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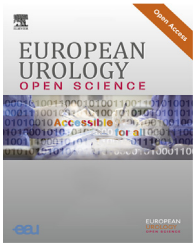

Urothelial Cancer

Survival and Long-term Effects of Kidney-sparing Surgery Versus Radical Nephroureterectomy on Kidney Function in Patients with Upper Urinary Tract Urothelial Carcinoma

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Abstract

Background: Current European Association of Urology (EAU) guidelines discriminate between high- and low-risk upper urinary tract urothelial carcinoma (UTUC) to determine treatment by means of radical nephroureterectomy (RNU) or kidney-sparing surgery (KSS).
Objective: To compare long-term oncological outcomes and renal function for patients with UTUC treated by RNU versus KSS.
Design, setting, and participants: A retrospective cohort study, including 186 renal units with nonmetastatic UTUC treated in a tertiary referral centre between 2010 and 2021, was conducted.
Intervention: RNU, ureterorenoscopy, percutaneous tumour resection, and segmental ureteral resection.
Outcome measurements and statistical analysis: Recurrence-free survival, metastasis-free survival (MFS), overall survival (OS), cancer-specific survival (CSS), and renal function were analysed by means of the log-rank test and the independent-sample *t* test.
Results and limitations: OS was 71.1% for the RNU group and 81.9% for the KSS group. In a cohort matched for propensity weight based on EAU risk stratification progression-free survival (PFS; RNU 96.0%; KSS 86.0%), MFS (RNU 72.0%; KSS 84.0%), CSS (RNU 84.0%; KSS 86.0%), and OS (RNU 76.0%; KSS 76.0%) were all similar between both groups. No significant differences in renal function were seen at 2 and 5 yr after the intervention. Although this series represents the largest cohort of (high-risk) UTUC patients treated by means of KSS to date, it is not suitable for performing a multivariate analysis.
Conclusions: PFS, MFS, CSS, and OS were all comparable when analysing the RNU and KSS groups. Similar results for groups with evenly distributed risk factors

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and a large percentage of high-risk disease suggest that current risk stratification might not be accurate in discriminating low-risk from high-risk disease.

Patient summary: In this report, we looked at outcomes for upper urinary tract urothelial carcinoma in a specialised hospital. We conclude that kidney-sparing surgery and radical nephroureterectomy have comparable outcomes and that risk factors for worse outcome might not be identified correctly.

1. Introduction

Urothelial carcinoma has a high incidence and prevalence; however, only 5–10% of these tumours are located in the upper urinary tract [1]. Owing to this rarity, knowledge on disease management of upper urinary tract urothelial carcinoma (UTUC) has historically been extrapolated from what is known from urothelial carcinoma of the bladder (UCB). Nonetheless, several studies indicate that UTUC shows significant aetiological, practical, and genomic differences when compared with UCB. Therefore, a different approach seems rational to achieve optimal management.

The gold standard treatment for UTUC is by radical nephroureterectomy (RNU). In a selected group of patients, kidney-sparing surgery (KSS) can be offered according to current guidelines [2]. The guidelines stress out the importance of risk stratification in patients with UTUC. Patients with low-risk disease or with an imperative indication for minimally invasive treatment can be offered KSS by means of ureteroscopy (URS) [3–5]. Alternative approaches within KSS consist of percutaneous tumour resection (PCTR) in case treatment by means of URS is not possible and segmental ureteral resection (SUR), which can be applied to both low- and high-grade tumours located in the distal ureter.

In high-risk disease, RNU is still the recommended choice of treatment. Although KSS has been proved to be safe and effective, European Association of Urology (EAU) guidelines underline the lack of evidence on patient selection based on risk stratification. The above-named characteristics demand a personalised approach and substantiate the significance of shared decision-making.

In the latest guidelines, KSS by URS has gained a more prominent position with strong recommendations in low-risk disease based on available data [6]. However, high-level evidence on the best treatment strategy concerning long-term oncological and functional outcomes is lacking. Prospective randomised trials are often a nonstarter in low-prevalence diseases. In addition, studies with standardised treatment protocols and long-term follow-up data are scarce due to both the rarity and the late onset of the disease.

In this study, we report and compare the oncological outcomes and renal function of patients treated by KSS and RNU for UTUC in a tertiary referral centre.

2. Patients and methods

In this retrospective single-centre cohort study, we included 186 renal units in 180 patients with nonmetastatic UTUC from January 2010 until December 2020 treated in the Amsterdam UMC, location AMC. Eligible patients were selected through screening of the histopathological reports for UTUC for the following items: ureterorenoscopy, diagnostic ureterorenoscopy, PCTR, (laparoscopic) RNU, and (distal) ureterectomy. All eligible patients were informed about the study in writing and were given the opportunity to refuse participation in accordance with local guidelines of the medical ethical advisory board.

