Impact of nephron sparing surgery on survival in upper urinary tract urothelial carcinoma patients stratified by tumor characteristics

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Research article

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Abstract

Background: We aimed to evaluate the impact of nephron sparing surgery (NSS) on survival in upper urinary tract urothelial carcinoma (UTUC) patients stratified by tumor grade and stage compared to radical nephroureterectomy (RNU) or no surgery.

Methods: Overall, 10319 UTUC patients between 2004 and 2015 were extracted from the SEER database. Patients were divided into no surgery group, NSS group and RNU group. Kaplan-Meier plots illustrated survival rates according to surgical method. Multivariable Cox regression analyses assessed the effect of different surgical methods on survival rates.

Result: Among the 10319 UTUC patients. Kaplan-Meier plots showed that NSS was associated with a higher overall survival (OS) and cancer-specific survival (CSS) in grade I and II and AJCC stage I patients (all $p < 0.05$). In multivariable Cox regression analyses, NSS was prone to a higher OS or CSS in grade I ($p > 0.05$). Moreover, NSS predisposed to a higher OS only in AJCC stage I ($p < 0.05$).

Conclusion: The beneficial effect of NSS was evident in grade I or AJCC stage I. NSS can be considered in grade I or stage I, for other grades or stages remains to be seen, both of which will be verified by further prospective research.

Background

Urothelial carcinomas are the fourth most common tumor, most of which are located in the lower urinary tract and upper tract urothelial carcinoma (UTUC) accounts for only 5% of urothelial tumors and 8% of renal tumors^[1, 2]. Radical nephroureterectomy (RNU) with bladder cuff excision is the gold standard treatment for UTUC. However, solitary kidney after RNU may lead to higher risk of dialysis, cardiovascular morbidity and overall mortality^[3, 4]. In an effort to decrease the potential risk, nephron sparing surgery deserves attention greatly in elaborately chosen patients with UTUC with the intention of obtaining acceptable oncological results^[5-7].

Although the stage of UTUC is usually determined by endoscopic biopsy during ureteroscopy, inadequate tissue sampling and concerns about ureteral perforation make accurate staging challenging^[8, 9]. Therefore, due to concerns of cancer progression, many clinicians are willing to perform radical eradication therapy even in patients with early-stage UTUC^[10, 11]. However, some scholars have suggested that NSS may play a curative role especially in low grades and early stages^[12, 13]. Nevertheless, evidence-based data are scarce to support the oncologic efficacy of NSS for its rarity.

Originally, NSS was exclusively considered for UTUC patients who are intolerance of RNU or those with imperative indications such as anatomically or functionally solitary kidneys. Recently, It is that elective risk-based indications were introduced for patients with bilateral functional kidneys when obtaining effective oncologic control for these emergency cases^[14]. As a result, all the contemporary reports comparing NSS versus RNU have included a mix of patients with imperative and elective indications, and

the available data are therefore highly heterogeneous^[15], which makes it difficult to draw any reasonable conclusions from the current literature. To clarify this issue, we evaluated and compared the treatment of NSS on overall survival (OS) and cancer-specific survival (CSS) when compared to RNU or no surgery.

Methods

Data source and patients

Within the Surveillance, Epidemiology and End Results (SEER) database from 2004 to 2015, we used the National Cancer Institute's SEER*Stat software (version 8.3.5) with UTUC (codes C65.9 and C66.9) to identified 10,319 patients treated with NSS, RNU or no surgery between January 1, 2004, to December 31, 2015. The exclusion criteria were as follows: (a) unknown survival time; (b) unclear grade or AJCC stage; (c) patients under 18 years of age; (d) unclear tumor location; (e) surgical code is not 00, 30, 40, 50. Finally, 10,319 eligible patients were identified in the present research.

