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Post-Surgical Outcomes of Kidney-Sparing Surgery vs. Radical Nephroureterectomy for Upper-Tract Urothelial Cancer in a Propensity-Weighted Cohort

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Abstract

Objectives: In localized upper-tract urothelial carcinoma (UTUC), radical nephroureterectomy (RNU) represents the surgical gold standard, but kidney-sparing surgery (KSS) offers an alternative. The surgical perspective, including complications, remains understudied in this context. This study aimed to compare KSS and RNU, assess kidney function and survival, and identify the surgical risk factors. Methods: This retrospective analysis included UTUC patients undergoing KSS (n = 46) or RNU (n = 46) at a single center from 2016 to April 2024, matched by propensity scores. The primary endpoint was Clavien–Dindo complications. Other endpoints included Days Alive and Out of the Hospital within 30 days (DAOH30), changes in the eGFR, cancer-specific survival (CSS), and disease-free survival (DFS). A UTUC Surgery Risk Score was developed to identify the surgical risk factors for severe complications. Results: KSS was significantly associated with higher rates of Clavien–Dindo grades $\geq$ 3 (KSS: 14; RNU: 3). DAOH30 was significantly longer following RNU. The UTUC Surgery Risk Score, based on a non-endoscopic KSS approach, an ASA score $\geq$ 3, and preoperative creatinine > 0.9 mg/dL, was significantly associated with overall and severe complications and DAOH30 (both $p < 0.001$). KSS showed significantly better early postoperative eGFR preservation (+0.55 mL/min vs. −4.3 mL/min for RNU, $p = 0.015$). No significant differences were observed in the median CSS or DFS between the groups. Conclusions: KSS is associated with a higher rate of certain postoperative complications, but offers superior kidney function preservation, with comparable oncological outcomes to RNU. The novel UTUC Surgery Risk Score can aid in patient counseling and personalized decision-making prior to surgery.

Keywords: kidney-sparing surgery; radical nephroureterectomy; upper-tract urothelial cancer; UTUC; complications; kidney function; survival

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1. Introduction

Upper-tract urothelial cancer (UTUC) represents a subset of urothelial carcinoma, located in the renal pelvis or ureter. Although its incidence is rather low, UTUC is frequently diagnosed in a locally advanced or metastatic stage (≥T3 or N+ in 33–58%; M1 in 8–11%) [1,2]. Following surgery, bladder recurrence (22–47%) and/or progression to metastatic disease (10–23%) need to be monitored [3,4]. The established gold standard for localized UTUC is a radical nephroureterectomy (RNU), as recommended by international guidelines [3,5]. However, RNU necessitates the loss of a renal unit, leading to the development of kidney-sparing surgery (KSS) as an organ-preserving alternative.

While the guidelines primarily reserve KSS for low-risk UTUC and select high-risk scenarios [3,5], a growing body of observational data suggests that KSS may offer comparable oncological outcomes to RNU even in high-risk patients [6–13]. These findings, though potentially subject to selection bias, highlight the need for individualized patient assessment and shared decision-making.

Previous studies have focused on the oncological and renal function outcomes, leaving the surgical perspective largely unexplored. KSS can be more technically complex and less standardized than RNU, which may lead to different surgical outcomes regarding hospitalization and complications.

Therefore, this study aimed to fill this knowledge gap by comparing the surgical outcomes of KSS versus RNU. We also describe the short- and long-term kidney function and survival. Ultimately, we sought to identify surgical risk factors within this comprehensive dataset to improve preoperative patient counseling.

2. Materials and Methods

2.1. Patient Cohort and Ethics

In this retrospective analysis, all patients who underwent KSS for UTUC at a tertiary referral center at University Hospital Bonn from 2016 until data cutoff in April 2024 were screened for eligibility. The KSS approach was based on shared decision-making, and cases without a viable RNU alternative, such as patients with a solitary kidney, were excluded from this analysis. Further inclusion criteria for this study were histologically confirmed and clinically organ-confined UTUC and the availability of baseline data and a sufficient 30-day postoperative follow-up.

Next, propensity scores were generated using a logistic regression model. The continuous variables, age and pre-surgical estimated glomerular filtration rate (eGFR), were included alongside age and the factors of sex, urinary tract localization (renal pelvis vs. ureter and right vs. left), EAU risk group, and ASA score. Afterward, we performed propensity-weighted matching with an institutional database of UTUC patients who underwent RNU at the same institution during this period. The cohort selection process is depicted in Supplementary Figure S1. This study was approved by the local ethics committee (University Bonn, vote #128-22) and conducted in accordance with the Declaration of Helsinki.