2.1. Objectives

The objective of this study was to compare long-term oncological outcomes and renal function for patients with UTUC treated by RNU versus KSS.

2.2. Inclusion criteria, treatment, and follow-up

Adult patients, aged ≥18 yr with histopathologically confirmed UTUC (by biopsy and/or resection specimen) without lymphogenic or haematogenous metastasis, and treated with RNU, SUR, PCTR, or URS were eligible for inclusion. Patients were managed, treated, and followed according to the local standard of practice based on the recommendations from the EAU guidelines over time. With the exception that KSS was also considered and often offered in high-risk disease based on size, multifocality, hydronephrosis, high-grade UCB, and, in case of an imperative indication, high-grade tumour in cytology or biopsy if the treatment was deemed feasible and effective during a multidisciplinary meeting.

2.3. Data collection

Data were collected from electronic patient files and stored into an encrypted database that was available only to the research team. Patient data were collected from first presentation to last follow-up, including data on presentation, the diagnostic process, treatment, and follow-up. All imaging data by computed tomography (CT) and magnetic resonance imaging (MRI) were re-examined by the researcher to conclude size, extent of invasion, and presence of hydronephrosis. Main study parameters include recurrence-free survival (RFS), progression-free survival (PFS), metastasis-free survival (MFS), overall survival (OS), cancer-specific survival (CSS), and kidney function. If there was any doubt regarding whether death was caused by comorbidities/old age or due to tumour progression, a consensus meeting was organised with the authors (J.B., G.K., H.B., and N.H.).

2.4. Statistical analysis

All data were summarised by descriptive statistics. Variables were described using mean and standard deviation for data with normal distribution, and median and interquartile range for skewed data. Frequency distributions of baseline characteristics, with an expected frequency of more than five, were compared with the Pearson χ^2 test. Oncological outcomes were analysed by means of Kaplan-Meier plots and the log rank test. Propensity scores were based on current EAU risk stratification and matched with a match tolerance of 0.05, with randomi-

sation of case order when drawing matches and with priority to exact matches. Differences in kidney function were investigated by means of the unpaired *t* test.

3. Results

3.1. Demographic characteristics

Included patients were predominantly males (72.6%), with a median age of 68.44 (±11.50) yr and a history of smoking (73.7%). The mean American Society of Anesthesiologists score was 2.03 (±0.65) and estimated glomerular filtration rate (eGFR) was 55.19 (±13.24) ml/min, and were comparable for the RNU and KSS groups. All demographic characteristics can be found in Table 1.

3.2. Tumour characteristics

Multifocality, invasive disease, hydronephrosis, and tumours >20 mm were found on CT scan in, respectively, 8.6%, 5.9%, 37.6%, and 58.6% of all cases. High-grade disease was found in 50.0% of all tumours. Significant differences were found in the distribution of tumour grade and invasiveness between the RNU and KSS groups (p = 0.000; Table 2). According to risk stratification in current EAU guidelines, 74.2% of all tumours treated with KSS and 93.8% of all tumours treated by means of RNU were considered to be of high risk.

3.3. Perioperative data

Adjuvant intravesical mitomycin C (MMC) was administered in 51.5% of all patients and in 52.7% of high-risk patients treated with RNU after initial treatment. None of the patients treated by means of KSS received MMC. The mean amount of procedures was 3.18 (standard deviation [SD] ± 2.21) for the RNU group and 8.76 (SD ±5.53) for the KSS group.

3.4. Survival

Intravesical recurrence was seen in 30.9% in the RNU group (mean time to recurrence 78.91 mo) and in 50.6% in the KSS group (mean time to recurrence 50.61 mo). Ipsilateral recurrence (in the ureteral stump) occurred in 12.4% of the RNU group (mean time to recurrence 115.80 mo) and 70.8% of the KSS group (mean time to recurrence 25.92 mo; Fig. 1).

Progression from low- to high-grade UTUC was seen in 4.1% of all tumours treated by means of RNU and in 13.5% of all tumours treated by means of KSS. The mean time to progression was 119.42 and 105.45 mo for the RNU and KSS groups, respectively (Fig. 1).

Metastases were seen in 33.0% in the RNU group and 13.5% in the KSS group. The mean time to metastasis was 76.69 and 108.69 mo for, respectively, the RNU and KSS groups.

