ORIGINAL PAPER

UROLOGICAL ONCOLOGY

Prognostic effect of renal collecting system invasion on survival of patients with renal cell carcinoma and tumor thrombus

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Citation: Przydacz M, Golabek T, Okon K, Dudek P, Chlosta P. Prognostic effect of renal collecting system invasion on survival of patients with renal cell carcinoma and tumor thrombus. Cent European J Urol. 2020; 73: 280-286.

Article history
Submitted: June 14, 2020
Accepted: Aug. 30, 2020
Published online: Sept. 8, 2020

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Introduction Urinary collecting system invasion (UCSI) has been found to have significant prognostic value for patients with renal cell carcinoma (RCC). However, for RCC patients with venous tumor thrombus (VTT), only contradictory data exist regarding the prognostic efficacy of UCSI. Therefore, the aim of this study is to assess the prognostic relevance of UCSI in survival of patients with RCC and VTT.

Material and methods Medical records in a prospectively maintained institutional database were analyzed for RCC-VTT patients who had undergone nephrectomy with thrombectomy. Then, the effect of UCSI on overall survival was analyzed.

Results The study examined data for 114 patients, including patients with VTT present in the renal vein (35 patients, 31%), infrahepatic inferior vena cava (28 patients, 24%), and suprahepatic inferior vena cava (51 patients, 45%). Nineteen percent of patients had UCSI. The median overall survival of patients with UCSI was 9 months, whereas median overall survival was 10 months for patients without collecting system invasion. Survival and regression analyses rejected UCSI as a prognostic marker for overall survival.

Conclusions UCSI has no effect on survival in our cohort of RCC-VTT patients. Therefore, it should not be considered in risk stratification models or in treatment decision-making for this patient group.

Key Words: renal carcinoma ‹› tumor thrombus ‹› histological features ‹› histopathology

INTRODUCTION

Renal cell carcinoma (RCC) represents 2–3% of all cancers, and RCC is the third most common urological malignant tumor [1, 2]. In some patients, RCC may extend into the venous system that organizes a tumor thrombus (VTT). RCC-related VTT affects 4–36% of RCC individuals. VTT may enter the renal vein (the most common location), inferior vena cava (IVC), or even the heart [3, 4, 5]. The presence of VTT has a strong effect on RCC patient prognosis because VTT is associated with less favorable cancer-related outcomes, extensive surgical procedures (including often cardiac surgery) and particular complications (e.g., lymphocele, thrombosis). In the absence of metastases, aggressive surgical treatment with intention to cure was associated with 5-year survival rates of 40–68% [6, 7].

To predict survival of patients with RCC, four groups of prognostic factors (anatomical, histological, clinical, molecular) have been identified. Among the four groups, pathological evaluation was the strongest predictor of survival of patients with RCC [8]. However, patients with RCC accompanied by VTT represent a unique population because of complex and multidisciplinary approach with individual classification systems [9]. Despite a relatively large body of literature on outcomes after radical surgery in patients with RCC and VTT, there remain controversies surrounding the prognostic significance

of histopathological features [10]. Numerous studies have investigated pathological stage, grade, histological subtype, nodal status, distant metastases, and fat invasion, yet findings are still debatable. Further, there are relatively few reports on the prognostic impact of urinary collecting system invasion (UCSI) in patients with RCC and VTT [9, 11]. The influence of UCSI has not been examined seriously, and the absence of study represents the greatest data paucity in histology-related prognosis of patients with RCC and VTT. Moreover, studies of all-stage RCC patients suggest that UCSI is associated with poor long-term outcome [12]. Prognosis of patients affected by RCC accompanied by VTT is even more challenging. Thus, to clarify the status of UCSI as a prognostic factor in a unique population of RCC-VTT patients, we analyzed the effect of UCSI on survival of patients with RCC and VTT.

MATERIAL AND METHODS

This study was a retrospective, single-center investigation. Data were extracted from a prospectively maintained database. We included 711 patients with RCC treated with partial, radical, or cytoreductive nephrectomy between 2007 and 2016 (KBET/101/B/2013). In this group, 114 individuals had RCC with concomitant VTT.

