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Long term survival in elderly patients with resectable upper tract urothelial carcinoma: analysis of hospital-based cancer registry data in Japan

Shuhei Suzuki[1], Yoshiyuki Nagumo[1*], Kosuke Kojo[1], Shuya Kandori[1], Hiromichi Sakurai[1], Reo Takahashi[1], Bunpei Isoda[1], Akane Yamaguchi[1], Kazuki Hamada[1], Kozaburo Tanuma[1], Satoshi Nitta[1], Masanobu Shiga[1], Atsushi Ikeda[1], Takashi Kawahara[1], Akio Hoshi[1], Hiromitsu Negoro[1], Bryan J. Mathis[2], Ayako Okuyama[3,4] and Hiroyuki Nishiyama[1]

Abstract

Background To clarify the long-term prognoses of elderly upper tract urothelial carcinoma (UTUC) patients after surgery.

Methods We used a hospital-based cancer registry data in Japan to extract patients with pT1-3N0M0 UTUC diagnosed in 2009 who underwent surgery, and classified them by age group (≤ 64, 65–74, ≥ 75 years old). We estimated the 10-year overall survival (OS) by a Kaplan-Meier analysis. For cancer survival estimation, we calculated the 10-year net survival (NS) by Pohar-Preme method using the Japanese life tables.

Results A total of 1139 UTUC patients (564 renal pelvic cancer [RPC] and 575 ureteral cancer [UrC]) were identified. The 10-year OS rates for elderly RPC patients (≥ 75 years old) were significantly worse than for younger patients (≤ 64 years old) in pT1 (43.1% vs. 80.1%) and pT2-3 (34.2% vs. 67.3%) stages. In contrast, the 10-year NS rates were comparable between elderly and younger RPC groups in pT1 (93.3% vs. 87.0%) and T2-3 (77.4% vs. 73.7%) stages. While the 10-year NS and OS rates of patients with pT1 UrC had similar trends as RPC patients, the NS and OS rates of elderly patients with pT2-3 UrC were significantly worse than younger patients.

Conclusions Among resectable UTUC, except for pT2-3 UrC patients, estimated cancer survival rates for elderly patients were similar to younger patients. These findings may be useful in shared decision making by informing discussions about treatment strategies with elderly patients and their families.

Keywords Hospital-based cancer registry, Upper tract urothelial carcinoma, Overall survival, Net survival, Elderly patients

*Correspondence:
Yoshiyuki Nagumo
ynagumo@md.tsukuba.ac.jp
[1]Department of Urology, University of Tsukuba, 1-1-1 Tennodai, Tsukuba 305-8575, Ibaraki, Japan
[2]Department of Cardiovascular Surgery, University of Tsukuba, 1-1-1 Tennodai, Tsukuba 305-8575, Ibaraki, Japan
[3]Graduate School of Nursing Science, St Luke's International University, 10-1 Akashicho, Chuo-ku, Tokyo 104-0044, Japan
[4]Center for Cancer Registries, Institute for Cancer Control, National Cancer Center, 5-1-1 Tsukiji, Chuo-ku, Tokyo 104-0045, Japan

Introduction

Upper tract urothelial carcinoma (UTUC) is uncommon, comprising from 5 to 10% of all urothelial carcinoma (UC) [1], and the incidence rate is estimated at approximately 2 per 100,000 persons [2]. UTUC is more common in the elderly and the incidence peaks between 70 and 90 years of age, with men afflicted at twice the rate of women [2, 3]. Patients with non-metastatic UTUC generally receive radical nephroureterectomy (RNU) [3] and, in addition, adjuvant platinum-based chemotherapy may improve prognoses for locally advanced UTUC [4].

On the other hand, treatment choices in the elderly must be based on a risk-benefit assessment. As Japan and other developed countries enter a demographic aging peak [5], elderly patients with frailty syndrome (decreased resistance to external stress and increased vulnerability) are expected to rise, increasing the risk of adverse events and poorer surgical outcomes. There are reports regarding treatment with respect to geriatric oncology, including urologic surgery [6–9], but there remains insufficient evidence regarding the prognoses of non-metastatic UTUC elderly patients after surgery. Optimal treatment choices for these elderly patients in daily clinical practice are facilitated by shared decision-making (SDM), using evidence from big-data studies that aid decision making for both patients and urologists [10].