OS (mortality rate: RNU 28.9%; KSS 19.1%) and CSS (mortality rate: RNU 20.6%; KSS 10.1%) were high after 11 yr. The mean time to death was 80.41 mo for the RNU group and 99.14 mo for the KSS group (Fig. 1).

3.5. Survival matched for propensity weight based on EAU risk stratification

After propensity score matching based on current EAU risk stratification with randomisation of case order when drawing matches and with priority to exact matches, a cohort of 100 patients was left. Of all tumours treated by means of RNU, 85% were considered to be of high risk in this propensity weighted cohort, as opposed to 90% of all tumours treated by means of KSS. In concordance with the forenamed method, all risk factors were distributed equally between both groups, as shown in Table 3.

Intravesical recurrence occurred in 32.0% of the RNU group (mean time to recurrence 69.14 mo) and 52.0% of the KSS group (mean time to recurrence 41.32 mo; log rank p = 0.029). Ipsilateral recurrence occurred in 8.0% (mean time to recurrence 93.85 mo) of the RNU group and 68.0% (mean time to recurrence 28.74 mo) of the high risk KSS group (log rank p = 0.000; Fig. 2).

In the RNU group, 4.0% showed progression in grade as opposed to 14.0% in the KSS group (log rank p = 0.147; Fig. 2). The mean time to progression was 73.39 and 103.38 mo for, respectively, the RNU and KSS groups.

Metastases were found in 28.0% in the RNU group as opposed to 18.0% in the KSS group (log rank p = 0.217; Fig. 2). The mean time to metastasis was 73.39 mo for the RNU group and 103.38 mo for the KSS group.

CSS (mortality rate: RNU 16.0% vs KSS 14.0%; log rank p = 0.490) and OS (mortality rate: RNU 24.0% vs KSS 24.0%; log rank p = 0.691) were similar in both groups (Fig. 2). The mean time to overall death was 77.76 mo for the RNU group versus 92.99 mo for the KSS group.

3.6. Renal function

Renal function was comparable at baseline for both the RNU group and the KSS group (eGFR p = 0.071). The greatest difference was seen during follow-up at 3 mo after intervention (eGFR p = 0.000). No significant difference was seen at 2 (p = 0.081) and 5 yr (p = 0.304) after intervention (Fig. 3).

4. Discussion

In this article, we describe the outcomes of patients with UTUC treated with either RNU or KSS.

To the best of our knowledge, this series represents the largest cohort of (high-risk) patients treated with KSS. We concluded that OS and CSS were relatively high after 11 yr. Furthermore, we compared high-risk UTUC treated with RNU or KSS matched for propensity weight based on EAU risk stratification. PFS, MFS, CSS, and OS were all similar when comparing the RNU group with the KSS group in the matched propensity weight cohort, whereas intravesical RFS and ipsilateral RFS were significantly higher in the RNU group.

Table 1 – Demographic characteristics

Characteristic	Overall (*n* = 186)	Radical nephroureterectomy (*n* = 97)	Kidney-sparing surgery (*n* = 89)	*p* value
Gender, *n* (%)				
Male	135 (72.6)	67 (69.1)	68 (76.4)	
Female	51 (27.4)	30 (30.9)	21 (23.6)	
Age (yr)	68.44 (±11.50)	68.77 (±10.14)	68.08 (±12.86)	
BMI (kg/m^2)	26.60 (±0.34)	26.37 (±0.48)	26.85 (±0.49)	
ASA score	2.03 (±0.65)	2.05 (±0.68)	2.00 (±0.60)	
Creatinine (μmol/l)	101.90 (±3.19)	107.66 (±4.84)	95.63 (±4.01)	
eGFR (ml/min/1.73 m^2)	55.19 (±13.24)	53.52 (±13.57)	57.02 (±12.69)	
History, *n* (%)				
Low-grade UCB	34 (18.3)	12 (12.4)	22 (24.7)	0.037
High-grade UCB	19 (10.2)	11 (11.3)	8 (8.9)	
Cystectomy	5 (2.7)	3 (3.1)	2 (2.2)	
Low-grade contralateral UTUC	9 (4.8)	4 (4.1)	5 (5.6)	
High-grade contralateral UTUC	8 (4.3)	1 (1.0)	7 (5.6)	
(Functional) solitary kidney	27 (14.5)	12 (12.4)	15 (16.9)	
Cardiovascular disease	97 (52.2)	50 (51.5)	47 (53.4)	
Diabetes mellitus	40 (21.5)	20 (20.6)	20 (22.5)	
CVA/TIA	15 (8.1)	8 (8.2)	7 (7.9)	
COPD	19 (10.2)	11 (11.3)	8 (9.0)	
Malignancy	75 (40.3)	35 (36.1)	40 (44.9)	
Smoking	137 (73.7)	70 (72.2)	67 (75.3)	
Burden according to Amsterdam II criteria	12 (6.5)	5 (5.2)	7 (7.9)	
Lynch	12 (6.5)	4 (4.1)	8 (9.0)	
Employment in chemical industry	18 (9.7)	7 (7.2)	11 (12.4)	