Preoperative evaluation

We used the TNM and the Neves and Zincke classification systems to assess the expanse of the VTT because these scales are used widely in research and routine clinical practice for patients with RCC and VTT [13, 14]. Computed tomography (CT) or magnetic resonance angiography with pre- and multiphasic post-contrast images were used to evaluate the degree of venous involvement (i.e. VTT level) in all patients. Volumetric datasets provided by CT scanners were reconstructed in multiple planes with variable slice thickness, preserving image quality to better investigate thrombus level. In patients with thrombus affecting the heart, a transoesophageal echocardiography was also performed. Chest CT or X-ray were used to detect chest metastases. Alternative imaging techniques with different imaging protocols or other tests, including brain CT and bone scans, were performed when indicated by the clinical scenario.

Surgery

All the included patients had been treated with radical or cytoreductive nephrectomy combined with thrombectomy. The expansion of the VTT reflected the surgical approach. Therefore, a laparoscopic approach or flank incision was used for level 0 of the VTT. In patients with VTT levels from I to IV, surgery was initiated with the chevron incision. Often, in this patient subgroup, extracorporeal circulation was considered to maintain dissemination of blood and body oxygen content. If cardiopulmonary bypass with or without hypothermic cardiac arrest was required, the incision was cranially increased, and a sternotomy was performed. This maneuver was also implemented if the surgeon needed to prepare and mobilize the liver for suprahepatic control of the IVC. All procedures were performed by a single surgical team. In high level VTT, cardiothoracic surgeons were also involved.

Pathological findings

Histopathological reports were retrieved from patients' medical records. Tumor size was evaluated on fixed pathologic specimens. If needed, the TNM staging was reconsidered according to the 2009 Union for International Cancer Control/American Joint Committee on Cancer TNM staging system [14]. Similarly, when the TNM was not clear, the histological slides were re-examined by a uropathologist blinded to the patient characteristics and outcome.

Follow-up after surgery

In this study, the overall survival (OS) was calculated from the date of surgery to the date of death from any cause or last follow-up. Because patients were sometimes followed outside of our institution, to acquire reliable data on their deaths, we applied for access to the Register of Births, Marriages and Deaths of the Polish Registry Office and access to the Death Register of the Polish Ministry of Health and Social Welfare.

Statistics

Patients were analyzed in terms of demographic factors, preoperative parameters, surgical factors, tumor histopathology, and oncological outcomes. The effect of UCSI from pathological reports on the study variables was assessed with Student's t test (or Welch test in the absence of variance homogeneity) or Mann-Whitney U test (if the Student's t-test could not be applied or for variables measured on the ordinal scale) and a test for two proportions. Spearman's rank correlation coefficient and multiple logistic regression analyses were used to assess the associations between parameters. Survival curves were es-

timated with the Kaplan-Meier estimator, and then the log-rank test was used to compare differences among survival curves. Statistical significance was considered when p value was <0.05. Data analysis was conducted with IBM SPSS Statistics, version 24.0 (IBM Corporation, Armonk, NY, USA).

RESULTS

We included 114 patients with concomitant RCC and VTT in our study. All patients had undergone radical or cytoreductive nephrectomy and tumor thrombectomy. Cardiopulmonary bypass with moderate hypothermic cardiac arrest was performed in 41 cases. We did not identify patients with neoadjuvant chemotherapy or embolization.

The mean age of the analyzed patients was 65.2 years (Table 1). There were more men than women (60% vs. 40%, respectively). Most patients were classified as pT3a (47; 41%). Twelve individuals (11%) were oncologically disseminated and 16 (14%) had positive lymph node involvement.

In our cohort, we found UCSI in 22 patients (19%). Table 1 presents the clinical and pathological details of the two subgroups classified as per UCSI status (i.e. UCSI vs. non-UCSI). Of note, demographic factors, clinical parameters, and pathological features were not statistically different between the two patient groups of different UCSI status (p >0.05).

Further analysis of the remaining histological features revealed that most patients had tumor size greater than 7 cm and clear cell RCC (Table 1). The most common Fuhrman grade was 3 and invasion of the venous wall by a thrombus was identified in 49 patients (43%). Table 2 further shows the distribution of the histopathological features classified as per VTT level and pathological T-stage.