2.2. Baseline Data

The baseline data collected for the patients included demographics (age, sex), type of surgery, and tumor characteristics (pre-surgical risk factors according to the EAU: size, grading, cytology, presence of hydronephrosis, and prior cystectomy [3]), alongside the American Society of Anesthesiologists physical status classification system (ASA) and the estimated eGFR based on serum creatinine according to the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula [14].

2.3. Outcomes and Follow-Up

The durations of the surgery and postoperative hospitalization, alongside any complications, were collected within a timespan of 30 days after surgery. The complications were classified according to the Clavien–Dindo grading system [15].

The postoperative kidney function data were collected at two different time points: the early post-surgical eGFR in the range of 5–30 days after surgery, and the long-term eGFR in the range of 12–24 months after surgery, based on their availability. In each case, the most recently obtained laboratory results for the corresponding time period were chosen.

Any follow-up information on disease recurrence or death and cause of death was collected. If no information was available, the date of the last follow-up was collected.

2.4. Endpoints

The primary endpoint was the frequency of complications according to Clavien–Dindo grading. To avoid biased results arising from the retrospective nature of this study, grade 1 events were deemed non-significant and included in the Clavien–Dindo 0–1 group.

We also assessed Days Alive and Out of the Hospital within 30 days (DAOH30), calculated as 30 minus the total days hospitalized within the postoperative period (initial stay and readmissions), with death resulting in a score of 0 [16].

Changes in kidney function were measured as differences between the pre- and post-surgical eGFR and were separately assessed by their early and long-term dynamics.

Cancer-specific survival (CSS) was defined as the timespan from surgery to death related to urothelial cancer or the last follow-up (censored). Death from other causes was censored. In addition, disease-free survival (DFS) was defined as the time until the recurrence of urothelial cancer, irrespective of localization or the last follow-up, with full information on the recurrence status (censored).

2.5. Risk Score

To assess any associations of complications with the baseline parameters, including the type of surgery, the baseline characteristics were fitted to a multivariable generalized linear model (GLM) as independent variables towards the binomial dependent outcome of severe complications (defined as complications with a Clavien–Dindo grade ≥ 3). We attributed one point to each of these independent risk factors, and these were added up to form the UTUC Surgery Risk Score. The predictive performance of the score was evaluated using a receiver operating characteristic (ROC) curve analysis.

2.6. Statistics

Baseline data are presented as medians with ranges. Inter-group comparisons were made using Fisher's exact test, Kruskal–Wallis tests, or Wilcoxon rank-sum tests. Survival comparisons were performed with Kaplan–Meier estimators and Log-Rank tests. p-values < 0.05 were considered statistically significant. All statistics were coded and analyzed in RStudio v2024.04.2 + 764 using packages "survival" (v3.8-3) and "survminer" (v0.5.0), and plotted with package "ggpubr" (v0.6.1).

3. Results

In total, 46 patients undergoing KSS met the inclusion criteria and were matched by propensity weights, with all 46 patients undergoing RNU. Their baseline characteristics are summarized in Table 1. They were balanced between KSS and RNU subgroups without displaying significant differences.

Table 1. Baseline characteristics in the propensity weight-matched cohort.

Parameter	RNU $n = 46$	KSS $n = 46$	Overall $n = 92$	p-Value [1]
Age (years)				0.867
Median [Range]	69.2 [43.8, 87.9]	69.8 [40.6, 93.2]	69.5 [40.6, 93.2]	
Sex (n, %)				1.000
Female	15 (32.6%)	15 (32.6%)	30 (32.6%)	

Table 1. *Cont.*

Parameter	RNU *n* = 46	KSS *n* = 46	Overall *n* = 92	*p*-Value [1]
Male	31 (67.4%)	31 (67.4%)	62 (67.4%)	
Localization (*n*, %)				1.000
Renal Pelvis	15 (32.6%)	14 (30.4%)	29 (31.5%)	
Ureter	31 (67.4%)	32 (69.6%)	63 (68.5%)	
Side (*n*, %)				1.000
Right	24 (52%)	23 (50%)	47 (51%)	
Left	22 (48%)	23 (50%)	45 (49%)	
EAU Risk Group (*n*, %)				0.479
High Risk	10 (22%)	14 (30%)	24 (26%)	
Low Risk	36 (78%)	32 (70%)	68 (74%)	
ASA Score (*n*, %)				0.197
1	3 (7%)	0 (0%)	3 (3%)	
2	20 (43%)	25 (54%)	45 (49%)	
3	23 (50%)	21 (46%)	44 (48%)	
eGFR (mL/min)				0.991
Median [Range]	56 [10, 103]	58 [14, 109]	57 [10, 109]	
Type of Surgery				NA
Radical Nephroureterectomy	46 (100%)	--	46 (50%)	
Segmental Ureterectomy	--	26 (56%)	26 (28%)	
Partial Nephrectomy/Pyeloplasty	--	10 (212%)	10 (11%)	
Ureterorenoscopy	--	10 (22%)	10 (11%)	