In this study, we revealed the long-term survival of elderly UTUC patients who underwent surgery and compared them to younger patients using the hospital-based cancer registry (HBCR) from nationwide, designated cancer care hospitals (DCCHs: with regions and representative facilities designated by the Ministry of Health, Labour and Welfare) and other core cancer care hospitals in Japan.

Patients and methods

Data sources

In this study, we used data from the 2009 cohort of the HBCR database, focusing on patients diagnosed with UTUC. This data included survival information for a period of 10 years after diagnosis, aggregated from newly identified cancer patients registered at DCCHs and core cancer care centers across Japan. Notably, this database consisted of data from a total of 281 institutions with at least 90% follow-up of cancer patients [11, 12]. The data collected include information on demographics, tumor characteristics, and initial treatment, recorded by trained cancer registrars.

Data extraction

We extracted eligible cases from the HBCR data using the following inclusion criteria: (i) patients with urothelial carcinoma of the renal pelvis (C65) and ureter (C66) diagnosed in 2009; (ii) patients with a histological diagnosis; and (iii) patients who were either treated with surgery alone or surgery with chemotherapy. Both open and laparoscopic surgeries were combined into the "surgery" group. The neoadjuvant or adjuvant chemotherapy was described as "chemotherapy" because the timing of chemotherapy was unavailable from the HBCR database. We also excluded cases with unknown pathological stages. Because the purpose of this study was to investigate the prognoses after surgery in elderly patients with non-metastatic UTUC, we excluded patients with distant metastases. In addition, patients with pT4 were excluded due to the small number of cases.

Statistical analyses

Pearson's chi-squared test was used to assess differences between age groups for sex, TNM (tumor, nodes, metastasis staging), and treatment method. Overall survival (OS) at 3-, 5-, and 10-year timepoints were evaluated using the Kaplan-Meier method, with comparisons between groups using the log-rank test. The prognoses of RPC and UrC are reported to be different, with UrC having a worse prognosis [13], so they were evaluated separately in the prognosis analysis. Multivariable analysis for the OS was performed by Cox regression analysis for time to death, with age group, sex, pT stage, tumor location, and treatment method as covariables. Since the HBCR data does not contain the cancer specific survival (CSS) status, we used net survival (NS), which estimates survival from cancer by adjusting for other causes of death [14]. The NS was calculated by the Pohar-Perme method [15] by the "relsurv" R package [16], using Japanese life tables, including mortality rates by sex and age in each year, provided by the National Cancer Center. Statistical analyses were performed using a two-sided approach, with a p-value of less than 0.05 considered indicative of statistical significance. R software (version 4.3.3 for Windows®), provided by the R Foundation [17], was used for all analysis.

Results

Patient characteristics

According to the eligibility criteria, a total of 1139 cases were extracted from the 1444 registered patients with UTUC (Fig. 1). The number of patients with renal pelvis cancer (RPC) and ureteral cancer (UrC) were 564 and 575. Table 1 summarizes patient characteristics by age groups. We did not exclude patients with stage 0 (TaN0M0 and TisN0M0) in the eligibility criteria but these patients were eventually excluded as a result of the extraction of eligible patients according to the aforementioned criteria. In elderly RPC patients over 75 years old, the proportion of females was significantly higher compared to patients under 74 years old (34.3%, $p = 0.009$), while the distribution of pT stage did not significantly