Ten months was the median follow-up in our cohort (range: 1–150 months). At the last follow-up, 55 patients (48%) were alive, and they did not present any evidence of the disease. This circumstance was after a median time of 13 months from surgical treatment. The median and the mean OS were 10 months and 19 months, respectively (Table 3). For patients with UCSI, the median OS was 9 months, and it was 10 months for patients without UCSI. The OS curves of these two patient groups with opposite UCSI status were not statistically different (p = 0.698; Figure 1). The p value for 1-, 2-, 3-, and 5-year OS of patients with UCSI vs. without was 0.191, 0.599, 0.339, and 0.674, respectively. Further subgroup analysis of the mean and the median OS for metastatic patients with UCSI vs. without UCSI did not show any significant differences (mean OS of 6.33 months and median OS of 9.00 months with UCSI

Table 1. *Patient characteristics and descriptive statistics*

	Overall	Urinary collecting system invasion	
		Yes (N = 22)	No (N = 92)
Mean age, years ±SD (range)	65.2 ±10.6 (26–84)	62.1 ±9.0 (41–77)	65.9 ±10.8 (26–84)
Sex, n (%)			
Male	68 (60%)	17 (77%)	51 (55%)
Female	46 (40%)	5 (23%)	41 (45%)
Side, n (%)			
Right	75 (66%)	17 (77%)	58 (63%)
Left	39 (34%)	5 (23%)	34 (37%)
Tumor size, n (%)			
>7 cm	85 (75%)	19 (86%)	66 (72%)
<7 cm	29 (25%)	3 (14%)	26 (28%)
Tumor/kidney diameter rate, n (%)			
>0.5	88 (77%)	18 (82%)	70 (76%)
<0.5	26 (23%)	4 (18%)	22 (24%)
Histological subtype, n (%)			
Clear cell RCC	100 (88%)	20 (91%)	80 (87%)
Others	14 (12%)	2 (9%)	12 (13%)
Sarcomatoid features, n (%)			
Yes	7 (6%)	1 (5%)	6 (7%)
No	107 (94%)	21 (95%)	86 (93%)
Fuhrman grade, n (%)			
1	4 (4%)	1 (5%)	3 (3%)
2	39 (34%)	5 (23%)	34 (37%)
3	40 (35%)	10 (45%)	30 (33%)
4	22 (19%)	6 (27%)	16 (17%)
Tumour necrosis, n (%)			
Yes	33 (29%)	9 (41%)	24 (26%)
No	81 (71%)	13 (59%)	68 (74%)
Surgical margin status, n (%)			
Positive	16 (14%)	4 (18%)	12 (13%)
Negative	98 (86%)	18 (82%)	80 (87%)
Perinephric fat invasion, n (%)			
Yes	74 (65%)	18 (82%)	56 (61%)
No	40 (35%)	4 (18%)	36 (39%)
Venous wall cancer invasion, n (%)			
Yes	49 (43%)	11 (50%)	38 (41%)
No	65 (57%)	11 (50%)	54 (59%)
Renal vein outlet invasion, n (%)			
Yes	5 (4%)	2 (9%)	3 (3%)
No	109 (96%)	20 (91%)	89 (97%)
VTT level, n (%)			
0	35 (31%)	3 (14%)	32 (35%)
I	13 (11%)	2 (9%)	11 (12%)
II	15 (13%)	3 (14%)	12 (13%)
III	15 (13%)	5 (23%)	10 (11%)
IV	36 (32%)	9 (41%)	27 (29%)
pT stage, n (%)			
pT3a	47 (41%)	6 (27%)	41 (45%)
pT3b	26 (23%)	6 (27%)	20 (22%)
pT3c	33 (29%)	7 (32%)	26 (28%)
pT4	8 (7%)	3 (14%)	5 (5%)
Nodal status			
pN0/cN0	98 (84%)	18 (82%)	80 (87%)
pN+	16 (16%)	4 (18%)	12 (13%)
Distant metastases			
cM0	102 (89%)	19 (86%)	83 (90%)
cM1	12 (11%)	3 (14%)	9 (10%)

n – number of patients; SD – standard deviation; RCC – renal cell carcinoma; VTT – venous tumour thrombus; pT stage – pathological tumour stage; c – clinical; p – pathological; N – lymph nodes; M – distant metastases

Table 2. *The distribution of selected histopathological features classified as per the venous tumour thrombus level and pathological T-stage*

