



# Does age impact clinical outcomes of radical nephroureterectomy in the elderly?—results from a multicenter retrospective study

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**Background:** Few studies have addressed the efficacy of nephroureterectomy for managing upper tract urothelial carcinoma (UTUC) in very elderly patients (those aged 85 years and older). We aimed to elucidate the association between age and clinical outcomes in patients with UTUC who underwent radical nephroureterectomy.

**Methods:** We retrospectively analyzed data from 847 patients who underwent nephroureterectomy for UTUC. These patients were classified into four age brackets: young ( $\leq 64$  years,  $n=177$ ), intermediate (65–74 years,  $n=300$ ), elderly (75–84 years,  $n=312$ ), and very elderly ( $\geq 85$  years,  $n=58$ ). We applied logistic regression models to ascertain predictors of postoperative complications. Cox's proportional hazards models were used to evaluate key prognostic factors affecting non-urothelial tract recurrence-free survival (NUTRFS), cancer-specific survival (CSS), and overall survival (OS).

**Results:** In all, 56 patients reported postoperative complications. An Eastern Cooperative Oncology Group performance status  $\geq 2$  was identified as a significant predictor for postoperative complications whereas age did not show a noteworthy correlation. Kaplan-Meier survival analyses indicated that very elderly patients had notably poorer OS than younger groups. Nevertheless, the differences in NUTRFS and CSS across the age brackets were not statistically significant. In multivariable analyses, very elderly age was a substantial independent determinant of OS but not NUTRFS or CSS.

**Conclusions:** The therapeutic benefits of surgical procedures are relatively consistent across age groups. This underscores the potential of considering surgical treatment for UTUC in patients aged 85 and above, provided they are deemed fit to withstand the surgical rigors and associated invasiveness.

**Keywords:** Upper tract urothelial carcinoma (UTUC); elderly patients; oncological outcome

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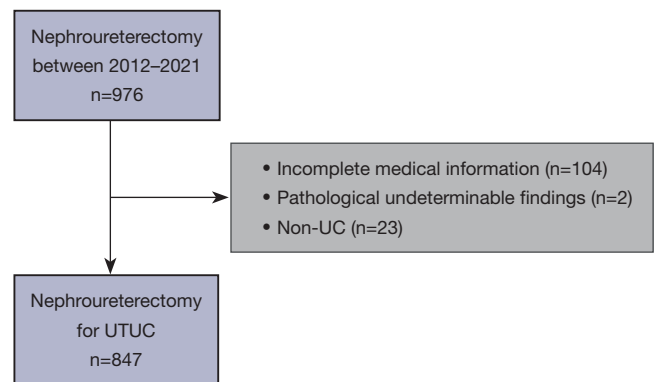
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## Introduction

The world is witnessing a significant surge in the elderly population, resulting in an increased percentage of individuals aged  $\geq 65$  years in the global populace (1). This could lead to increased public health issues. For example, Japan has experienced an upswing in cancer incidence rates among patients aged  $\geq 75$  years old (2). When managing elderly cancer patients, there is a tendency to employ less-aggressive treatment modalities. This has triggered continual debate over the appropriateness and implications of such approaches, particularly in relation to surgical procedures (3).

Upper tract urothelial carcinoma (UTUC) remains a relatively rare diagnosis, representing about 10% of renal tumors and 5% of urothelial malignancies. Nevertheless, its incidence has been increasing in recent years (4,5). Radical nephroureterectomy coupled with bladder cuff excision is the accepted primary treatment for UTUC, offering prospects for durable disease remission. However, high-risk UTUC, typified by features such as high-grade pathology or marked invasiveness, is frequently associated with notable recurrence and progression risks (6).