Study variables

Study variables included age of diagnosis, year of diagnosis, sex, race, marital status, urban-rural residence, insurance, summary AJCC stage, grade, surgical method, radiotherapy and chemotherapy information. According to the surgical code, patients were divided into three groups: no surgery (code 00, no cancer-directed surgery of primary site), NSS group (code 30, Partial or subtotal nephrectomy or partial ureterectomy, including Cryosurgery, Electrocautery, Excisional biopsy, Laser, Segmental resection, Thermal ablation, Wedge resection) and RNU group (code 40,50. Radical nephrectomy). AJCC stage is refer to AJCC Cancer Staging Manual, 7th Edition. Meanwhile these group are divided into four groups according to the 2016 WHO classification (grade I, grade II, grade III and grade IV). Demographic and clinicopathological characteristics including age at diagnosis (18-50, 51-65, 66-80 and >80), sex (male and female), race (white, black and others), marital status (married, unmarried and unknown), urban-rural residence (metropolitan and nonmetropolitan), summary stage (localized, regional, distant), radiotherapy (yes or no) and chemotherapy (yes or no). Household income was divided into three group: lower group (<4219), middle group (4219-5210) and upper group (>5210). OS and CSS are the primary endpoints of our study.

Statistical analysis

Statistical Package for the Social Sciences software (version 24.0; SPSS Inc, Chicago, IL, USA) was used for all statistical analyses. The chi-square test was used to analyze factors related to the surgical method. Kaplan-Meier curves analyses using a log-rank test was used to analyze the OS and CSS rate. Multivariate Cox regression was used to analyses factors associated with OS and CSS. P value ≤ 0.05 was considered statistically significant.

Results

General characteristics

A total of 10,319 eligible UTUC patients were identified in our study cohort between 2004 and 2015. Among them, 963 (9.3%) patients did not received surgery, 1,273 (12.3%) received NSS and 8,083 (78.3%) received RNU. Table 1 demonstrated the demographic and clinicopathological characteristics of patients with UTUC. Chi-square test showed some risks had an impact on therapeutic decision making.

Of the 10,319 patients, the proportion of NSS remained stable from 2004 to 2015, while the proportion of NSS decreased in pelvis patients (Figure 1).

Survival related variables

Kaplan-Meier curves analysis the influence of risk factors on OS and CSS of UTUC patients (Table 2). Patients undergoing NSS had the longest OS median survival time (MST) (70.00 months) and highest CSS MST (115.10 months) compared with the other groups.

Survival analyses according to surgical method

As shown in **Table S1**, the 3,5,10-year OS for the population who received NSS was significantly longer than RNU patients in WHO grade III (58.3 % vs 50.3%, 46.5% vs 37.1%, 27.1% vs 22.8%, $p < 0.001$). In addition, In the stage IV, NSS patients have longer survival ratio when compared with RNU patients (33.4 % vs 22.0%, 20.8% vs 14.9%, 16.3% vs 8.7%, $p < 0.001$).

Multivariate cox regression analysis revealed some risk factors in UTUC patients (Table 3). After adjusting for risk factors, The results shown that compared with the patients who receive RNU treatment , no surgery patients (HR: 3.78, 95% CI: 3.51-4.08, $p < 0.001$) may be at increased risk. In term of CSS, no surgery patients (HR: 2.46, 95% CI: 2.18-2.77, $p < 0.001$) associated more commonly with low-risk CSS, while the people performed with NSS (HR: 0.78, 95% CI: 0.67-0.91, $p = 0.002$) may also associated with significantly greatest odds of CSS.