	Overall	VTT level					Pathological T-stage			
		0	I	II	III	IV	pT3a	pT3b	pT3c	pT4
Mean age, years ±SD (range)	65.2 ±10.6 (26–84)	64 ±13.4 (26–84)	68.5 ±6.7 (55–83)	62.5 ±10.9 (39–80)	66.5 ±8.9 (49–80)	65.6 ±9 (44–79)	63.2 ±12.4 (26–84)	66.9 ±8.7 (49–83)	65.5 ±9.2 (44–79)	69.5 ±8.5 (55–80)
Sex, n (%)										
Male	68 (60%)	17 (49%)	5 (38%)	12 (80%)	9 (60%)	25 (69%)	23 (49%)	17 (65%)	23 (70%)	5 (63%)
Female	46 (40%)	18 (51%)	8 (62%)	3 (20%)	6 (40%)	11 (31%)	24 (51%)	9 (35%)	10 (30%)	3 (37%)
Side, n (%)										
Right	75 (66%)	20 (57%)	8 (62%)	9 (60%)	13 (87%)	30 (83%)	29 (62%)	18 (69%)	22 (67%)	6 (75%)
Left	39 (34%)	15 (43%)	5 (38%)	6 (40%)	2 (13%)	6 (17%)	18 (38%)	8 (31%)	11 (33%)	2 (25%)
Tumor size, n (%)										
>7 cm	85 (75%)	18 (51%)	11 (85%)	10 (67%)	12 (80%)	34 (94%)	27 (57%)	21 (81%)	30 (91%)	7 (88%)
<7 cm	29 (25%)	17 (49%)	2 (15%)	5 (33%)	3 (20%)	2 (6%)	20 (43%)	5 (19%)	3 (9%)	1 (12%)
Tumor/kidney diameter rate, n (%)										
>0.5	88 (77%)	22 (63%)	10 (77%)	12 (80%)	13 (87%)	31 (86%)	30 (64%)	23 (88%)	29 (88%)	6 (75%)
<0.5	26 (23%)	13 (37%)	3 (23%)	3 (20%)	2 (13%)	5 (14%)	17 (36%)	3 (12%)	4 (12%)	2 (25%)
Histological subtype, n (%)										
Clear cell RCC	100 (88%)	28 (80%)	10 (77%)	11 (73%)	15 (100%)	36 (100%)	37 (79%)	23 (88%)	33 (100%)	7 (88%)
Others	14 (12%)	7 (20%)	3 (23%)	4 (27%)	0	0	10 (21%)	3 (12%)	0	1 (12%)
Sarcomatoid features, n (%)										
Yes	7 (6%)	4 (11%)	0	2 (13%)	0	1 (3%)	4 (9%)	1 (4%)	1 (3%)	1 (12%)
Fuhrman grade, n (%)										
1	4 (4%)	2 (6%)	0	0	2 (13%)	0	2 (4%)	1 (4%)	1 (3%)	0
2	39 (34%)	7 (20%)	4 (31%)	5 (33%)	5 (33%)	18 (50%)	10 (21%)	8 (31%)	19 (58%)	2 (25%)
3	40 (35%)	13 (37%)	5 (38%)	2 (13%)	6 (40%)	14 (39%)	13 (28%)	10 (38%)	12 (36%)	5 (63%)
4	22 (19%)	6 (17%)	3 (23%)	7 (47%)	2 (13%)	4 (11%)	16 (34%)	4 (15%)	1 (3%)	1 (12%)
Tumour necrosis, n (%)										
Yes	33 (29%)	14 (40%)	7 (54%)	2 (13%)	4 (27%)	6 (17%)	15 (32%)	11 (42%)	5 (15%)	2 (25%)
No	81 (71%)	21 (60%)	6 (46%)	13 (87%)	11 (73%)	30 (83%)	32 (68%)	15 (58%)	28 (85%)	6 (75%)
Surgical margin status, n (%)										
Positive	16 (14%)	2 (6%)	3 (23%)	2 (13%)	2 (13%)	7 (19%)	4 (9%)	4 (15%)	5 (15%)	2 (25%)
Negative	98 (86%)	33 (94%)	10 (77%)	13 (87%)	13 (87%)	29 (81%)	43 (91%)	22 (85%)	28 (85%)	6 (75%)
Perinephric fat invasion, n (%)										
Yes	74 (65%)	19 (54%)	9 (69%)	11 (73%)	9 (60%)	26 (72%)	28 (60%)	16 (62%)	22 (67%)	8 (100%)
No	40 (35%)	16 (46%)	4 (31%)	4 (27%)	6 (40%)	10 (28%)	19 (40%)	10 (38%)	11 (33%)	0
Venous wall cancer invasion, n (%)										
Yes	49 (43%)	3 (9%)	7 (54%)	10 (67%)	4 (27%)	25 (72%)	11 (23%)	10 (38%)	22 (67%)	6 (75%)
No	65 (57%)	32 (91%)	6 (46%)	5 (33%)	11 (73%)	11 (28%)	36 (77%)	16 (62%)	11 (33%)	2 (25%)
Urinary collecting system invasion, n (%)										
Yes	22 (19%)	3 (9%)	2 (15%)	3 (20%)	5 (33%)	9 (25%)	6 (13%)	6 (23%)	7 (21%)	3 (37%)
No	92 (81%)	32 (91%)	11 (85%)	12 (80%)	10 (67%)	27 (75%)	41 (87%)	20 (77%)	26 (79%)	5 (63%)
Renal vein outlet invasion, n (%)										
Yes	5 (4%)	0	2 (15%)	0	0	3 (8%)	2 (4%)	0	2 (6%)	1 (12%)
No	109 (96%)	35 (100%)	11 (85%)	15 (100%)	15 (100%)	33 (92%)	45 (96%)	26 (100%)	31 (94%)	7 (88%)
Nodal status										
pN0/cN0	98 (84%)	30 (86%)	12 (92%)	10 (67%)	15 (100%)	31 (86%)	40 (85%)	25 (96%)	28 (85%)	5 (63%)
pN+	16 (16%)	5 (14%)	1 (8%)	5 (33%)	0	5 (14%)	7 (15%)	1 (4%)	5 (15%)	3 (37%)
Distant metastases										
cM0	102 (89%)	33 (94%)	12 (92%)	9 (60%)	13 (87%)	35 (97%)	40 (85%)	24 (92%)	32 (97%)	6 (75%)
cM1	12 (11%)	2 (6%)	1 (8%)	6 (40%)	2 (13%)	1 (3%)	7 (15%)	2 (8%)	1 (3%)	2 (25%)