The appropriateness of nephroureterectomy in elderly patients with UTUC has received little attention



**Figure 1** Flowchart detailing patient inclusion in the study. UC, urothelial carcinoma; UTUC, upper tract urothelial carcinoma.

in the literature. Published studies have presented variable and sometimes contrasting clinical outcomes. As such, the potential benefits and prognosis of radical nephroureterectomy in elderly populations continue to be debated (7-11). In this context, we aimed to elucidate the association between age and clinical outcomes in patients with UTUC who underwent radical nephroureterectomy. We present this article in accordance with the STROBE reporting checklist (available at <https://tau.amegroups.com/article/view/10.21037/tau-24-37/rc>).

## Methods

### Patient demographics

We analyzed patients subjected to nephroureterectomy from January 2012 to December 2021 at the Jikei University Hospital and its 16 associated facilities (JIKEI-YAYOI Collaborative Group). Patients with incomplete clinical records (n=104), ambiguous pathological results (n=2), or those diagnosed with non-urothelial carcinoma (n=23) were removed from the study, leaving 847 qualified patients for analysis (Figure 1). Genitourinary surgeons conducted the operations, and the decision between open and laparoscopic methodologies depended on the circumstances of each individual patient and the judgment of the surgeon. A standard radical nephroureterectomy with bladder cuff removal was uniformly performed across all participating centers. The scope and performance of lymph node dissection were made by the overseeing physician. Induction for neoadjuvant chemotherapy and adjuvant chemotherapy was primarily based on clinical and pathological confirmation of T3/4 and N+ disease,

### Highlight box

#### Key findings

- In carefully selected cases, radical nephroureterectomy can be a safe and effective option, even for elderly (75–84 years old) and very elderly ( $\geq 85$  years old) upper tract urothelial carcinoma (UTUC) patients.

#### What is known and what is new?

- The appropriateness of nephroureterectomy in elderly UTUC patients has received little attention in the literature. Published studies have presented variable and sometimes contrasting clinical outcomes.
- There have been few reports on UTUC patients in very elderly patients due to its rarity.
- This study, using the largest database, investigates the clinical outcomes of Japanese UTUC patients aged  $\geq 85$  years old who had undergone radical nephroureterectomy.

#### What is the implication, and what should change now?

- The efficacy of surgical interventions for UTUC appears to be consistent across different age groups. This finding suggests that patients aged 85 years and older could also be considered for nephroureterectomy, assuming they are physically robust enough to endure the surgery and its associated demands.

respectively. The final decision regarding the type of chemotherapy induction was made after a comprehensive discussion between the patient and the urologist or medical oncologist. Data procured for evaluation included baseline demographic and clinicopathological metrics, operation specifics, and subsequent postoperative and oncological outcomes. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The research was approved by the Jikei University Institutional Review Board [protocol No. 33-260(10878)]. Informed consent was obtained from all subjects involved in the study.

### ***Pathological evaluation***

We collected data including baseline demographics, clinicopathological traits, operative specifics, and subsequent oncological outcomes. Patients who underwent nephroureterectomy were stratified into four age groups at the time of the procedure: young ( $\leq 64$  years), intermediate (65–74 years), elderly (75–84 years), and very elderly ( $\geq 85$  years). Tumor staging adhered to the American Joint Committee on Cancer guidelines (8th edition, 2017). Lymphovascular invasion (LVI) was determined based on the presence of tumor cells within the endothelial linings of the vascular or lymphatic channels. Tumor grading and variant histology classification followed the criteria delineated by the World Health Organization in 2016 (12).

### ***Follow-up***

Non-urothelial tract recurrence (NUTR) was characterized by the manifestation of disease outside the urinary tract and bladder. Postoperative surveillance involved routine evaluations including complete blood count, hepatic and renal function assays, and abdominal computed tomography (CT) scans every 3–6 months for the initial 2 postoperative years, transitioning to biannual evaluations after that. Perioperative complications were assessed using the Clavien-Dindo classification.

