral metastases. In the UUT group, patients with liver metastasis had a median survival of only 2 months, compared to 14 months for those without (95% CI: 0–4.44 vs 5.90–22.10). Similarly, in the Kidney group, lung metastasis was associated with a poor median

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Table 2. Median Survival Estimates for the Study Population

Variable	UUT group (n=54) median survival estimate (months), (95%CI)	Kidney group (n=41) median survival estimate (months), (95%CI)
All	10 (6.241- 13.759)	6 (4.696- 7.304)
Age		
<70 years	11 (0- 25.758)	10 (4.526- 15.474)
≥70 years	9 (4.48- 13.52)	6 (4.631- 7.369)
Sex		
Female	12 (6.02- 17.98)	6 (3.614- 8.386)
Male	9 (5.187- 12.813)	6 (1.975- 10.025)
Race/Ethnicity		
NHW	10 (5.098- 14.902)	6 (4.56- 7.44)
NHAPI	12 (2.2- 21.8)	3 (1.4- 4.6)
NBH	1 (*)	1 (*)
Hispanic	*	6 (0.12- 11.88)
NHAIA	*	12 (*)
Marital status		
Married	10 (6.289- 13.711)	6 (2.519- 9.481)
Unmarried	12 (0- 25.016)	6 (4.655- 7.345)
Residence type		
Metropolitan	10 (6.54- 13.46)	6 (4.744- 7.256)
Non-metropolitan	15 (0- 31.41)	3 (1.4- 4.6)
Median household income		
<70,000 dollars	15 (1.056- 28.944)	6 (3.911- 8.085)
≥70,000 dollars	10 (6.821- 13.179)	6 (3.524- 8.476)
Laterality		
Left	15 (0- 31.64)	6 (3.061- 8.939)
Right	10 (6.933- 13.067)	6 (3.145- 8.855)
Stage		
Localised- regional	15 (8.523- 21.477)	6 (2.013- 9.987)
Distant	9 (6.198- 11.802)	6 (3.709- 8.291)
Surgery		
No	9 (3.931- 14.069)	3 (0.171- 5.829)
Yes	12 (8.185- 15.815)	11 (0- 26.431)
Chemotherapy		
No/unknown	6 (0- 12.126)	6 (2.886- 9.114)
Yes	11 (4.241- 17.759)	6 (3.922- 8.078)
Radiotherapy		
No/unknown	10 (5.842- 14.158)	6 (4.159- 7.841)
Yes	21 (5.793- 36.207)	10 (7.108- 12.892)
Bone metastasis		
No/unknown	14 (6.455- 21.545)	6 (1.979- 10.021)
Yes	8 (0.423- 15.577)	6 (0.233- 11.767)
Brain metastasis		
No/unknown	*	6 (3.138- 8.862)
Yes	*	6 (1.509- 10.491)
Liver metastasis		
No/unknown	14 (5.902- 22.098)	8 (4.123- 11.877)
Yes	2 (0- 4.44)	6 (0.074- 11.926)
Lung metastasis		
No/unknown	11 (3.852- 18.148)	7 (3.88- 10.12)
Yes	1 (*)	2 (0.4- 3.6)

Note: Note: Median survival estimates are shown with 95% confidence intervals (CI). p-values were calculated using the Log-rank test. * indicates that the median survival estimate could not be calculated due to insufficient events or small sample size. UTT: Upper Urinary Tract, NHW: Non-Hispanic White, NHAPI: Non-Hispanic Asian/Pacific Islander, NBH: Non-Black Hispanic, NHAIA: Non-Hispanic American Indian/Alaska Native

survival of 2 months, versus 7 months for patients without lung involvement.

Adjuvant Therapies: UUT patients receiving radiotherapy reached a remarkable median survival of 21 months, compared to 10 months for those who did not. UUT patients receiving chemotherapy had a median survival of 11 months, while it was 6 months for those who did not.

Kaplan-Meier Survival Analyses and Prognostic Factors

CSS rates of the study population were analysed using the Kaplan-Meier method, and differences between groups were evaluated using the Log-rank test. Notably, the Kaplan-Meier curve exhibited a sharp decline within the first 6 months of diagnosis, reflecting the highly aggressive nature and significant early mortality associated with this malignancy (Figure 1).