Subgroup analysis stratified by AJCC stage and WHO grade

Based on summary stage and WHO grade, we further discussed the difference between surgical method and prognosis among the subgroups of patients (Table 4). We found that for OS and CSS, surgical method was still associated with them among different stage and various grade subgroups patients. Kaplan-Meier plots showed that NSS was associated with a higher overall survival (OS) and cancer-specific survival (CSS) in grade I and II and AJCC stage I patients (all $p < 0.05$) (Figure 2, Figure 3). In multivariable COX regression analyses, NSS patients had a higher OS rate in stage IV group (OS: HR: 0.74, 95% CI 0.60-0.90, $p = 0.003$) and a higher OS or CSS rate in grade III group compared to RNU patients. However, for other subgroup patients, the surgical method had no obvious effect in terms of OS ,as well as CSS ($p > 0.05$). When classified according to the primary organ, the related results are shown in the supplementary materials (**Table S2-S3**). **Supplemental Figure 1-4** was performed to verify the NSS group was prone to a higher OS or CSS in the former periods.

Discussion

Our study was based on a large number of population database to quantitatively compare the impact of NSS on survival in patients with UTUC compared to RNU or no surgery. UTUC is a rare disease with an annual incidence of one to two cases per 100 000 individuals in Western countries. We explored the effect of surgical methods on OS and CSS in UTUC patients and discovery that surgical method was an independent prognostic factor. Moreover, the mean survival time was higher in NSS group than in RNU patients. Kaplan-Meier plots showed that NSS was associated with a higher OS and CSS in grade I and II and AJCC stage I patients. In multivariable Cox regression analyses, NSS was prone to a higher OS or CSS in grade I, and NSS predisposed to a higher OS only in AJCC stage I.

In our research, the OS and CSS of NSS and RNU were not significant for low-grade or early-stage with the selected UTUC patients. This result is similar to the previous report. Jay Simhan et al.^[16] reported that patients with similar situation when treated with NSS have analogous cancer-specific mortality (CSM) rates to those patients managed with RNU. Jeldres et al.^[17] thought segmental ureterectomy (SU) may be operated to UTUC patients when it is technically feasible, especially when detected in T3 or even T4 lesions. Moreover, Giovanni Lughezzani^[18] report a stage and grade migration at NU or SU towards more aggressive disease among surgically treated patients between 1983 and 2004. But the CSM rates are not higher than former that validates the two surgical ways as effective treatments for UTUC. However, In another research, Chen GL^[12] reported acceptable oncological outcomes were observed in 23 patients undergoing laser ablation with strict ureteroscopic surveillance. In another side, the use of NSS has become an acceptable alternative in select patients with non-high grade, early-stage UTUC who are at low risk of disease progression^[19, 20], However, the risk of cancer progression or recurrence is estimated to be as high as 30% within 5 years^[21]. A large part of the difference in these results is due to competing model factors for the selected patient sample as well as aspects of the patient profile. In addition, radiotherapy is usually administered in symptomatic patients or patients unable to undergo radical surgery^[22], however, Li Xiaoying^[23] concluded radiotherapy can reduce local recurrence rate in patients with radical nephroureterectomy. In our research, we also found radiotherapy may benefit in UTUC patients. It may result from the population with surgery and high grade occupy most of the population, and radiotherapy may further improve the survival rate of patients. Meanwhile, there are studies focusing on the role of chemotherapy on survival for UTUC patients, and the therapeutic effects differ for different patients. In Zhai Ting-Shuai's research^[24], The beneficial effect of chemotherapy on survival probability was evident in pT3/pT4 or patients with lymph node metastasis, this may be involved more population with distant metastasis and more people are may have strong will of survival, so they have to face more treatment including receive extra chemotherapy. In other side, we observed that NSS has higher a OS or CSS when compared to RNU methods especially in Grade III and AJCC stage IV. In a multi cental research, Kaag et al.^[25] identified a reduction in mean estimated GFR by $\approx 24\%$ after RNU in tumor patients. Thus, patients when operated with RNU have notable decreases in renal function and leading to chronic kidney disease^[26]. Importantly, such a decline in renal function after radical surgery in patients with UTUC may affect eligibility in the event of disease progression^[27]. We concerned more about NSS surgery because

NSS could protect the nephron, and it could better maintain the life of the patient with solitary kidney, thereby prolonging the survival period. Previous studies examining the oncological efficacy in patients managed conservatively were limited by small sample sizes, lack of generalizability, and inclusion of patients with aggressive disease characteristics. Using national registry data, the present multicenter large-sample study might be more convincing.