### ***Statistical analysis***

Associations between categorical and continuous variables were assessed using chi-square and Kruskal-Wallis tests, respectively. A logistic regression model was adopted to identify determinants of postoperative complications. Survival analyses including non-urothelial tract recurrence-free survival (NUTRFS), cancer-specific survival (CSS),

and overall survival (OS) were conducted using the Kaplan-Meier method with log-rank tests as needed, commencing from the nephroureterectomy date. In the analysis of NUTRFS, patients who had no documented recurrence or death by the time of the final follow-up were considered censored. For CSS, patients were censored at the final follow-up if there was no documented cancer-specific death or death from causes other than UTUC. In the assessment of OS, patients who had not been documented as deceased by the final follow-up were also censored. Variables impacting intravesical recurrence-free survival (RFS), NUTRFS, CSS, and OS were evaluated via Cox proportional hazards regression models. P value  $< 0.05$  was taken to indicate statistical significance. All statistical analyses were performed using Stata (version 13.1, TX, USA).

## **Results**

### ***Patient characteristics***

Descriptive statistics for the patients are presented in *Table 1*. Of the 847 participants, 177 (20.9%) were in the young category, 300 (35.4%) were intermediate, 312 (36.8%) were elderly, and 58 (6.8%) were very elderly. The median age was 74 years, with a spread from 32 to 94 years. The median follow-up duration was 28 months. Lymph node dissection was performed in 318 patients (37.5%). Of those who underwent lymph node dissection, 70 (22.0%) exhibited positive lymph node involvement. Laparoscopic nephroureterectomy was the choice for 615 patients (72.6%), with no instances of open conversion. Neoadjuvant and adjuvant chemotherapy were prescribed to 70 (8.3%) and 120 (14.2%) patients, respectively.

### ***Clinical outcomes***

During the surveillance period, 225 (26.6%) patients experienced metastases. In total, 137 (16.2%) experienced cancer-specific death and 182 (21.5%) had any case of death. The 3-year NUTRFS, CSS, and OS rates were 71.7%, 82.3%, and 77.9%, respectively (refer to *Table S1*). Kaplan-Meier analyses did not indicate significant differences in RFS and CSS among the age groups (*Figure 2*). However, OS rates were notably lower for the intermediate, elderly, and very elderly groups compared to the young group. *Table S1* lists the 3-year NUTRFS, CSS, and OS rates stratified by age.