ASA = American Society of Anesthesiologists; BMI = body mass index; COPD = chronic obstructive pulmonary disease; CVA = cerebrovascular accident; eGFR = estimated glomerular filtration rate; *n* = number of renal units; TIA = transient ischaemic attack; UCB = urothelial cancer of the bladder; UTUC = upper tract urothelial carcinoma.

Table 2 – Tumour characteristics

Characteristic	Overall (*n* = 186)	Radical nephroureterectomy (*n* = 97)	Kidney-sparing surgery (*n* = 89)	*p* value
CT scan, *n* (%)				
Suspicion of UTUC	167 (89.8)	90 (92.8)	77 (86.5)	
Distal ureter [a]	54 (29.0)	30 (30.9)	24 (27.0)	
Proximal ureter [a]	24 (12.9)	12 (12.4)	12 (13.5)	
Renal pelvis [a]	57 (30.6)	31 (32.0)	26 (29.2)	
Lower pole [a]	5 (2.7)	4 (4.1)	1 (1.1)	
Interpolar pole [a]	5 (2.7)	1 (1.0)	4 (4.5)	
Upper pole [a]	21 (11.3)	11 (11.3)	10 (11.2)	
Unifocal disease	151 (81.2)	78 (80.4)	73 (82.0)	
Multifocal disease	16 (8.6)	11 (11.3)	5 (5.6)	
Invasive disease	11 (5.9)	9 (9.3)	2 (2.2)	
Hydronephrosis	70 (37.6)	47 (48.5)	23 (25.8)	0.026
Tumour >2 cm	109 (58.6)	68 (70.1)	41 (46.1)	0.001
Grade [b], *n* (%)				
High grade	93 (50.0)	71 (73.2)	22 (24.7)	0
Low grade	96 (51.6)	29 (31.5)	67 (75.3)	0
T stage, *n* (%)				
Ta	126 (67.7)	49 (50.5)	77 (86.5)	0
T1	20 (10.8)	16 (16.5)	4 (4.5)	0
T2	14 (7.5)	9 (9.3)	5 (5.6)	
T3	25 (13.4)	22 (22.7)	3 (3.4)	0
T4	1 (0.5)	1 (1.0)	0 (0.0)	
Bilateral disease, *n* (%)	7 (3.8)	2 (2.1)	5 (5.6)	
Concomitant bladder cancer, *n* (%)	24 (12.9)	12 (12.4)	12 (13.5)	0
High risk based on EAU guideline, *n* (%)	155 (83.3)	91 (93.8)	66 (74.2)	0
Follow-up (mo), mean (min. – max.)	42.33 (0–126)	37.29 (0–126)	47.81 (4–126)	0.029

CT = computed tomography; EAU = European Association of Urology; KSS = kidney-sparing surgery; max. = maximum; min. = minimum; *n* = number of renal units; RNU = radical nephroureterectomy; UTUC = upper tract urothelial carcinoma.

[a] Location is based on the highest tumour volume.

[b] Either based on biopsy in case of KSS or RNU specimen in case of RNU. The cumulated percentage is >100% because of multiple biopsies with different tumour grades in a selected group of patients. Risk stratification was based on the highest grade.

4.1. *Comparison with earlier studies*

To the best of our knowledge, this article is the first to compare outcomes within a cohort matched for propensity weight based on EAU risk stratification in patients with UTUC treated by RNU versus KSS. Furthermore, this cohort is unique because of the relatively high number of high-risk patients in both groups. Previous literature comparing these treatment modalities either focused on all patients treated for UTUC or divided groups based on tumour grade or invasion.