There are limitations in our research. First, the SEER database is a retrospective dataset. Second, the patient's physical condition was unclear, patients with much complications might pursue more conservative treatment. Third, patients receiving NSS may have a selection bias relative to RNU. In addition, for chemotherapy and radiotherapy, we didn't distinguish whether adjuvant or neoadjuvant therapy, and there is no information on specific RT technique (dose, fractionation, beam energy) or chemotherapy regimens.

Conclusions

To conclude, we demonstrated that the beneficial effect of NSS was evident in grade Ⅲ or AJCC stage Ⅲ. NSS can be considered in grade Ⅲ or stage Ⅲ, for other grades or stages remains to be seen, both of which will be verified by further prospective research.

Abbreviations

NSS: nephron sparing surgery; UTUC: upper urinary tract urothelial carcinoma; RNU: radical nephroureterectomy; OS: overall survival; CSS: cancer-specific survival; SEER: the Surveillance, Epidemiology and End Results; MST: median survival time

Declarations

Ethics approval and consent to participate

For the institutional cohorts, data were extracted from the Surveillance, Epidemiology, and End Results database. This article does not contain any studies with human participants performed by any of the authors. For this type of study, formal consent is not required.

Consent for publication

Not applicable.

Availability of data and material

The datasets used and/or analyzed during this current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

L J contributed to study designation, data analysis, methodology, data validation and original draft writing. TS Z contributed to data collection, manuscript preparation and edition. Z Z contributed to data collection, formal analysis, investigation and visualization. X L contributed to formal analysis, methodology and validation. JX Z contributed to formal analysis and methodology. XC N contributed to formal analysis and methodology. HQ L contributed to data collection. XD Y contributed to conceptualization and supervision. LM F contributed to conceptualization, supervision and editing. L Y contributed to conceptualization, funding acquisition, resources, supervision and writing-review and editing. All authors have read and approved the manuscript.

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Tables

Table 1. Characteristics for UTUC patients stratified by surgical method.