KSS = kidney-sparing surgery; RNU = radical nephroureterectomy; EAU = European Association of Urology; ASA = American Society of Anesthesiologists physical status classification system; eGFR = estimated glomerular filtration rate. [1] Calculated with Wilcoxon rank-sum test for continuous variables and Fisher's exact test for categorical variables. Note: Data rounded to whole numbers.

3.1. Surgical Complications and Risk Score

In total, 59 patients (64.1%) experienced no significant complications (Clavien–Dindo 0–1). Clavien–Dindo grade 2, 3a, 3b, and 4a complications were seen in 10, 6, 9, and 8 patients, respectively (10.9%, 6.5%, 9.8%, and 8.7%). Kidney-sparing surgery was significantly associated with this outcome; in particular, the rates of grade 3a ($n = 8$ in KSS vs. $n = 1$ in RNU) or 3b complications ($n = 6$ in KSS vs. $n = 0$ in RNU) were considerably higher, while 4a complications occurred predominantly in the RNU patients ($n = 3$ in KSS; $n = 5$ in RNU). All of these events were of acute kidney failure. DAOH30 was significantly longer following RNU than KSS (Table 2, Supplementary Figure S2A).

In the GLM, among the baseline variables, the non-endoscopic kidney-sparing surgical techniques of segmental ureterectomy (estimate: 1.39; $p = 0.038$) or partial nephrectomy/pyeloplasty (estimate: 3.87; $p = 0.003$) were significantly associated with severe complications, with a Clavien–Dindo ≥ 3. Furthermore, a baseline pre-surgical creatinine level > 0.9 mg/dL was strongly associated with this outcome (estimate = 3.09; $p = 0.041$). An ASA score of 3 showed a non-significant trend (estimate = 1.03; $p = 0.125$). Based on strong clinical reasoning and the belief that this factor would likely be significant in a larger cohort, it was retained in the final score. All the other variables did not provide meaningful associations with severe complications (Supplementary Table S1).

Therefore, we set up the UTUC Surgery Risk Score as follows: one point each was attributed for a non-endoscopic KSS approach, an ASA score ≥ 3, and a preoperative creatinine level > 0.9 mg/dL. This risk score was significantly associated with overall complications and severe complications of Clavien–Dindo grade ≥ 3 (both $p < 0.001$). No patients (0%) with a score of 0 experienced complications $\geq$ grade 2, compared to

$n = 5$ (17.9%) with a risk score of 1, $n = 17$ (42.5%) with a risk score of 2, and $n = 11$ (73.3%) with a risk score of 3. These included $n = 2$ (7.1%), $n = 12$ (30.0%), and $n = 9$ (60.0%) major complications ≥ grade 3 for scores of 1, 2, and 3, respectively. The UTUC Surgery Risk Score showed strong predictive ability for severe complications (Clavien–Dindo grade ≥ 3), with an area under the curve (AUC) of 77.3% (95% CI: 51.7–91.3%). At the optimal cutoff point of a score of ≥2, the sensitivity was 91.3% and the specificity was 50.7%, with a positive predictive value (PPV) of 38.2% and a negative predictive value (NPV) of 94.6%. The occurrence of complications according to the risk score is illustrated in Figure 1. Furthermore, the risk score was a significant predictor of DAOH30. The linear regression analysis showed that for each one-point increase in the score, DAOH30 decreased by an average of 3.91 days ($\beta = -3.91$, $p < 0.001$). This association was further confirmed with a Kruskal–Wallis test ($p < 0.001$, Supplementary Figure S2B).

Table 2. Complications and DAOH30 stratified according to type of surgery.