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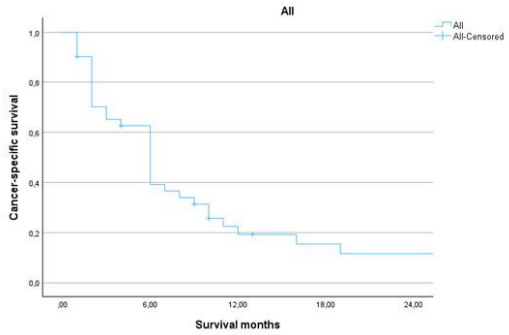


Figure 1. Kaplan-Meier estimates of cancer-specific survival for the entire study cohort, demonstrating early mortality rates. Cancer-specific survival rates decline sharply within the first six months

Kidney Group: Univariate analyses in the Kidney group identified surgical treatment as the most determinant factor for survival. The cumulative survival rate in patients who underwent surgery (nephrectomy) was significantly higher than in those who did not (Log-rank p<0.001) (Figure 2). In the kidney cancer cohort, lung metastasis was identified as a significant prognostic factor. Patients with lung metastasis demonstrated significantly lower survival rates compared to the non-metastatic group (Log-rank p=0.030) (Figure 3). In contrast, factors such as age (p=0.482), sex (p=0.622), tumour laterality (p=0.227), and stage (p=0.317) did not show a statistically significant effect on survival in the Kidney group. Furthermore, the administration of chemotherapy (p=0.272) and radiotherapy (p=0.111) did not provide a survival advantage in this group.

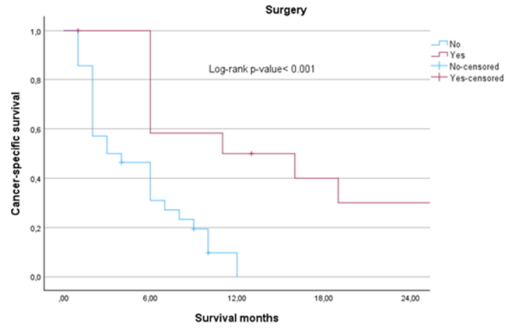


Figure 2. Kaplan-Meier survival curves for the Kidney Group stratified by surgical intervention (Surgery vs. No Surgery).

UUT Group: In the UUT group, tumour stage was identified as the primary prognostic factor affecting survival. The survival curve of the group with localised/regional disease was significantly better than that of the distant metastatic group (Log-rank p=0.033) (Figure 4). Regarding sex, female patients showed a trend toward better survival compared to males, although this difference remained borderline significant (p=0.064). The

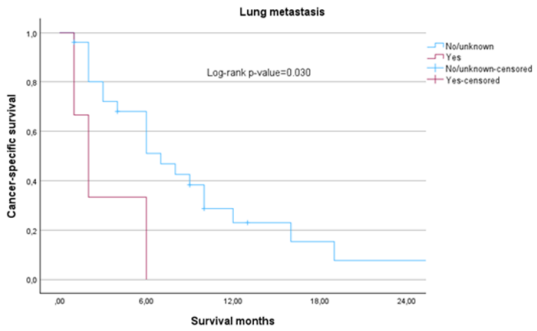


Figure 3. Kaplan-Meier estimates of cancer-specific survival in patients with Kidney carcinoma stratified by lung metastasis status.

presence of liver metastasis was associated with a dramatic reduction in survival. Patients with liver metastasis exhibited significantly poorer CSS compared to those without liver involvement (Log-rank p=0.002) (Figure 5). Interestingly, contrary to the Kidney group, surgical treatment did not create a statistically significant difference in survival in the UUT group (p=0.704). Similarly, other covariates such as age, race, marital status, and receipt of radiotherapy/chemotherapy did not reach statistical significance in the UUT group (p>0.05).

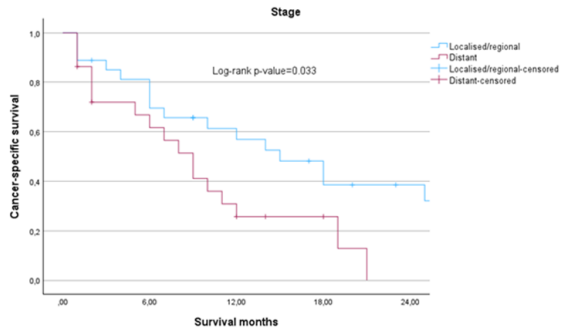


Figure 4. Kaplan-Meier survival curves for the Upper Urinary Tract (UUT) Group stratified by tumour stage (Localised/Regional vs. Distant).