Characteristic	Total No. (%)	No Surgery No. (%)	NSS No. (%)	RNU No. (%)	P value
Total	10319	963 (9.3)	1273 (12.3)	8083 (78.3)	
Age at diagnosis					<0.001
18-50	348 (3.4)	20 (0.2)	25 (0.2)	303 (2.9)	
51-65	2275 (22.0)	154 (1.5)	275 (2.7)	1846 (17.9)	
66-80	5177 (50.2)	438 (4.2)	649 (6.3)	4090 (39.6)	
>80	2519 (24.4)	351 (3.4)	324 (3.1)	1844 (17.9)	
Year of diagnosis					<0.001
2004	840 (8.1)	70 (0.7)	118 (1.1)	652 (6.3)	
2005	792 (7.7)	56 (0.5)	92 (0.9)	644 (6.2)	
2006	895 (8.7)	61 (0.6)	114 (1.1)	720 (7.0)	
2007	869 (8.4)	66 (0.6)	116 (1.1)	687 (6.7)	
2008	895 (8.7)	84 (0.8)	128 (1.2)	683 (6.6)	
2009	893 (8.7)	79 (0.8)	103 (1.0)	711 (6.9)	
2010	882 (8.5)	75 (0.7)	114 (1.1)	693 (6.7)	
2011	837 (8.1)	97 (0.9)	112 (1.1)	628 (6.1)	
2012	787 (7.6)	89 (0.9)	85 (0.8)	613 (5.9)	
2013	830 (8.0)	81 (0.8)	91 (0.9)	658 (6.4)	
2014	867 (8.4)	102 (1.0)	106 (1.0)	659 (6.4)	
2015	932 (9.0)	103 (1.0)	94 (0.9)	735 (7.1)	
Sex					<0.001
Male	6139 (59.5)	543 (5.3)	843 (8.2)	4753 (46.1)	
Female	4180 (40.5)	420 (4.1)	430 (4.2)	3330 (32.3)	
Race					0.03
White	9026 (87.4)	824 (8.0)	1103 (10.7)	7099 (68.8)	
Black/Other	1293 (12.6)	139 (1.3)	170 (1.6)	984 (9.5)	
Marital status					<0.001
Married	6193 (60.0)	500 (4.8)	784 (7.6)	4909 (47.6)	
Unmarried	3716 (36.0)	412 (4.0)	425 (4.1)	2879 (27.9)	
Unknown	410 (4.0)	51 (0.5)	64 (0.6)	295 (2.9)	
Urban-rural residence					0.604
Metropolitan	9798 (95.0)	913 (8.8)	1214 (11.8)	7671 (74.3)	
Non-metropolitan	521 (5.1)	50 (0.5)	59 (0.6)	412 (4.0)	
Insurance					0.012
Yes	7571 (73.4)	746 (7.2)	918 (8.9)	5907 (57.2)	
No	88 (0.9)	8 (0.1)	6 (0.1)	74 (0.7)	
Unknown	2660 (25.8)	209 (2.0)	349 (3.4)	2102 (20.4)	
Income					0.491
Lower	4303 (41.7)	421 (4.1)	520 (5.0)	3362 (32.6)	
Middle	2906 (28.2)	258 (2.5)	350 (3.4)	2298 (22.3)	
Upper	3110 (30.1)	284 (2.8)	403 (3.9)	2423 (23.5)	
Summary stage					<0.001
Localized	2732 (26.5)	230 (2.2)	421 (4.1)	2081 (20.2)	
Regional	6403 (62.1)	260 (2.5)	813 (7.9)	5330 (51.7)	
Distant	1184 (11.5)	473 (4.6)	39 (0.4)	672 (6.5)	
Grade					<0.001
I	434 (4.2)	50 (0.5)	71 (0.7)	313 (3.0)	

II	1511 (14.6)	117 (1.1)	195 (1.9)	1199 (11.6)	
III	3135 (30.4)	386 (3.7)	387 (3.8)	2362 (22.9)	
IV	5239 (50.8)	410 (4.0)	620 (6.0)	4209 (40.8)	
AJCC Stage					<0.001
I	2976 (28.8)	253 (2.5)	444 (4.3)	2279 (22.1)	
II	1683 (16.3)	28 (0.3)	342 (3.3)	1313 (12.7)	
III	3143 (30.5)	41 (0.4)	339 (3.3)	2763 (26.8)	
IV	2517 (24.4)	641 (6.2)	148 (1.4)	1728 (16.7)	
Radiotherapy					<0.001
Yes	455 (4.4)	15 (0.1)	47 (0.5)	393 (3.8)	
No/Other	9864 (95.6)	948 (9.2)	1226 (11.9)	7690 (74.5)	
Chemotherapy					<0.001
Yes	2164 (21.0)	381 (3.7)	208 (2.0)	1575 (15.3)	
No/Other	8155 (79.0)	582 (5.6)	1065 (10.3)	6598 (63.1)	

Abbreviations: NSS: Nephron Sparing Surgery; RNU: Radical Nephroureterectomy.

Table 2. Kaplan-Meier analysis overall survival and cancer-specific survival for UTUC patients.