Outcome	RNU $n = 46$	KSS $n = 46$	Overall $n = 92$	*p*-Value [1]
Clavien–Dindo grade (*n*, %)				**0.005 ****
0–1	34 (74%)	25 (54%)	59 (64%)	
2	6 (13%)	4 (9%)	10 (11%)	
3a	0 (0%)	6 (13%)	6 (7%)	
3b	1 (2%)	8 (17%)	9 (9%)	
4a	5 (11%)	3 (7%)	8 (9%)	
DAOH30 (days)				**0.011 ***
Median [range]	23 [0–28]	16 [0–20]	20 [0–29]	

KSS = kidney-sparing surgery; RNU = radical nephroureterectomy; DAOH30 = Days Alive and Out of the Hospital within 30 days. [1] Calculated with Wilcoxon rank-sum test for continuous variables and Fisher's exact test for categorical variables. * $p < 0.05$, ** $p < 0.01$ Note: Data rounded to whole numbers.

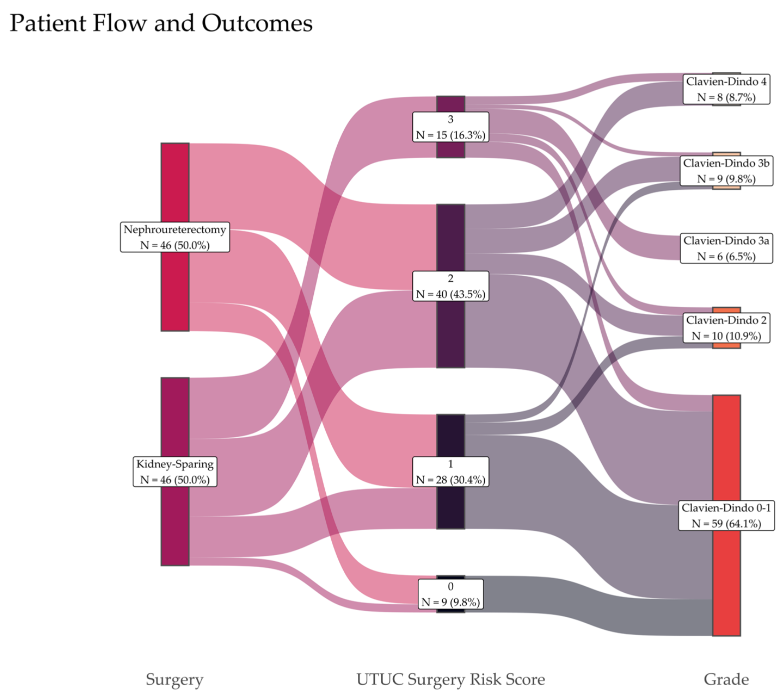

Figure 1. Sankey diagram of surgical complications based on pre-surgical risk score (1 point each for non-endoscopic kidney-sparing surgery, ASA score ≥ 3, and pre-surgery creatinine > 0.9 mg/dL). The columns represent the sequential stages in the patient pathway. The height of each node (bar) is proportional to the number of patients (N) and percentage (%) in that state, while the thickness of the connecting flows indicates the number of patients transitioning between states.

3.2. Kidney Function

In the early postoperative period (7–30 days), the eGFR decreased by a median of −4.3 mL/min in the RNU group, while the median difference in the KSS group was +0.55 mL/min (p = 0.015, Supplementary Figure S3A). In the long-term course (12–24 months), the eGFR remained decreased by a median of −3.25 in the RNU patients, while it increased by +11.1 mL/min in the KSS group compared to the pre-surgical baseline. The between-group differences displayed a strong non-significant trend (p = 0.051, Supplementary Figure S3B).

3.3. Survival Outcomes

The median CSS was not reached (NR) in either the RNU or KSS group (95% CI: NR–NR; Log-Rank p = 0.60; Figure 2A). The median DFS was 16.0 months in the KSS group (95% CI: 11.8–33.3 months) and 11.3 months (95% CI: 7.0 months–NR) in the RNU group. These differences remained non-significant (Log-Rank p = 0.57; Figure 2B).