n – number of patients; SD – standard deviation; RCC – renal cell carcinoma; VTT – venous tumour thrombus; pT stage – pathological tumour stage; c – clinical; p – pathological; N – lymph nodes; M – distant metastases

vs. mean OS of 8.00 months and median OS of 7.00 months without UCSI; p = 0.458).

Among the remaining histopathological features, the median OS was decreased for patients with non-clear cell RCC, sarcomatoid features, low Fuhrman grade, tumor necrosis, and positive surgical margins. However, in the univariate and multivariate analyses, only the Fuhrman grade and the status of surgical margins

Table 3. *Median and mean overall survival in patients with renal cell carcinoma and venous tumour thrombus*

	Mean OS ±SD ±SE	Median OS ±SE
Overall	19 ±26 ±0.23	10 ±0.29
Tumor size		
>7 cm	18 ±22 ±0.26	10 ±0.33
<7 cm	22 ±35 ±1.21	8 ±1.52
Tumor/kidney diameter rate		
>0.5	17 ±23 ±0.35	9 ±0.44
<0.5	11 ±12 ±0.67	8 ±0.84
Histological subtype		
Clear cell RCC	21 ±27 ±0.27	11 ±0.34
Others	6 ±5 ±0.36	3 ±0.45
Sarcomatoid features		
Yes	5 ±8 ±1.14	3 ±1.43
No	20 ±27 ±0.25	10 ±0.31
Fuhrman grade		
1	29 ±2 ±8	21 ±10.03
2	22 ±26 ±0.67	14 ±0.84
3	17 ±18 ±0.45	10 ±0.56
4	6 ±5 ±0.23	4 ±0.29
Tumour necrosis		
Yes	15 ±19 ±0.58	6 ±0.73
No	20 ±28 ±0.35	10 ±0.44
Surgical margin status		
Positive	6 ±9 ±0.6	3 ±0.75
Negative	21 ±28 ±0.29	13 ±0.36
Perinephric fat invasion		
Yes	18 ±22 ±0.3	11 ±0.38
No	21 ±32 ±0.8	9 ±1
Venous wall cancer invasion		
Yes	17 ±17 ±0.35	14 ±0.44
No	20 ±31 ±0.48	8 ±0.6
Urinary collecting system invasion		
Yes	23 ±34 ±1.55	9 ±1.94
No	18 ±24 ±0.26	10 ±0.33
Renal vein outlet invasion		
Yes	12 ±12 ±2.4	9 ±3
No	19 ±27 ±0.25	10 ±0.31
Nodal status		
pN0/cN0	20 ±28 ±0.29	10 ±0.36
pN+	13 ±13 ±0.81	9 ±1.02
Distant metastases		
cM0	20 ±27 ±0.26	10 ±0.33
cM1	8 ±5 ±0.42	8 ±0.53