Characteristic	OS MST (months)	Kaplan-Meier		CSS MST (months)	Kaplan-Meier	
		Log Rank χ^2 test	P value		Log Rank χ^2 test	P value
Age at diagnosis		720.68	≤ 0.001		93.79	≤ 0.001
18-50	92.08			104.84		
51-65	80.70			104.64		
66-80	61.56			100.82		
>80	37.74			87.31		
Sex		0.90	0.344		28.45	≤ 0.001
Male	61.25			100.79		
Female	60.88			95.56		
Race		1.89	0.169		18.45	≤ 0.001
White	61.32			100.32		
Black/Other	59.62			91.81		
Marital status		71.99	≤ 0.001		27.84	≤ 0.001
Married	64.84			101.41		
Unmarried	54.75			94.85		
Unknown	60.53			101.02		
Urban-rural residence		1.74	0.188		3.66	0.160
Metropolitan	61.24			99.25		
Non-metropolitan	58.31			98.68		
Income		15.84	≤ 0.001		12.21	0.002
Lower	58.42			96.62		
Middle	62.68			100.51		
Upper	63.29			101.68		
Summary stage		2854.23	≤ 0.001		2853.40	≤ 0.001
Localized	85.21			125.18		
Regional	58.84			97.00		
Distant	14.16			26.85		
Grade		305.38	≤ 0.001		271.73	≤ 0.001
I	81.70			124.43		
II	82.63			119.98		
III	54.03			91.74		
IV	56.79			94.06		
AJCC Stage		2468.48	≤ 0.001		2478.87	≤ 0.001
I	85.61			125.23		
II	72.92			115.23		
III	58.99			96.48		
IV	25.87			49.76		
Radiotherapy		133.54	≤ 0.001		161.07	≤ 0.001
Yes	33.81			58.27		
No	62.34			100.94		
Chemotherapy		98.78	≤ 0.001		267.48	≤ 0.001
Yes	50.37			76.85		
No	63.80			104.80		
Surgery methods		1476.78	≤ 0.001		1255.92	≤ 0.001
No	17.66			40.04		
NSS	70.70			115.10		
RNU	64.65			102.07		

Abbreviations: OS: Overall Survival; CSS: Cancer Specific Survival; MST: Mean Survival Time; NSS: Nephron Sparing Surgery; RNU: Radical Nephroureterectomy.

Table 3. Risk factors for survival: outcome is overall survival and cancer-specific survival.