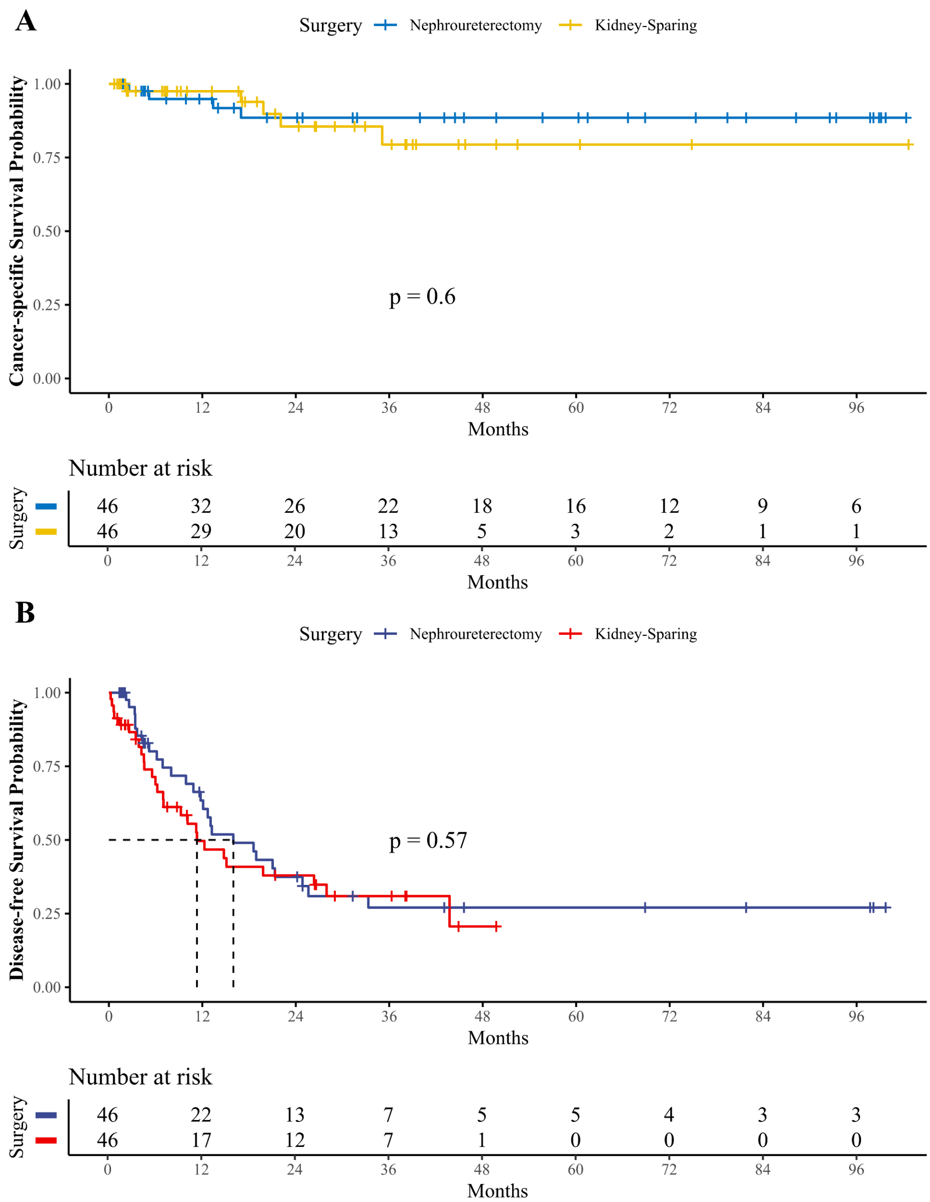

Figure 2. Kaplan–Meier estimators of the endpoints (**A**) CSS and (**B**) DFS for patients treated with either RNU or KSS.

4. Discussion

UTUC frequently presents at advanced stages, typically necessitating RNU or KSS as a viable alternative in selected patients. This study uniquely addresses the critical gap in the comprehensive understanding of perioperative complications, providing a detailed comparison of KSS and RNU with regard to surgical outcomes, short- and long-term kidney function, and survival, in addition to identifying the crucial surgical risk factors.

Our finding that KSS is associated with a higher rate of grade $\geq$ 3 complications adds a nuanced perspective to the literature, where the reported complication rates vary widely depending on the surgical approach (e.g., robotic, endoscopic), patient population, and specific KSS technique [17–21]. However, most studies have not reported on this outcome [22]. Specific procedures within KSS carry unique risks, such as ureteral stenosis following endoscopic treatment or reconstruction, which remains a key concern during patient follow-up. This underscores the importance of identifying systemic patient risk factors, as markers of inflammation and nutrition, such as the albumin/fibrinogen ratio, have been suggested as risk factors for ureteral stenosis in surgical contexts [23].