**Table 1** Patients' characteristics

Variables	Total (n=847)	Young (n=177)	Intermediate (n=300)	Elderly (n=312)	Very elderly (n=58)	P value
Age (years)	74 [67–79]	61 [55–63]	71 [68–73]	79 [77–81]	87 [86–89]	<0.001
Follow-up (months)	28 [15–53]	34 [15–62]	30 [17–57]	25 [12–44]	25 [12–37]	<0.001
Sex						0.15
Male	606 (71.5)	135 (76.3)	218 (72.7)	217 (69.6)	36 (62.1)	
Female	241 (28.5)	42 (23.7)	82 (27.3)	95 (30.4)	22 (37.9)	
Body mass index (kg/m <sup>2</sup> )	22.8 [13.5–50.2]	23.4 [15.4–50.2]	22.75 [14.0–32.0]	22.39 [15.2–33.0]	22.13 [13.5–31.2]	<0.001
ECOG performance status						<0.001
0	644 (76.0)	155 (87.6)	245 (81.7)	217 (69.6)	27 (46.6)	
1	154 (18.2)	16 (9.0)	42 (14.0)	74 (23.7)	22 (37.9)	
≥2	49 (5.8)	6 (3.4)	13 (4.3)	21 (6.7)	9 (15.5)	
Laterality						0.39
Right	410 (48.4)	84 (47.5)	136 (45.3)	162 (51.9)	28 (48.3)	
Left	437 (51.6)	93 (52.5)	164 (54.7)	150 (48.1)	30 (51.7)	
Hydronephrosis						0.19
Absent	406 (47.9)	87 (49.2)	156 (52.0)	140 (44.9)	23 (39.7)	
Present	441 (52.1)	90 (50.8)	144 (48.0)	172 (55.1)	35 (60.3)	
Operative method						0.16
Open	234 (27.6)	59 (33.3)	73 (24.3)	88 (28.2)	14 (24.1)	
Laparoscopic	615 (72.6)	118 (66.7)	227 (75.7)	224 (71.8)	44 (75.9)	
Tumor location						0.005
Renal pelvis	412 (48.6)	106 (56.9)	145 (48.3)	140 (44.9)	21 (36.2)	
Ureter	381 (45.0)	59 (33.3)	141 (47.0)	151 (48.4)	30 (51.7)	
Both	54 (6.4)	12 (6.8)	14 (4.7)	21 (6.7)	7 (12.1)	
Clinical T stage						0.40
cTis/Ta/T1	36 (4.3)	3 (1.7)	14 (4.7)	15 (4.8)	4 (6.9)	
cT2	385 (45.5)	72 (40.7)	147 (49.0)	139 (44.6)	27 (46.6)	
cT3	235 (27.7)	58 (32.8)	74 (24.7)	89 (28.5)	14 (24.1)	
cT4	170 (20.1)	37 (20.9)	57 (19.0)	65 (20.8)	11 (19.0)	
NR	21 (2.5)	7 (4.0)	8 (2.7)	4 (1.3)	2 (3.4)	
Clinical N stage						0.65
cN0	781 (92.2)	160 (90.4)	280 (93.3)	283 (90.7)	58 (100.0)	
cN1	66 (7.8)	17 (9.6)	20 (6.7)	29 (9.3)	0 (0.0)	
Neoadjuvant chemotherapy						0.01
Absent	777 (91.7)	156 (88.1)	270 (90.0)	293 (93.9)	58 (100.0)	
Present	70 (8.3)	21 (11.9)	30 (10.0)	19 (6.1)	0 (0.0)	

**Table 1** (continued)

Table 1 (continued)

Variables	Total (n=847)	Young (n=177)	Intermediate (n=300)	Elderly (n=312)	Very elderly (n=58)	P value
Pathological findings						
Histology						0.009
Pure UC	813 (96.0)	172 (97.2)	295 (98.3)	293 (93.9)	53 (91.4)	
UC with variant	34 (4.0)	5 (2.8)	5 (1.7)	19 (6.1)	5 (8.6)	
Pathological T stage						
pTis/pTa/pT1	366 (43.2)	89 (50.3)	128 (42.7)	128 (41.0)	21 (36.2)	0.50
pT2	102 (12.0)	21 (11.9)	35 (11.7)	38 (12.2)	8 (13.8)	
pT3	334 (39.4)	58 (32.8)	125 (41.7)	125 (40.1)	26 (44.8)	
pT4	45 (5.3)	9 (5.1)	12 (4.0)	21 (6.7)	3 (5.2)	
Pathological N stage						
pN0	248 (29.3)	65 (36.7)	76 (25.3)	92 (29.5)	15 (25.9)	0.043
pN+	70 (8.3)	19 (10.7)	21 (7.0)	29 (9.3)	1 (1.7)	
pNx	529 (62.4)	93 (52.5)	203 (67.7)	191 (61.2)	42 (72.4)	
Tumor grade						
High	632 (74.6)	115 (65.0)	221 (73.7)	246 (78.9)	50 (86.2)	0.004
Low	145 (17.1)	45 (25.4)	56 (18.7)	39 (12.5)	5 (8.6)	
NR	70 (8.3)	17 (9.6)	23 (7.7)	27 (8.7)	3 (5.2)	
Concomitant CIS						
Absent	713 (84.2)	155 (87.6)	250 (83.3)	262 (84.0)	46 (79.3)	0.43
Present	134 (15.8)	22 (12.4)	50 (16.7)	50 (16.0)	12 (20.7)	
LVI						
Absent	565 (66.7)	129 (72.9)	207 (69.0)	189 (60.6)	40 (69.0)	0.02
Present	282 (33.3)	48 (27.1)	93 (31.0)	123 (39.4)	18 (31.0)	
Adjuvant chemotherapy						
Absent	727 (85.8)	147 (83.1)	252 (84.0)	271 (86.9)	57 (98.3)	0.02
Present	120 (14.2)	30 (16.9)	48 (16.0)	41 (13.1)	1 (1.7)	