Characteristic	OS				CSS			
	univariate COX analysis		Multivariate Cox analysis		univariate COX analysis		Multivariate Cox analysis	
	Hazard Ratio (95% CI)	<i>P</i> value	Hazard Ratio (95% CI)	<i>P</i> value	Hazard Ratio (95% CI)	<i>P</i> value	Hazard Ratio (95% CI)	<i>P</i> value
Age at diagnosis								
18-50	Reference		Reference		Reference		Reference	
51-65	1.36 (1.13-1.64)	<0.001	1.33 (1.11-1.60)	0.003	1.03 (0.82-1.29)	0.810	1.03 (0.82-1.29)	0.815
66-80	2.04 (1.71-2.44)	<0.001	1.96 (1.64-2.35)	<0.001	3.88 (3.65-4.12)	0.200	1.16 (0.93-1.44)	0.192
>80	3.43 (2.87-4.12)	<0.001	3.16 (2.63-3.79)	<0.001	5.98 (5.57-6.43)	<0.001	1.64 (1.31-2.06)	<0.001
Race								
White	Reference				Reference		Reference	
Black/Other	1.06 (0.98-1.14)	0.173			1.27 (1.14-1.41)	<0.001	1.24 (1.10-1.38)	<0.001
Marital status								
Married	Reference		Reference		Reference		Reference	
Unmarried	1.26 (1.19-1.33)	<0.001	1.12 (1.06-1.18)	<0.001	1.23 (1.13-1.33)	<0.001	1.13 (1.04-1.23)	0.003
Unknown	1.07 (0.93-1.23)	0.374	1.04 (0.90-1.19)	0.614	0.91 (0.73-1.14)	0.428	0.92 (0.73-1.14)	0.440
Urban-rural residence								
Metropolitan	Reference		Reference		Reference			
Non-metropolitan	1.06 (1.02-1.10)	0.007	1.09 (0.97-1.22)	0.169	1.10 (0.93-1.30)	0.276		
Income								
Lower	Reference		Reference		Reference		Reference	
Middle	0.91 (0.85-0.97)	0.003	0.93 (0.87-0.99)	0.017	0.88 (0.80-0.96)	0.006	0.91 (0.82-0.99)	0.040
Upper	0.90 (0.84-0.95)	<0.001	0.90 (0.84-0.06)	0.001	0.87 (0.79-0.95)	0.002	0.86 (0.78-0.94)	0.001
Summary stage								
Localized	Reference		Reference		Reference		Reference	
Regional	1.87 (1.75-2.00)	<0.001	0.69 (0.51-0.93)	0.015	3.06 (2.70-3.47)	<0.001	0.84 (0.51-1.38)	0.488
Distant	7.84 (7.19-8.55)	<0.001	1.36 (0.99-1.86)	0.053	17.75 (15.43-20.41)	<0.001	1.75 (1.04-2.93)	0.035
Grade								
I	Reference		Reference		Reference		Reference	
II	5.14 (4.24-6.23)	<0.001	0.95 (0.81-1.11)	0.510	1.45 (1.05-2.00)	0.022	1.28 (0.93-1.77)	0.133
III	10.25 (8.44-12.46)	<0.001	1.29 (1.11-1.49)	0.001	3.90 (2.89-5.26)	<0.001	2.04 (1.51-2.77)	<0.001
IV	17.69 (14.61-21.42)	<0.001	1.33 (1.15-1.54)	<0.001	3.58 (2.66-4.82)	<0.001	2.14 (1.59-2.89)	<0.001
AJCC stage								
I	Reference		Reference		Reference		Reference	
II	1.34 (1.23-1.46)	<0.001	1.91 (1.42-2.58)	<0.001	1.58 (1.34-1.86)	<0.001	1.86 (1.12-3.08)	0.016
III	1.89 (1.76-2.04)	<0.001	2.72 (2.02-3.66)	<0.001	3.07 (2.69-3.50)	<0.001	3.44 (2.10-5.66)	<0.001

IV	4.84 (4.50-5.21)	<0.001	4.97 (3.68-6.71)	<0.001	10.39 (9.16-11.79)	<0.001	7.34 (4.46-12.10)	<0.001
Surgery								
No surgery	3.78 (3.51-4.08))	<0.001	2.94(2.71-3.19)	<0.001	4.69 (4.24-5.19)	<0.001	3.02(2.70-3.39)	<0.001
NSS	0.86 (0.79-0.94)	<0.001	0.96(0.88-1.04)	0.332	0.62 (0.54-0.72)	<0.001	0.76(0.66-0.88)	<0.001
RNU	Reference		Reference		Reference		Reference	
Radiotherapy								
Yes	Reference		Reference		Reference		Reference	
No	0.53 (0.48-0.60)	<0.001	0.70 (0.63-0.78)	<0.001	0.41 (0.36-0.47)	<0.001	0.67 (0.58-0.69)	<0.001
Chemotherapy								
Yes	Reference		Reference		Reference		Reference	
No	0.73 (0.69-0.78)	<0.001	1.24 (1.16-1.33)	<0.001	0.51 (0.46-0.55)	<0.001	1.22 (1.10-1.34)	<0.001

Abbreviations: OS: Overall Survival; CSS: Cancer Specific Survival; MST: Mean Survival Time; NSS: Nephron Sparing Surgery; RNU: Radical Nephroureterectomy.

Table 4. Subgroup analyses stratified by summary stage and grade for overall survival and cancer-specific survival.