OS – overall survival; SD – standard deviation; SE – standard error; RCC – renal cell carcinoma; c – clinical; p – pathological; N – lymph nodes; M – distant metastases

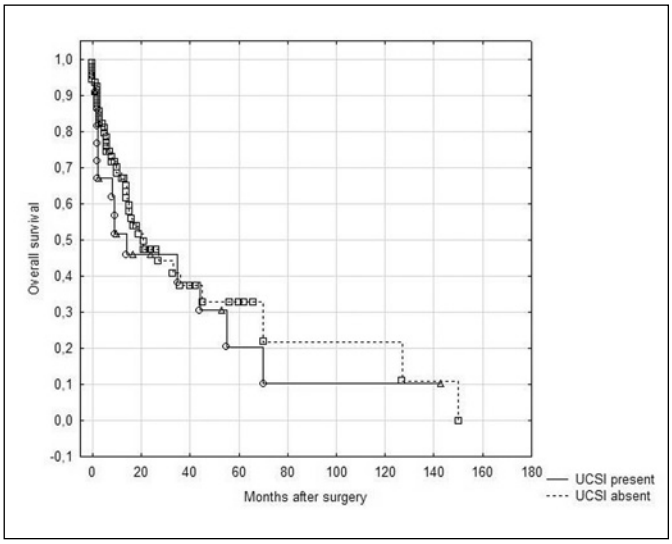

Figure 1. *Association between urinary collecting system invasion (UCSI) and clinical outcome in all included patients. The overall survival (OS) curves of these two patient groups with opposite UCSI status were not statistically different (p = 0.698).*

were statistically significant predictors of OS. We did not find any survival effect for UCSI, pathological tumor stage, tumor thrombus level, lymph node status, distant metastases, tumor side, histological tumor subtype, tumor necrosis, invasion of the venous wall by a thrombus, and tumor fat invasion.

DISCUSSION

We have comprehensively analyzed prognostic histological features of concurrent RCC and VTT with emphasis on UCSI in patients treated with nephrectomy and thrombectomy. Although investigators have analyzed the effects of histological features on survival of such patients, the influence of UCSI has not been examined seriously, and this lack of attention is the greatest data gap in histology-related prognosis of patients with RCC and VTT.

Chen et al., in a meta-analysis, found that UCSI had a significant negative impact on OS and recurrence-free survival in RCC patients, and UCSI predicted cancer-specific survival [15]. Thus, RCC patients with invasion of collecting system should receive greater attention from clinicians and pathologists because RCC patients require close follow-up for their poor prognoses. However, a further subgroup analysis suggested that UCSI was not significantly associated with poor cancer-specific survival with stage T3–T4 tumors. More recently, Chen et al. found that UCSI was an independent prognostic factor in pT3 RCC patients [16]. Unfortunately, the study authors neither performed a subgroup analysis for different T3-stages nor did they report the number of patients with RCC accompanied by VTT. Results presented by Bailey et al. concurred with the findings of Chen et al [12]. They evaluated the prognostic significance of UCSI in 859 patients with clear cell RCC, 325 patients with pT3a stage, 97 with pT3b, and 30 with pT3c. The authors demonstrated the significance of UCSI in both univariate and multivariate analyses of the pT3 patients. Nevertheless, these investigators also failed to report the number of patients with VTT, and they did not perform a statistical analysis of this specific group.