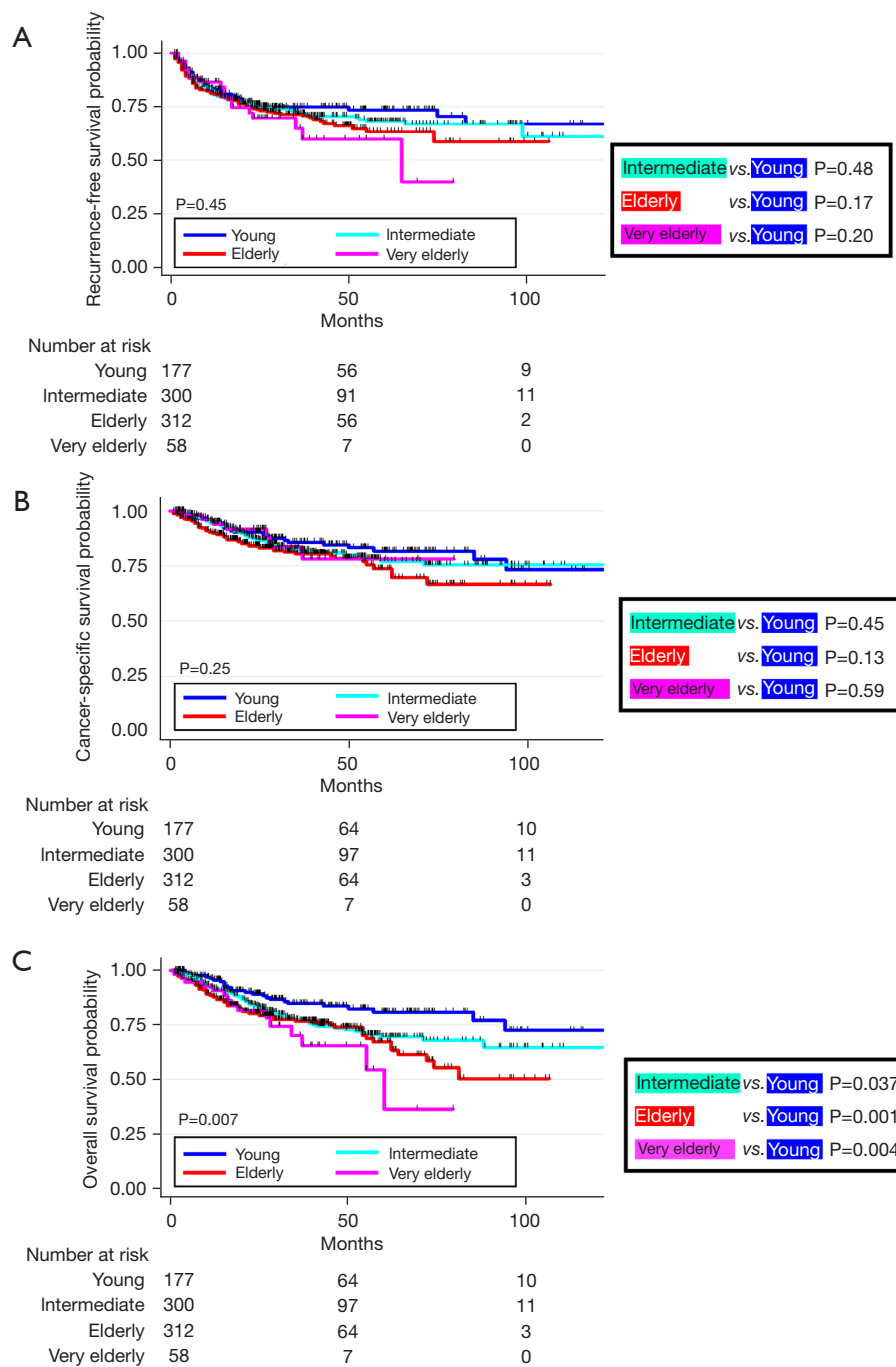
Data are presented as median [IQR] or n (%). ECOG, Eastern Cooperative Oncology Group; NR, not reported; UC, urothelial carcinoma; CIS, carcinoma in situ; LVI, lymphovascular invasion; IQR, interquartile range.