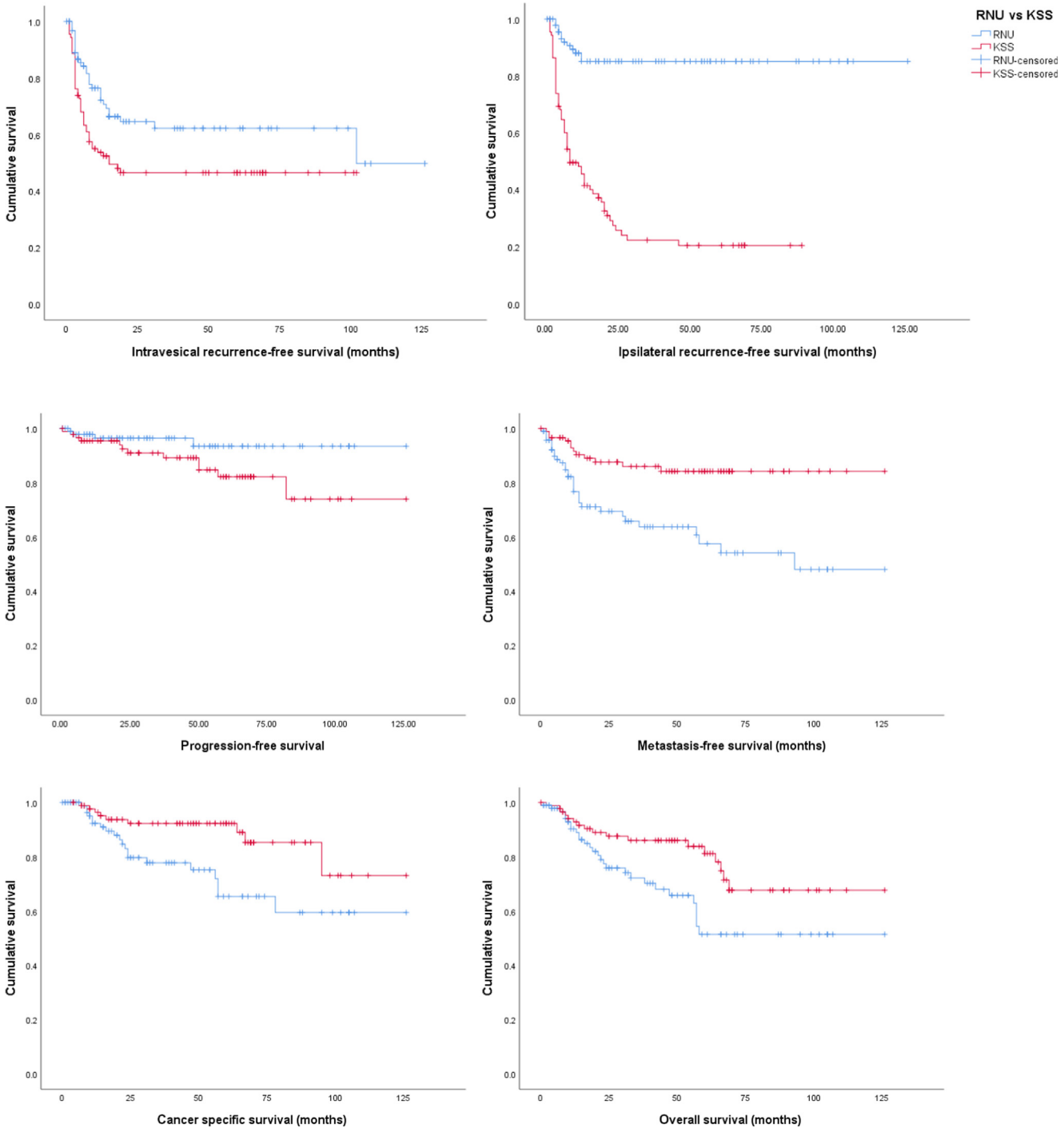

Fig. 1 – Survival for RNU and KSS. Numbers at risk after 11 yr are as follows: intravesical recurrence—number at risk RNU 49.7 and number at risk KSS 46.5; ipsilateral recurrence—number at risk RNU 88.3 and number at risk KSS 8.5; progression—number at risk RNU 93.5 and number at risk KSS 74.0; metastasis—number at risk RNU 48.1 and number at risk KSS 84.2; cancer specific—number at risk RNU 59.5 and number at risk KSS 74.1; and overall—number at risk RNU 51.5 and number at risk KSS 67.7. KSS = kidney-sparing surgery; RNU = radical nephroureterectomy.

Grasso et al [3] described oncological outcomes of the overall RNU group. They concluded that CSS and OS after 10 yr were 56.0% and 36.0%, respectively. These were lower than our results, showing CSS of 59.5% and OS of 51.5% within the whole RNU group. Differences can be explained by dissimilarities in study population in the RNU group as Grasso et al [3] included more T4 tumours (5.0% vs 1.0%), patients with positive lymph nodes (12.5% vs 0.0%), and two patients treated by SUR within the RNU group. The URS group consisted of patients with low-grade and mostly low-risk disease, or with a palliative treatment goal consisting of minimisation of hazardous haematuria. Therefore, the group described by Grasso et al [3] is difficult to compare with our study population.