Cox Regression Analysis Univariate and multivariate Cox regression analyses were performed to evaluate independent predictors of CSS (Table 3). In the UUT group, univariate analysis identified distant stage (HR: 2.09, p=0.042) and liver metastasis (HR: 3.94, p=0.007) as significant predictors of poor survival. However, in the multivariate model, the impact of stage became borderline significant (HR: 1.87, p=0.095). In the Kidney group, surgical intervention emerged as a significant factor associated with improved survival in the multivariate analysis (HR: 0.18, 95% CI: 0.07–0.49, p<0.001). Notably, while radiotherapy was not statistically significant in the univariate analysis (p=0.150), it emerged as a significant

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Table 3. Univariate and Multivariate Cox Regression Analysis for Cancer-Specific Survival

Variables	UUT Group (Univariate)		UUT Group (Multivariate)		Kidney Group (Univariate)		Kidney Group (Multivariate)	
	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p
Sex (Female vs Male)	0.55 (0.29–1.06)	0.076	0.58 (0.29–1.19)	0.138	1.17 (0.59–2.33)	0.652	-	-
Age (≥70 vs <70)	1.21 (0.59–2.50)	0.606	-	-	1.28 (0.60–2.71)	0.520	-	-
Stage (Distant vs Loc/Reg)	**2.09 (1.03–4.24)**	**0.042**	1.87 (0.90–3.91)	0.095	1.61 (0.59–4.38)	0.352	-	-
Surgery (Yes vs No)	0.88 (0.46–1.71)	0.712	-	-	**0.25 (0.10–0.63)**	**0.004**	**0.18 (0.07–0.49)**	**<0.001**
Chemotherapy (Yes vs No)	0.73 (0.39–1.39)	0.337	-	-	0.70 (0.35–1.40)	0.318	-	-
Radiotherapy (Yes vs No)	0.71 (0.27–1.82)	0.472	-	-	0.54 (0.23–1.25)	0.150	**0.35 (0.15–0.85)**	**0.020**
Metastasis Site (vs None)								
Bone	2.11 (0.83–5.36)	0.118	NA*	-	1.35 (0.59–3.08)	0.480	NA**	-
Liver	**3.94 (1.47–10.59)**	**0.007**	NA*	-	1.60 (0.70–3.64)	0.267	NA**	-
Lung	4.40 (0.51–37.66)	0.176	NA*	-	3.41 (0.96–12.17)	0.059	NA**	-

NA*: Not included in multivariate analysis as it is covered by the stage variable. NA**: Excluded due to excessive missing data. HR: Hazard Ratio, CI: Confidence Interval. Note: Only variables with p < 0.20 in univariate analysis were included in the multivariate model. (-) indicates variables not meeting the inclusion criteria.

independent prognostic factor associated with better survival in the multivariate model (HR: 0.35, 95% CI: 0.15–0.85, p=0.020). Site-specific analysis of metastasis revealed that liver metastasis was associated with significantly worse outcomes in the UUT group (p=0.007), whereas lung metastasis showed a trend toward poor prognosis in the kidney group (HR: 3.41, p=0.059), although it did not reach statistical significance.

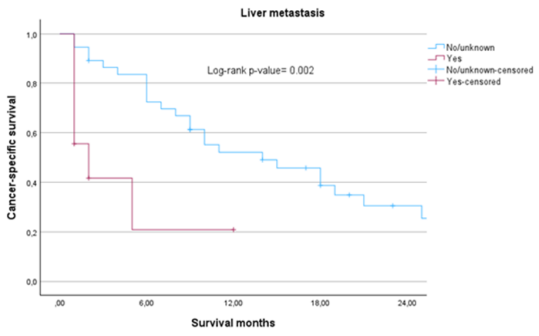


Figure 5. Kaplan-Meier estimates of cancer-specific survival in patients with Upper Urinary Tract (UUT) carcinoma stratified by liver metastasis status

DISCUSSION

To the best of our knowledge, this is the largest population-based study to compare SCCK and SCC UUT. In this study, the clinicopathological characteristics and survival outcomes of 95 patients diagnosed with SCCK and SCC UUT were examined. The most notable finding of our exploratory analysis is that, although both tumour groups follow an aggressive course, surgical treatment and radiotherapy were associated with prolonged survival, particularly in the kidney group.