### Multivariate analysis

Employing the Cox regression model, pathological staging  $\geq$  T3, residual lymph node involvement, and LVI were identified as independent determinants for RFS. The same factors significantly influenced CSS and OS. While NUTRFS and CSS did not significantly differ by age, OS rates were again notably lower for the intermediate, elderly, and very elderly groups than for the young group (Table 2).

### Postoperative complications

Table S2 provides a breakdown. Grade III and above complications encompassed wound infections (n=3), ileus (n=2), subcutaneous hematoma (n=1), postoperative bleeding (n=1), cardiovascular events (n=1), and pancreatic fistulas (n=1). Postoperative complications did not lead to any fatalities. Multivariable logistic regression revealed age wasn't a significant predictor for postoperative



**Figure 2** Non-urothelial tract recurrence-free survival (A), cancer-specific survival (B), and overall survival (C) rates for upper tract urothelial carcinoma, segmented by age group: young ( $\leq 64$  years), intermediate-aged (65–74 years), elderly (75–84 years), and very elderly ( $\geq 85$  years).

**Table 2** Multivariate analysis for oncological outcomes

Covariant	Non-urothelial tract RFS			CSS			OS		
	HR	95% CI	P value	HR	95% CI	P value	HR	95% CI	P value
Age									
Young	Ref.			Ref.			Ref.		
Intermediate	1.03	0.66–1.60	0.91	1.14	0.63–2.05	0.67	1.83	1.03–3.27	0.03
Elderly	0.94	0.60–1.47	0.77	1.34	0.75–2.40	0.33	2.06	1.16–3.67	0.01
Very elderly	0.97	0.50–1.86	0.92	0.94	0.37–2.38	0.89	2.43	1.14–5.18	0.02
Sex									
Male	Ref.			Ref.			Ref.		
Female	1.13	0.83–1.53	0.43	0.87	0.58–1.31	0.51	0.72	0.50–1.04	0.08
ECOG performance status									
0–1	Ref.			Ref.			Ref.		
≥2	1.26	0.63–2.51	0.51	1.15	0.50–2.64	0.75	1.22	0.61–2.42	0.57
Tumor location									
Renal pelvis	Ref.			Ref.			Ref.		
Ureter	1.18	0.83–1.66	0.36	1.12	0.71–1.76	0.62	1.19	0.82–1.75	0.36
Both	1.12	0.64–1.96	0.69	0.56	0.23–1.37	0.21	0.74	0.34–1.58	0.44
Hydronephrosis									
Absent	Ref.			Ref.			Ref.		
Present	1.08	0.77–1.51	0.65	1.25	0.80–1.96	0.33	1.13	0.78–1.65	0.52
Pathological T stage									
≤ pT2	Ref.			Ref.			Ref.		
≥ pT3	2.51	1.72–3.65	<0.001	2.78	1.67–4.64	<0.001	2.05	1.36–3.08	<0.001
Histology									
Pure UC	Ref.			Ref.			Ref.		
UC with variant histology	1.43	0.80–2.58	0.23	1.52	0.72–3.20	0.27	1.77	0.95–3.27	0.07
Lymph node status									
pN0	Ref.			Ref.			Ref.		
pN+	2.01	1.26–3.20	0.003	2.2	1.24–3.88	0.007	2.02	1.21–3.39	0.007
pNx	1.04	0.74–1.46	0.83	1.05	0.68–1.62	0.83	0.98	0.68–1.41	0.91
LVI									
Absent	Ref.			Ref.			Ref.		
Present	3.36	2.39–4.72	<0.001	3.17	2.06–4.87	<0.001	2.64	1.84–3.80	<0.001
Tumor grade									
Low	Ref.			Ref.			Ref.		
High	1.88	0.99–3.58	0.053	4.27	1.31–13.90	0.01	1.50	0.82–2.76	0.19
NR	1.21	0.54–2.69	0.64	2.63	0.70–9.84	0.15	0.75	0.32–1.75	0.50
Adjuvant chemotherapy									
Absent	Ref.			Ref.			Ref.		
Present	1.01	0.70–1.45	0.96	1.18	0.77–1.83	0.45	1.11	0.74–1.66	0.62