Table 3 – Distribution of risk factors according to EAU risk stratification within propensity weighted cohort

	Radical nephroureterectomy (n = 50), n (%)	Kidney-sparing surgery (n = 50), n (%)	p value
High-grade tumour in biopsy	22 (44.0)	22 (44.0)	1.000
Invasive disease on CT scan	0 (0.0)	2 (4.0)	1.000
Tumour >2 cm	33 (66.0)	31 (62.0)	1.000
Multifocality on CT scan	2 (4.0)	1 (2.0)	1.000
Hydronephrosis	19 (38.0)	19 (38.0)	1.000
Cystectomy	1 (2.0)	0 (0.0)	1.000

CT = computed tomography.

Cutress et al [4] reported their oncological outcomes in patients with nonmetastatic UTUC treated with KSS. They reported CSS of 77.4% and OS of 40.3%. Patient population is comparable with the current study, except for T stage where we describe higher rates of T2 (0.0% vs 5.6%) and T3 (0.0% vs 3.4%) tumours in our study. Although CSS is comparable (CSS in the current study 75.1%), OS is considerably higher in our study (OS in the current study 67.7%). Looking at the descriptive characteristics in both cohorts, no clear explanation can be given for this difference. However, the median follow-up was longer than in the current study (54.0 vs 47.81 mo), which might explain the difference in OS.

A meta-analysis of studies analysing treatment modalities for UTUC showed CSS of 64–92% for the RNU group and 67–87% for the KSS group [7]. OS was 58–78% for the RNU group and 45–74% for the KSS group. They concluded that there was no significant difference in oncological outcomes for both groups. However, with I^2 of 78% and 63% for OS and CSS, respectively, heterogeneity of included studies is deemed substantial. This is predominantly based on the variety in follow-up regimen, small study populations, and a strong selection bias with regard to tumour invasiveness.

With regard to renal function, Singla et al [8] showed similar results with a mild decline in 118 patients undergoing RNU for UTUC from baseline (58.4 ml/min/1.73 m^2) to last follow-up (51.3 ml/min/1.73 m^2). Campi et al [9] analysed kidney function after 66 RNU procedures and showed a median decline of 15 ml/min/1.73 m^2 from baseline (61 ml/min/1.73 m^2) 3 mo after RNU (46 ml/min/1.73 m^2), similar to our results 3 mo after RNU (43 ml/min/1.73 m^2). These are somewhat lower than the results of Singla et al [8]. This could be explained by the time it takes for the contralateral kidney to compensate for the loss of renal function due to the removed kidney. Our results, however, most likely represent an underestimation of renal function as up until recently an eGFR above 60 ml/min/1.73 m^2 was expressed as >60 ml/min/1.73 m^2 in laboratory results, therefore limiting the upper limit to 60 as opposed to Singla et al's study [8], which used a limit of 90.

4.2. *Strengths, weaknesses, and interpretation*

One of the main strengths of this study is the relatively large population of high-risk tumours treated with KSS. According to EAU guidelines, high-risk disease ought to be treated by RNU in the absence of imperative arguments such as bilateral disease, a solitary kidney, or severe comorbidities. This progressive minimally invasive take on treating UTUC revealed insight on oncological outcomes in a group where outcomes were expected to be poor. This study showed and confirmed that guidelines on risk stratification in UTUC are based on limited evidence. As the guideline on UTUC is still relatively young and RNU was historically deemed the gold standard treatment, moving towards less strict criteria will take time and is performed with caution. Therefore, it is only natural when creating these guidelines that a conscientious approach is taken when it comes to risk stratification.

As presenting comparable survival data between the RNU and KSS groups with evenly distributed risk factors with a large number of high-risk patients is only a tip of the iceberg on further insights into correct risk stratification, a multivariate analysis is needed. Our data consisted of very few events (death, metastasis, or recurrence) to comply with statistical conditions to perform a multivariate analysis on predictive factors for worse oncological outcome.