In the kidney group, median survival was 11 months for patients who underwent nephrectomy, compared to 3 months for those who did not (p<0.001). Our multivariate Cox regression analysis identified surgery as a strong, independent factor associated with improved survival (HR: 0.18, 95% CI: 0.07–0.49, p<0.001). However, these findings must be interpreted with extreme caution. The observed associations should not be interpreted as definitive treatment effects due to the high risk of selection bias and confounding by indication. It is highly probable that patients selected for surgery and radiotherapy had a better performance status, lower disease burden or fewer comorbidities than those managed conservatively. Due to the small sample size within these treatment subgroups, advanced statistical methods such as Propensity Score Matching could not be reliably performed to mitigate this confounding by indication. Consequently, while cytoreductive nephrectomy or local tumour burden reduction may be considered for a small number of patients, our data cannot definitively confirm a stage-independent survival advantage for aggressive local control, particularly in advanced metastatic settings.

While we acknowledge the debated histogenesis and the diagnostic challenge of distinguishing true primary SCCK from invasive SCCs UUT (8), and recognise that a

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definitive confirmation of tumour origin is not possible without central pathology review, our findings demonstrate that tumours presenting as primary kidney SCCs exhibit significantly different clinical behaviours, such as a higher rate of distant metastasis and a distinct response to surgical intervention. Therefore, despite potential classification overlaps inherent to registry data, stratifying these patients by their primary coded site provides highly relevant prognostic information and justifies site-specific management strategies.

In the UUT group, although the median survival was numerically higher in surgically treated patients (12 months) compared to those who were not (9 months), this difference did not reach statistical significance (p=0.704). This lack of significance may be attributed to the small sample size of the UUT group or selection bias regarding patients eligible for surgery. While surgery improves survival rates for people with SCCs outside the lung, definitive evidence regarding its survival benefits for the GU subgroup specifically remains limited (13). In early-stage (localised) disease, surgery (radical cystectomy or prostate surgery), particularly when combined with platinum-based chemotherapy, significantly increases survival (14, 15). Although not specific to SCC, the contribution of surgery to survival in advanced-stage (metastatic) disease is generally considered limited, with systemic therapy (chemotherapy) taking precedence. Surgery may only provide additional benefits to a highly selected group of patients, such as those with a solitary metastatic site (16).

SCCK is generally diagnosed in patients aged 50 and older, with limited data suggesting a slightly higher prevalence in women (1). Our cohort's demographic data confirm that this disease predominantly affects the elderly population; approximately 70% of the patients were aged 70 years or older. The balanced sex distribution in both groups (UUT: 50% Male, Kidney: 48.8% Male) delineates an epidemiological profile distinct from that of classic urothelial carcinomas and renal cell carcinomas, where male dominance is more pronounced (17, 18).

SCCs UUT typically present as advanced disease (1). SCCK is frequently associated with regional lymph node involvement (up to 56%) and distant metastasis (approximately 33%), with bone being the most common site of distant spread (19). According to our results, only 11.1% of SCC UUT patients and 2.4% of SCCK patients had localised disease at diagnosis; the remaining patients presented with locally advanced or metastatic disease.

As expected, tumour stage emerged as the most important prognostic factor in the UUT group. UUT patients with localised/regional disease achieved a median survival of 15 months, whereas this duration was 9 months for those with distant metastasis (p=0.033). In contrast, no survival difference was observed between stages in the kidney group (median 6 months for both); this suggests that SCCK possesses a highly aggressive biology independent of stage. Similarly, a study on bladder SCC reported that median survival was not reached in early-stage patients, whereas it was 9 months in advanced-stage patients (20). Likewise, median survival has been reported as 22 months in limited disease versus 4.1 months in extensive disease (10). In SCC UUT, survival is significantly worse in patients with high-stage disease (21). Our study also highlighted the prognostic significance of metastatic sites; specifically, liver metastasis was associated with a nearly four-fold increase in the risk of death in the UUT group (HR: 3.94, p=0.007), underscoring the aggressive nature of visceral involvement. For the kidney cohort, lung metastasis was identified as a significant prognostic factor. This can be attributed to the anatomical venous drainage of the kidney, making the lungs the primary site for haematogenous spread.