Characteristic	OS	OS		CSS	CSS	
	MST (months)	Hazard Ratio (95% CI)	<i>P</i> value	MST (months)	Hazard Ratio (95% CI)	<i>P</i> value
Grade I						
No surgery	28.23	4.28(2.91-6.29)	<0.001	74.77	3.17(1.38-7.28)	0.006
NSS	88.76	1.01(0.67-1.51)	0.97	126.13	0.89(0.34-2.33)	0.814
RNU	90.59	Reference		128.08	Reference	
Grade II						
No surgery	25.10	3.73(2.91-4.77)	<0.001	54.29	4.37(2.98-6.41)	<0.001
NSS	84.76	1.04(0.83-1.30)	0.748	130.43	0.66(0.39-1.10)	0.111
RNU	90.59	Reference		128.08	Reference	
Grade III						
No surgery	15.00	2.60(2.28-2.97)	<0.001	32.87	2.73(2.28-3.27)	<0.001
NSS	68.30	0.86(0.74-0.99)	0.033	112.12	0.69(0.54-0.88)	0.003
RNU	90.59	Reference		128.08	Reference	
Grade IV						
No surgery	16.66	2.91(2.57-3.29)	<0.001	36.02	3.02(2.56-3.56)	<0.001
NSS	64.57	1.02(0.90-1.15)	0.797	107.99	0.82(0.67-1.00)	0.053
RNU	90.59	Reference		128.08	Reference	
Stage I						
No surgery	31.24	3.41(2.88-4.04)	<0.001	73.17	4.99(3.73-6.69)	<0.001
NSS	89.25	1.02(0.87-1.21)	0.799	129.80	0.83(0.58-1.19)	0.310
RNU	90.59	Reference		128.08	Reference	
Stage II						
No surgery	34.22	2.94(1.97-4.61)	<0.001	60.52	4.69(2.46-8.95)	<0.001
NSS	72.58	0.93(0.79-1.10)	0.416	121.56	0.73(0.52-1.02)	0.062
RNU	90.59	Reference		128.08	Reference	
Stage III						
No surgery	19.53	2.96 (2.13-4.12)	<0.001	44.17	2.65(1.58-4.44)	<0.001
NSS	55.61	1.16 (0.99-1.34)	0.056	98.08	0.91(0.72-1.15)	0.430
RNU	90.59	Reference		128.08	Reference	
Stage IV						
No surgery	11.39	1.81(1.62-2.01)	<0.001	22.16	2.02(0.49-0.86)	<0.001
NSS	43.20	0.74(0.60-0.90)	0.003	79.21	1.15(0.95-1.40)	0.144
RNU	90.59	Reference		128.08	Reference	

Abbreviations: OS: Overall Survival; CSS: Cancer Specific Survival; MST: Mean Survival Time; NSS: Nephron Sparing Surgery; RNU: Radical Nephroureterectomy.

Figures

Figure 1

Trend of NSS rate from 2004 to 2015 stratified by tumor location. A show the distribution trend of all populations in different years. The population of Pelvis and Ureter was showed separately in B and C.

Figure 2

Overall survival and cancer-specific survival curves of UTUC patients according to surgical method in different Grades. A and B, Overall survival (left) and cancer-specific survival (right) in Grade 1 patients. C and D, Overall survival (left) and cancer-specific survival (right) in Grade 2 patients. E and F, Overall survival (left) and cancer-specific survival (right) in Grade 3 patients. G and H, Overall survival (left) and cancer-specific survival (right) in Grade 4 patients. C.E, cumulative number of events; N.R, number at risk.

Figure 3

Overall survival and cancer-specific survival curves of UTUC patients according to surgical method in different Grades. A and B, Overall survival (left) and cancer-specific survival (right) in Stage I patients. C and D, Overall survival (left) and cancer-specific survival (right) in Stage II patients. E and F, Overall survival (left) and cancer-specific survival (right) in Stage III patients. G and H, Overall survival (left) and cancer-specific survival (right) in Stage IV patients. C.E, cumulative number of events; N.R, number at risk.

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