Previous research predominantly showed differences in survival when analysing high-versus low-grade tumours as opposed to a subanalysis for other risk factors [3–5]. This might be a hint that different risk factors should be weighed discordantly and should not be viewed in a dichotomous on/off manner, but rather on a scale with different weights placed on both the favourable and the unfavourable side. Recently, a large international collaborative study by Marcq et al [10] tried to identify risk factors by performing multivariate regression analysis in 1214 patients with non–organ-confined UTUC (>pT2) as a primary endpoint. They concluded that it might be better to use a three-category system as opposed to a dichotomous system to stratify for risk. Predictors for progressing to more invasive disease consist of non–organ-confined disease ($\geq$cT3) on preoperative imaging (CT urography/MRI), large tumour size (>2 cm), a sessile tumour, the presence of ipsilateral hydronephrosis, high-grade cytology, and high-grade biopsy. However, the primary endpoint is progression instead of MFS or CSS. Furthermore, data from this database might not be applicable to other hospitals as these come from a high-volume tertiary referral centre.

Finally, by choosing KSS as a treatment modality, renal function will be spared, and this can prevent dialysis in case of a solitary kidney. However, meticulous and stringent

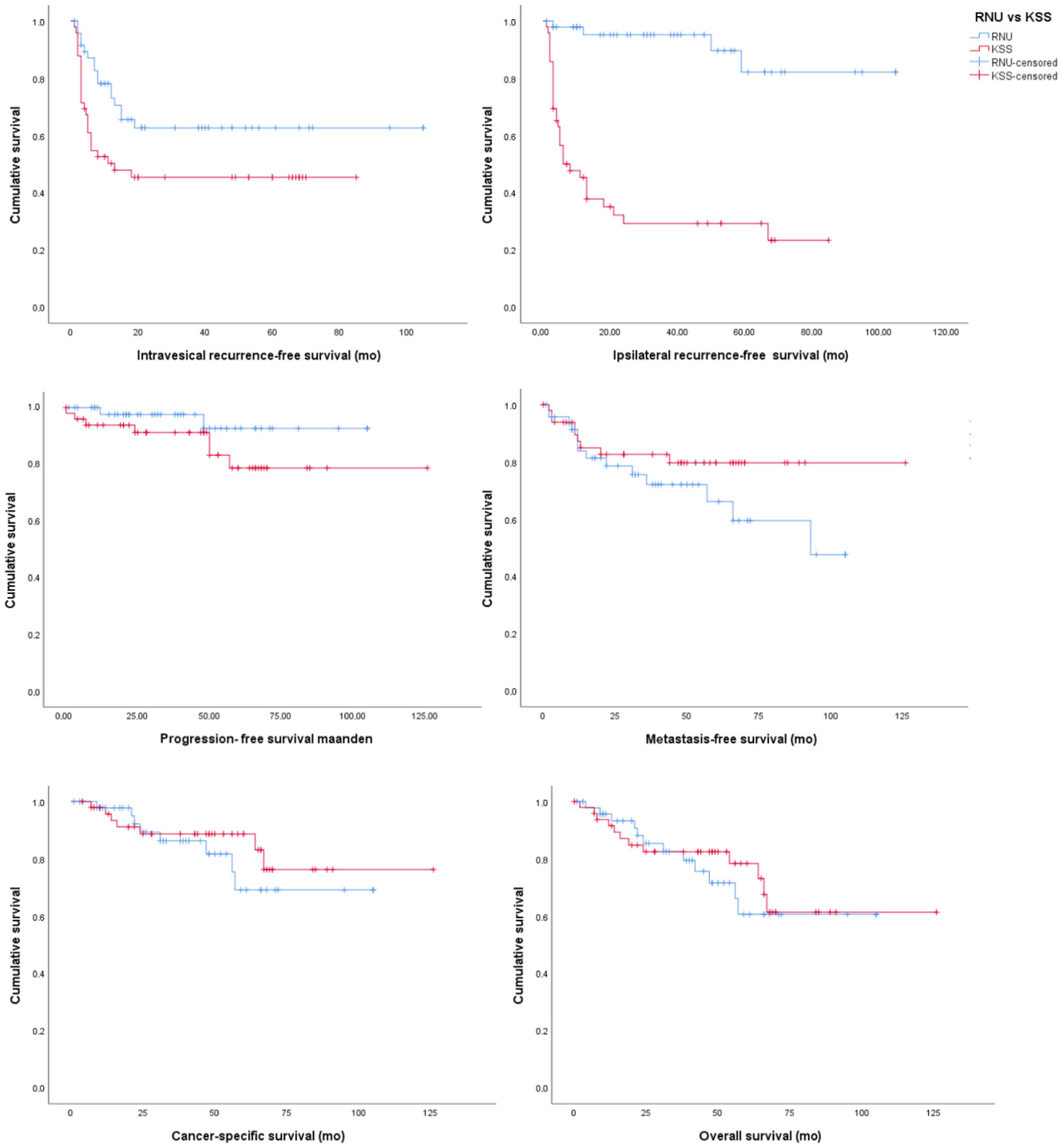

Fig. 2 – Survival in a cohort matched for propensity weight based on EAU risk stratification. Numbers at risk after 11 yr are as follows: intravesical recurrence-free survival—log rank $p = 0.029$, number at risk RNU 62.7, and number at risk KSS 54.6; ipsilateral recurrence-free survival—log rank $p < 0.0001$, number at risk RNU 82.2, and number at risk KSS 24.4; progression-free survival—log rank $p = 0.147$, number at risk RNU 92.7, and number at risk KSS 79.7; metastasis-free survival—log rank p = 0.217, number at risk RNU 47.6, and number at risk KSS 79.7; cancer-specific survival—log rank $p = 0.490$, number at risk RNU 69.1, and number at risk KSS 76.2; and overall survival—log rank $p = 0.691$, number at risk RNU 60.6, and number at risk KSS 61.4. KSS = kidney-sparing surgery; RNU = radical nephroureterectomy.