Our survival analyses revealed the high lethality of the disease. The median OS was 10 months in the UUT group and 6 months in the kidney group. Notably, the Kaplan-Meier curves exhibited a sharp decline in survival rates within the first 6 months following diagnosis, indicating that a significant proportion of patients succumb to the disease in this early period. The numerically higher mortality in the kidney group compared to the UUT group may be explained by the difference in stage at diagnosis. In our study, 58.5% of patients in the kidney group were in the distant metastasis stage, compared to 40.7% in the UUT group. The rich vascular structure of the renal parenchyma may facilitate haematogenous spread before the tumour becomes symptomatic. In the literature, the median OS for bladder SCC patients across all stages is generally reported between 10–16 months (22). This rate has been calculated as 12–15 months for SCC UUT patients (21). For SCCK, median OS ranges from 8 to 20 months (19). In our study, CSS was calculated as 9 months in the UUT group and 6 months in the kidney group. A review reported CSS as 15 months in SCC UUT (21). In bladder SCC, median CSS is generally around 12–15 months (22). Consequently, it can be concluded that the prognosis of the disease is poor, and the majority of patients die from the disease within one year.

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When evaluating treatment modalities, approximately 50% of patients in both groups received chemotherapy, and 20% received radiotherapy. Although no statistically significant difference was detected regarding the impact of these treatments, clinically important trends were observed. Particularly in the UUT group, patients receiving radiotherapy reached a remarkable median survival of 21 months, compared to 10 months for those who did not. Similarly, UUT patients receiving chemotherapy had a median survival of 11 months. These findings support the view that systemic chemotherapy and local radiotherapy should be part of a multimodal treatment approach for SCC. In the literature, platinum-based combination chemotherapy (cisplatin or carboplatin with etoposide) is accepted as the standard systemic treatment for both adjuvant and metastatic disease (1, 11). Patients receiving active treatment (chemotherapy, radiotherapy, or surgery) have been shown to have longer survival compared to those receiving best supportive care (median 12.3 vs. 2.3 months) (10). Combining local treatment (radical nephrectomy, nephroureterectomy) with systemic chemotherapy is recommended (1). In a case report of localised ureteral SCC, no recurrence was observed for 10 months following surgery with adjuvant chemotherapy and radiation therapy (11). Furthermore, in our study, radiotherapy was identified as a significant protective factor in the kidney cohort (HR: 0.35, 95% CI: 0.15–0.85, p = 0.020). Although SCC is typically considered a systemic disease, these findings imply that effective locoregional control through radiotherapy could improve overall survival. However, it is important to note that the SEER database does not specify whether radiotherapy was administered to the primary tumour bed with curative intent or as palliative care for distant metastases (e.g. in the bone or brain). Therefore, the observed survival benefit should be interpreted with caution. Consequently, our data support the consideration of a multimodal treatment strategy combining surgery and radiotherapy for carefully selected patients with SCCK.

However, the aggressive nature of SCC and its resistance to conventional therapies highlight the need for novel molecular targets (23). In lung SCC, the addition of immune checkpoint inhibitors (e.g., atezolizumab, durvalumab) to etoposide-platinum chemotherapy has become the standard of care (24). Delta-like protein 3 (DLL3), which is highly expressed in bladder SCC and associated with poor prognosis, is the focus of novel clinical trials targeting it with bispecific T-cell engagers such as Tarlatamab (25). These findings suggest that the future management of SCCK and SCC UUT will shift towards new therapeutic strategies involving immune checkpoint inhibitors and molecular targets like DLL3, in addition to standard platinum-based chemotherapy and local treatments.