One potential explanation for the discrepancy in the results, beyond the small size of the retrospective cohorts, may be a disregard for patient-derived factors. In proposing our UTUC Surgery Risk Score, we aimed to create a pragmatic stratification tool. The score showed a strong predictive ability for severe complications (AUC: 77.3%). Its clinical strength lies in its NPV of 94.6%, which allows clinicians to confidently identify patients at minimal risk of severe complications. This finding suggests its potential as a valuable "rule-out" tool during patient counseling. Conversely, its modest PPV of 38.2%, coupled with its high sensitivity (91.3%), means that a high score is not a definitive prediction but rather an effective flag for identifying patients who will require more detailed discussions about elevated surgical risks. This simple, clinically integrated tool, reminiscent of established systems like the R.E.N.A.L. score in renal cancer [24], offers a novel step towards personalizing the surgical approach for UTUC.

Furthermore, the UTUC Surgery Risk Score is associated with a novel and patient-centered endpoint: DAOH30 [25]. DAOH30 has not been reported in the context of UTUC surgery to date, and our finding that DAOH30 was significantly longer following RNU than KSS provides a more holistic and clinically relevant measure of early postoperative recovery and overall patient well-being. The emphasis on quality-of-life surrogate endpoints, such as DAOH30, marks a progressive step in surgical outcome reporting, moving beyond purely technical success rates to incorporate a patient's lived experience [26,27].

Regarding traditional endpoints, our findings corroborate the existing literature. We observed no significant differences in cancer-specific or disease-free survival between the RNU and KSS groups, reinforcing the oncological safety of KSS in appropriately selected patients [6–13]. It is noteworthy that the median DFS was numerically longer in our KSS group (16.0 vs. 11.3 months). While not statistically significant, likely due to the cohort size, this trend suggests that KSS does not compromise oncological control in appropriately selected patients. Similarly, our study emphatically confirms the nephron-sparing benefits of KSS, which is associated with a significantly better preservation of both short- and long-term renal function compared to RNU [28]. This advantage is critical, given the established link between kidney function preservation and reduced cardiovascular mortality in other urologic cancers [29].

This study has limitations inherent to its retrospective design, though propensity score matching was used to mitigate the confounding factors. The relatively small sample size limits the statistical power and increases the risk of overfitting in multivariable models, warranting external validation of our risk score. Furthermore, the wide time window for eGFR assessment, a consequence of real-world data collection, may introduce variability.

Finally, our analysis combined renal pelvis and ureteral tumors. Although this is standard practice as they are both considered UTUC and managed under unified guidelines, we acknowledge that tumor location can be a prognostic variable itself. Despite these limitations, our study provides a valuable, focused analysis of surgical outcomes, which is an underrepresented area in the UTUC literature.

5. Conclusions

In conclusion, our study highlights KSS as an independent risk factor for higher-grade complications, while confirming its benefits for renal function preservation and comparable oncological outcomes to RNU. The proposed UTUC Surgery Risk Score offers a valuable tool for personalized patient counseling and shared decision-making, emphasizing perioperative outcomes alongside traditional considerations in UTUC management.

Supplementary Materials: The following supporting information can be downloaded at https://www.mdpi.com/article/10.3390/surgeries6030071/s1, Figure S1. Cohort selection process; Figure S2. Days alive and out of the hospital (DAOH30) depending on type of surgery (A) or the UTUC surgery risk score (B); Figure S3. Violin-boxplots of estimated glomerular filtration rate (eGFR) dynamics in (A) the early post-surgery stage (7–30 days) and (B) long-term course (12–24 months); Table S1. Multivariable Generalized Linear Model of baseline parameters and the dependent binomial outcome Clavien-Dindo grade ≥ 3 complications.

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Institutional Review Board Statement: Ethical review and approval were waived for this retrospective study by the responsible Ethics Committee of the Medical Faculty at the University of Bonn (vote. no. 128/22).

Informed Consent Statement: Patient consent was waived due to the sole reliance on data collected within clinical routine.

Data Availability Statement: The data presented in this study are available on request from the corresponding author due to ethical reasons.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

ASA	American Society of Anesthesiologists Physical Status Classification System
AUA	American Urological Association
CI	Confidence Interval
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
CSS	Cancer-Specific Survival
CT	Computed Tomography
DAOH30	Days Alive and Out of the Hospital within 30 days
DFS	Disease-Free Survival
EAU	European Association of Urology

eGFR	Estimated Glomerular Filtration Rate
GLM	Generalized Linear Model
KSS	Kidney-Sparing Surgery
NR	Not Reached
RCC	Renal Cell Carcinoma
RNU	Radical Nephroureterectomy
UTUC	Upper-Tract Urothelial Cancer

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