surveillance is absolutely mandatory, and this certainly applies for high-risk tumours. Comparable results for KSS and RNU, as presented in this study, are feasible only when a clearly defined follow-up protocol is applied by means of regular URS (second look at 6 wk and third look at 3 mo afterwards), cystoscopy, and CT urography. As shown in our results, there is a great difference in the number of procedures when comparing the RNU group (3.18 procedures) with the KSS group (8.76 procedures). The number of procedures as well as the confrontation of having a recurrence might influence quality of life or cause anxiety in patients treated for UTUC.

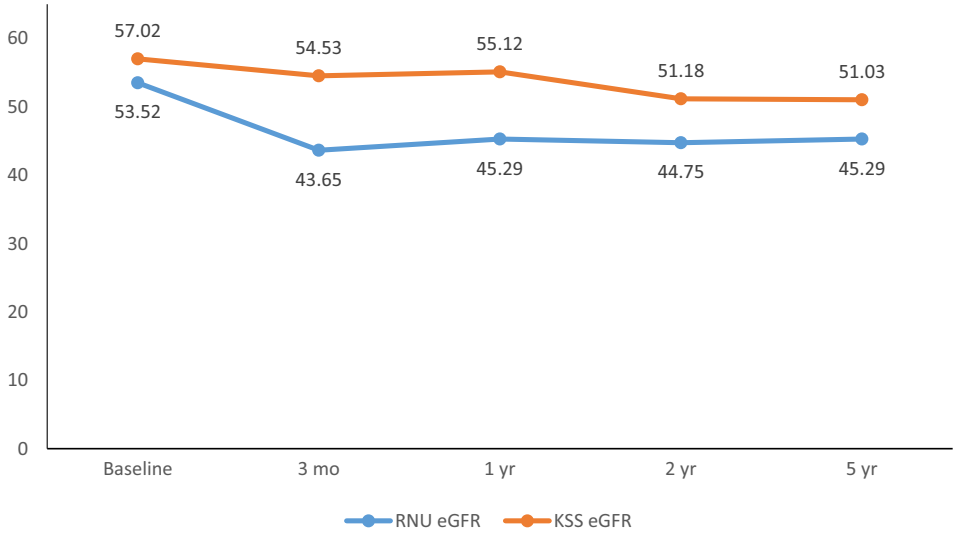

Fig. 3 – Renal function for patients treated with RNU or KSS over time. eGFR = estimated glomerular filtration rate; KSS = kidney-sparing surgery; RNU = radical nephroureterectomy.

5. Conclusions

At present, this series represents the largest cohort of (high-risk) UTUC patients treated with KSS. In this article, we concluded that OS and CSS were comparable with previous studies after 11 yr. Furthermore, we compared UTUC treated with RNU or KSS in a cohort with matched propensity weight based on EAU risk stratification. PFS, MFS, CSS, and OS were all comparable when analysing the RNU and KSS groups in this cohort. Similar results for groups with evenly distributed risk factors and a large percentage of high-risk disease suggest that current risk stratification might not be accurate in discriminating low- from high-risk disease. Subsequently, the adage that all high-risk tumours are best treated by means of RNU might be incorrect.

***Author contributions*:** Nora Hendriks had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Hendriks, Baard, Kamphuis, Beerlage.
Acquisition of data: Hendriks, Doherty.
Analysis and interpretation of data: Hendriks, Baard, Kamphuis, Beerlage.
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