This study has several limitations that are inherent to its retrospective nature and the SEER database. Firstly, the extremely small sample sizes (n = 41 for SCCK and n = 54 for SCC UUT), particularly after stratification by metastatic site and treatment type, significantly reduce the statistical power and reliability of the multivariate Cox models. Therefore, our analyses should be viewed strictly as exploratory and hypothesis-generating. Secondly, the absence of central pathology review means that misclassification between renal pelvis and parenchymal origins cannot be definitively excluded. Thirdly, excluding patients with a survival of less than one month, while intended to minimise bias due to perioperative mortality, may have inadvertently introduced selection bias. By excluding patients with the most aggressive disease phenotypes who might have been unfit for surgical intervention, the survival advantage observed in the surgical cohort, particularly in the kidney group, may be overestimated. Finally, granular data such as patient performance status, specific chemotherapy regimens (e.g., the exact platinum-based agents used or the potential integration of modern immune checkpoint inhibitors over the 22-year study period), the exact extent and purpose of surgical interventions (e.g. radical versus partial, or cytoreductive intent), and comorbidities were unavailable, preventing adjustment for these vital confounders.

CONCLUSION

SCCK and SCC UUT are extremely aggressive conditions characterised by high early mortality rates. Our exploratory analysis suggests that there are distinct prognostic associations between the two anatomical classifications. In the kidney group, surgical resection and radiotherapy were associated with improved survival. However, these findings should be interpreted with caution due to the inherent biases of retrospective registry data, such as confounding by indication. Conversely, the prognosis for UUT tumours is heavily influenced by tumour stage and visceral metastases, particularly to the liver. These findings highlight the need for site-specific, multimodal strategies that incorporate systemic therapy and carefully selected local control measures. Further prospective, multi-institutional studies are needed to validate these results and determine the most effective way to integrate emerging immunotherapies.

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Authorship contributions
YA contributed to surgical and medical practices, concept, design, literature search, and writing. MG was responsible for data collection or processing, and analysis or interpretation. All authors read and approved the final manuscript.

Data availability statement
The datasets analysed during the current study are available in the SEER (Surveillance, Epidemiology and End Results) Research Data Repository, https://seer.cancer.gov/. The dataset is de-identified and publicly accessible.

Declaration of competing interest
The authors declare that they have no competing financial interests or personal relationships which could have influenced the work reported in this paper.

Ethics
The study protocol was approved by the Uşak University Clinical Research Ethics Committee (ethics no: 993-993-12, date: 17.12.2025). The study was conducted in full accordance with the ethical standards of the Declaration of Helsinki and respected the privacy rights of all human subjects. Because the SEER dataset is de-identified and publicly accessible, the need for individual patient consent to participate was waived.