Currently, there are only four published studies that investigated the effect of UCSI on survival of patients with RCC accompanied by VTT. These studies produced conflicting results. Klatte et al. analyzed 321 patients with RCC accompanied by gross extension into the venous system [17]. Their analysis included 166 patients with VTT within renal vein, 137 patients with IVC involvement, and 18 patients with tumor thrombus within the atrium. The investigators concluded that UCSI significantly affected disease-specific survival. However, the authors did not prove this correlation in a multivariate regression analysis. Thus, UCSI was not independently associated with a disease-specific survival. Gu et al. proposed a post-operative nomogram for OS in patients with RCC and VTT [18]. They analyzed 185 patients, including 109 patients with VTT in the renal vein, 68 patients with VTT in infrahepatic IVC, and only 8 patients with VTT in suprahepatic IVC. Among different prognostic factors for OS, the authors included UCSI. Notably, the results for patients with high level VTT were grossly limited because of a small sample size of patients with VTT involving suprahepatic IVC (i.e., the sample included 3 patients (1.6%) with VTT in the IVC above the hepatic veins but below the diaphragm and 5 patients (2.7%) with VTT in the IVC above the diaphragm). This small sample size may have led to inherent selection bias and uncontrolled confounding factors. The nomogram also lacked external validation; only internal validation was performed. Sameh et al. assessed recurrence pattern in patients with locally advanced RCC [19]. Their group of 112 patients included 64 cases with VTT. Renal vein was affected in 34 cases, infrahepatic IVC in 23 cases, and suprahepatic in 7 patients. Even though their statistical analyses revealed that UCSI had no effect on patient survival, the authors' conclusion was based on comparison of all the patients. The authors did not perform a subgroup analysis of patients affected by both RCC and VTT versus patients without VTT. Chen et al. also investigated the impact of renal pelvis invasion on survival in patients with RCC and VTT [20]. Fifty-three patients had level 0 VTT, 16 level I, 11 level II, and 6 level III. No patients had level IV VTT. The authors did not find any correlation between renal pelvis invasion and patient survival.

In our study, we found that UCSI had no impact on prognosis of patients with RCC and VTT, thus, UCSI should not serve as a prognostic marker of survival in this specific population. Further subgroup analysis of metastasized and non-metastasized patients showed the same results for each subgroup. Moreover, of all the studies that have tested the effect of UCSI on survival, our analysis included the largest number of individuals with level 4 VTT.

In accordance with published data, our study confirmed the impact of Fuhrman grade and status of surgical margins on survival [21, 22]. Our results also agree with studies by Ficarra et al. and Patard et al. [23, 24]. Tilki et al., in their large international retrospective analysis, further confirmed that Fuhrman grade was associated with cancer-specific survival (the surgical margin status was not analyzed) [25].

Our study was not free from limitations. The study was a retrospective analysis with a one-institution design. Nevertheless, we used the data from a prospectively maintained database. We recognize that the included patients represented a highly selected cohort, treated at a single, high-volume academic center. This circumstance likely accounts for the relatively high percentage of patients with upper-level VTT in our study. We also did not identify patients with neoadjuvant chemotherapy or embolization. Although our sample size was large enough for powerful statistical analysis, given the relative rarity of some histological features, it is possible that still larger patient numbers would reveal significant differences in survival. In addition, we did not conduct a centralized, same-pathologist review. However, expert genitourinary pathologists at our institution evaluated all samples according to common definitions. The relatively short-term follow-up was another limitation because it may have limited interpretation of outcomes. After surgery, follow-up was executed at the discretion of the urologists and medical oncologists. Because the further treatment differed among consultant physicians (metastasectomy, immunotherapy, targeted therapy, chemotherapy), we did not consider it in the analyses. Moreover, we used only OS as the endpoint in our study because the causes of death were not reliably determined for all patients. Without reliable information about cause of death, we could not accurately determine cancer-specific survival. Nonetheless, OS is considered the gold standard for cancer clinical analyses, and it is recommended as the most reliable cancer endpoint [26].

CONCLUSIONS

To summarize, this large cohort study provides distinctive data to determine the role of UCSI in patients RCC and VTT. Patients with or without UCSI did not show any difference in OS. Consequently, UCSI was not of significance in prediction of survival. Commonly used prognostic markers such as Fuhrman grade and status of surgical margins had greater importance in survival.

Accurate estimates of the likelihood of treatment success, complications, and long-term morbidity and mortality are essential for counselling of, and informed decision-making by, patients with urological malignancies, and these estimates guide cancer treatment. In RCC with VVT patients UCSI failed to predict OS. Hence, it should not be used in risk stratification models or as an aid in treatment decision-making.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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