Young: ≤64 years; intermediate: 65–74 years; elderly: 75–84 years; very elderly: ≥85 years. RFS, recurrence-free survival; CSS, cancer-specific survival; OS, overall survival; HR, hazard ratio; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; UC, urothelial carcinoma; LVI, lymphovascular invasion; NR, not reported; Ref., reference.

**Table 3** Multivariate analysis for predictive factors of complication

Covariant	Complication		
	OR	95% CI	P value
ECOG performance status			
0–1	Ref.		
≥2	2.73	1.01–7.42	0.048
Body mass index	0.97	0.89–1.06	0.55
Sex			
Male	Ref.		
Female	1.09	0.56–2.12	0.79
Lymph node dissection			
Absent	Ref.		
Present	1.34	0.68–2.62	0.39
Age			
Young	Ref.		
Intermediate	1.31	0.46–3.75	0.62
Elderly	1.88	0.68–5.18	0.22
Very elderly	2.37	0.63–8.94	0.20

Young: ≤64 years; intermediate: 65–74 years; elderly: 75–84 years; very elderly: ≥85 years. ECOG, Eastern Cooperative Oncology Group; OR, odds ratio; CI, confidence interval; Ref., reference.

complications. Notably, an Eastern Cooperative Oncology Group (ECOG) performance status ≥2 was the sole significant risk contributor (odds ratio =2.73; 95% confidence interval: 1.01 to 7.42; P value =0.048, *Table 3*).

## Discussion

We investigated the clinical ramifications of age post-nephroureterectomy in patients diagnosed with localized UTUC. Postoperative complication rates after surgery did not significantly differ among the age groups. Similarly, there were no pronounced statistical differences in NUTRFS or CSS by age. Consequently, our results indicate that radical nephroureterectomy might be safely and effectively adopted in judiciously chosen cases, including elderly and very elderly patients. Therefore, age alone should not dictate the viability of this surgical technique for such patients. To the best of our understanding, this research represents the most expansive study to have probed the oncological outcomes in older patients undergoing radical nephroureterectomy within an Asian context (7,8). Notably, this was also the first study to explore the safety of

this procedure in very elderly patients (age ≥85 years). We collated an extensive dataset from diverse centers, which may have potentially countered biases due to individual clinician preferences and varying patient demographics across institutions.

Several studies have considered the clinical consequences of advancing age on the oncological outcomes of UTUC patients (7–10). Shariat *et al.* studied 1,453 patients that had undergone radical nephroureterectomy across 13 establishments. They reported that older age at the time of surgery correlated with diminished survival rates. In multivariate analysis with age treated as a categorical variable, they found that the HR was significantly elevated for CSS and OS for those aged above 80 years (9). Moreover, Ferro *et al.* evaluated 1,387 patients who underwent the same procedure and reported that those who were 70 years or older had inferior CSS and OS versus younger counterparts (10). Two Japanese studies presented different outcomes (7,8). Yamada *et al.* assessed 451 UTUC patients after radical nephroureterectomy and found that while OS was lower in patients aged ≥80 years old, CSS remained comparable across age groups (7). Koterazawa *et al.* studied 283 patients