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REFERENCES

1. Liao RS, Ruan HT, Jang A, Huynh M, Nadal Rios R, Hoffman-Censits JH, et al. Emerging Insights in Small-Cell Carcinoma of the Genitourinary Tract: From Diagnosis to Novel Therapeutic Horizons. Am Soc Clin Oncol Educ Book. 2024;44:e430336.
2. Brambilla E. Small Cell Carcinoma. In: Zander DS, Popper HH, Jagirdar J, Haque AK, Cagle PT, Barrios R, editors. Molecular Pathology of Lung Diseases. New York, NY: Springer New York; 2008. p. 293-300.
3. Jiang J, Han D, Wang J, Wen W, Zhang R, Qin W. Neuroendocrine transdifferentiation in human cancer: molecular mechanisms and therapeutic targets. MedComm (2020). 2024;5(10):e761.
4. Yang G, Bondaruk J, Cogdell D, Wang Z, Lee S, Lee JG, et al. Urothelial-to-Neural Plasticity Drives Progression to Small Cell Bladder Cancer. iScience. 2020;23(6):101201.
5. Frazier SR, Kaplan PA, Loy TS. The pathology of extrapulmonary small cell carcinoma. Semin Oncol. 2007;34(1):30-8.
6. Shahab N. Extrapulmonary small cell carcinoma of the bladder. Semin Oncol. 2007;34(1):15-21.
7. Baralo B, Schneider M, Baralo I. Survival analysis of small cell carcinomas of the genitourinary system. Proc (Bayl Univ Med Cent). 2023;36(1):8-14.
8. Si Q, Dancer J, Stanton ML, Tamboli P, Ro JY, Czerniak BA, et al. Small cell carcinoma of the kidney: a clinicopathologic study of 14 cases. Hum Pathol. 2011;42(11):1792-8.
9. Xie K, Li XY, Liao BJ, Wu SC, Chen WM. Primary renal small cell carcinoma: A case report. World J Clin Cases. 2022;10(17):5884-92.
10. Pervez N, El-Gehani F, Joseph K, Dechaphunkul A, Kamal M, Pertschy D, et al. Genitourinary small-cell carcinoma: a single-institution experience. Curr Oncol. 2013;20(5):258-64.
11. Jang H, Yuk SM, Kim JO, Han DS. A rare case of primary malignant small cell carcinoma combined with urothelial cell carcinoma in the ureter. World J Surg Oncol. 2013;11(1):181.
12. Yeung HM, Jeurkar C, Pompa T, Styler M. Small Cell Cancer of the Genitourinary Tract: A Case Report and Review of the Literature. Case Rep Oncol. 2017;10(2):489-92.
13. Mandish SF, Gaskins JT, Yusuf MB, Little BP, Dunlap NE. Extrapulmonary small cell carcinoma: Prognostic factors, patterns of care, and overall survival. Eur J Surg Oncol. 2020;46(9):1596-604.
14. Teo MY, Guercio BJ, Arora A, Hao X, Regazzi AM, Donahue T, et al. Long-term Outcomes of Local and Metastatic Small Cell Carcinoma of the Urinary Bladder and Genomic Analysis of Patients Treated With Neoadjuvant Chemotherapy. Clin Genitourin Cancer. 2022;20(5):431-41.
15. Luzzago S, Palumbo C, Rosiello G, Knipper S, Pecoraro A, Nazzani S, et al. Survival of Contemporary Patients With Non-metastatic Small-cell Carcinoma of Urinary Bladder, According to Alternative Treatment Modalities. Clin Genitourin Cancer. 2020;18(4):e450-e6.
16. Moschini M, Xylinas E, Zamboni S, Mattei A, Niegisch G, Yu EY, et al. Efficacy of Surgery in the Primary Tumor Site for Metastatic Urothelial Cancer: Analysis of an International, Multicenter, Multidisciplinary Database. Eur Urol Oncol. 2020;3(1):94-101.
17. Papatsoris AG, Chrisofos M, Skolarikos A, Varkarakis I, Lekas A, Dellis A, et al. Upper urinary tract transitional cell carcinoma. A 10-year experience. Tumori. 2008;94(1):75-8.
18. Hew MN, Zonneveld R, Kümmerlin IP, Opondo D, de la Rosette JJ, Laguna MP. Age and gender related differences in renal cell carcinoma in a European cohort. J Urol. 2012;188(1):33-8.

19. Majhail NS, Elson P, Bukowski RM. Therapy and outcome of small cell carcinoma of the kidney: report of two cases and a systematic review of the literature. Cancer. 2003;97(6):1436-41.
20. Lim JH, Sundar S. Prognosis of early stage small cell bladder cancer is not always dismal. ESMO Open. 2019;4(6):e000559.
21. Jiang N, Tian D, Shen Z, Wu P, Hou Y, Xie L, et al. Small cell carcinoma of the upper urinary tract and factors associated with progress survival: a systematic review and pooled analysis. Minerva Urol Nefrol. 2020;72(2):115-22.
22. Pasquier D, Barney B, Sundar S, Poortmans P, Villa S, Nasrallah H, et al. Small Cell Carcinoma of the Urinary Bladder: A Retrospective, Multicenter Rare Cancer Network Study of 107 Patients. Int J Radiat Oncol Biol Phys. 2015;92(4):904-10.
23. Kouba EJ, Cheng L. Understanding the Genetic Landscape of Small Cell Carcinoma of the Urinary Bladder and Implications for Diagnosis, Prognosis, and Treatment: A Review. JAMA Oncol. 2017;3(11):1570-8.
24. Goldman JW, Dvorkin M, Chen Y, Reinmuth N, Hotta K, Trukhin D, et al. Durvalumab, with or without tremelimumab, plus platinum-etoposide versus platinum-etoposide alone in first-line treatment of extensive-stage small-cell lung cancer (CASPIAN): updated results from a randomised, controlled, open-label, phase 3 trial. Lancet Oncol. 2021;22(1):51-65.
25. Koshkin VS, Garcia JA, Reynolds J, Elson P, Magi-Galluzzi C, McKenney JK, et al. Transcriptomic and Protein Analysis of Small-cell Bladder Cancer (SCBC) Identifies Prognostic Biomarkers and DLL3 as a Relevant Therapeutic Target. Clin Cancer Res. 2019;25(1):210-21.