and reported negligible differences in 5-year CSS rates between elderly ( $\geq 80$  years old) and those  $< 80$  years old. Their 5-year OS rates were 43% for the elderly and 63% for the others, revealing discernible, albeit statistically nonsignificant, variation (8). In addition, Chromecki *et al.* found that older age at the time of nephroureterectomy was associated with worse clinical results after surgery. However, in multivariable analyses that incorporated ECOG performance status, age was solely correlated with diminished OS not impacting CSS (11).

Our findings align with these latter three studies (7,8,11). There are two potential explanations for the variation in results across different studies. First, differences in life expectancy across racial demographics could be in play. Japan ranks fourth in global life expectancy, averaging approximately 85.0 years, outpacing both the United States and many European nations (13). This might correlate with resilience to surgical stress, particularly in older cohorts. Second, as Chromecki *et al.* (11) underscored, ECOG performance status is pivotal in forecasting oncological outcomes. When patients present with optimal performance status, age might not be the primary determinant, encouraging surgeons to advocate for radical nephroureterectomy. Recently, the Geriatric 8 (G8) assessment tool has demonstrated utility in selecting older candidates suitable for uro-oncologic procedures (14). Although we used the ECOG performance metric, G8 data were not captured. As the G8 has been reported to provide a more precise assessment of surgical tolerance (15), we plan to focus on its impact in future research.

The aggregate rates of postoperative complications and grade III or higher complications were 6.61% and 1.06%, respectively. Ileus was the most prevalent postoperative complication, with 21 out of the 56 patients experiencing it after surgery (1.1%, 2.0%, 3.5%, and 3.4% across the age categories from youngest to oldest). In multivariable analysis, there was no significant correlation between age groups and complication rates. Thus, our data suggest that even the very elderly can safely undergo UTUC treatment. Generally, aging is concomitant with a waning physiological reserve, even in those without manifest comorbidities (16). This can compromise an older individual's stress tolerance, potentially heightening postoperative complication risks and in-hospital mortality rates (17). It is pertinent to highlight that most patients nowadays opt for laparoscopic or robot-assisted laparoscopic radical nephroureterectomy, both of which are associated with lower complication rates than open surgery (8). In our cohort, approximately 80% of the

elderly underwent laparoscopic radical nephroureterectomy. Our results are in line with Koterazawa *et al.*, indicating analogous postoperative complication rates among elderly and younger patients following laparoscopic radical nephroureterectomy (8). In terms of postoperative complication risk factors after such surgery, ECOG performance status  $\geq 2$  was the sole significant predictor. This is in line with several previous studies that have reported that suboptimal performance status is linked to heightened postoperative risks for complications such as myocardial infarction and wound infections (18-20). Hence, when UTUC patients show a commendable performance status, their age should not deter clinicians from recommending nephroureterectomy.

Our study had some inherent limitations to acknowledge. Although multi-centric, its retrospective design and relatively short follow-up period are notable constraints. Further, our follow-up protocols lacked robust standardization, evident in the variation in examination types and imaging intervals. In addition, lymph node dissection decisions were made by individual physicians, potentially impacting oncological outcomes. Finally, given that pathology data were sourced from individual centers without a centralized review, diagnostic inconsistencies might have arisen.

## Conclusions

In conclusion, we demonstrate there were no statistically significant differences in NUTRFS or CSS across the four assessed age groups. This suggests that even for patients aged 85 years old and older, surgical treatment might be a viable therapeutic choice, assuming they can withstand the inherent surgical stress and procedure invasiveness.

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The research was approved by the Jikei University Institutional Review Board [protocol No. 33-260(10878)]. Informed consent was obtained from all subjects involved in the study.

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