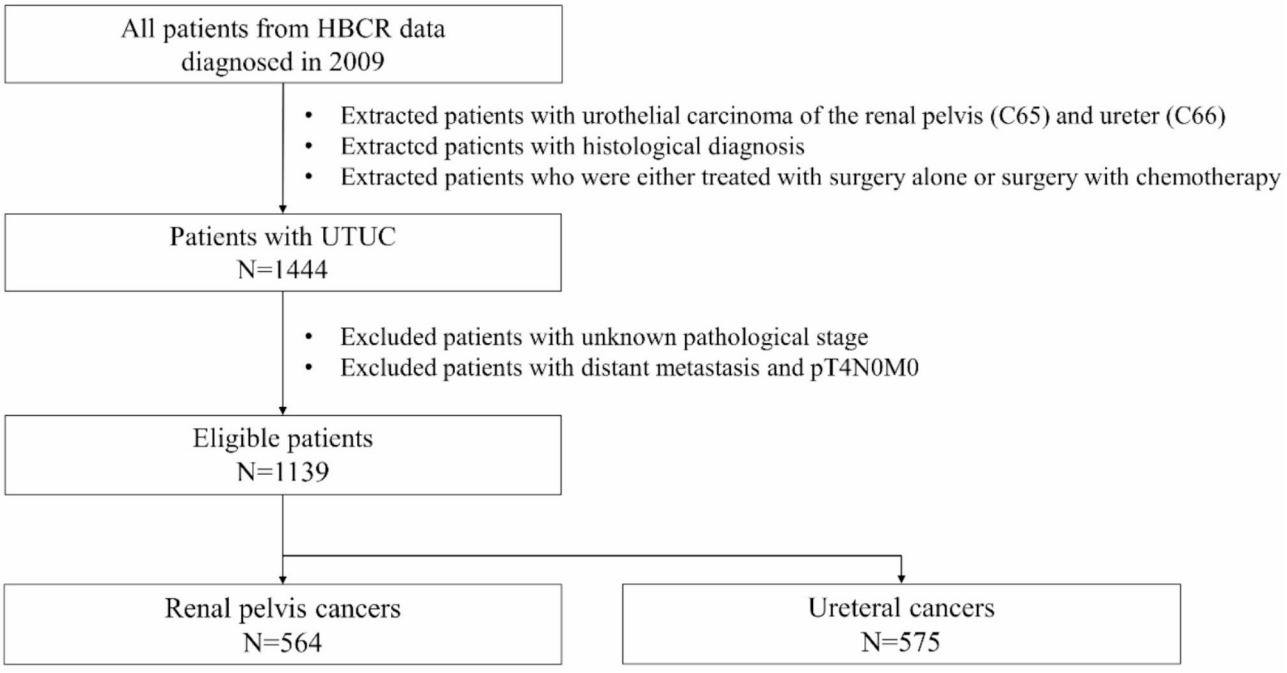

Fig. 1 Eligibility flowchart for patients with upper tract urothelial cancers

Table 1 Characteristics of patients with RPC and urc

		RPC *n* = 564			*P* value	UrC *n* = 575			*P* value
		≤ 64 years *n* = 144	65–74 years *n* = 178	≥ 75 years *n* = 242		≤ 64 years *n* = 99	65–74 years *n* = 191	≥ 75 years *n* = 285	
Sex, *n* (%)					0.024				0.073
	Male	108 (75.0)	137 (77.0)	159 (65.7)		75 (75.8)	127 (66.5)	180 (63.2)	
	Female	36 (25.0)	41 (23.0)	83 (34.3)		24 (24.2)	64 (33.5)	105 (36.8)	
TNM, *n* (%)					0.266				0.437
	pT1N0M0	41 (28.5)	43 (24.2)	76 (31.4)		29 (29.3)	46 (24.1)	83 (29.1)	
	pT2-3N0M0	103 (71.5)	135 (75.8)	166 (68.6)		70 (70.7)	145 (75.9)	202 (70.9)	
Treatment, *n* (%)					< 0.001				0.001
	Surgery Only	104 (72.2)	123 (69.1)	217 (89.7)		67 (67.7)	139 (72.8)	238 (83.5)	
	Surgery and Chemotherapy	40 (27.8)	55 (30.9)	25 (10.3)		32 (32.3)	52 (27.2)	47 (16.5)	

differ among the age groups. In both groups, patients who received chemotherapy had significantly lower rates in patients over 75 years old than those under 75 years old ($p < 0.001$, respectively).

The OS rates of UTUC patients stratified by location of cancer and age groups

Figure 2A and B display OS rates by age groups in each pT stage for RPC. In patients with pT1, the 10-year OS rates were the worst in patients over 75 years old (43.1%, 95% confidence interval [CI]: 33.3–55.9) and there were significant differences compared to patients under 64 years old (80.1%, 95% CI: 68.6–93.5, $p < 0.001$). Similarly, pT2-3 patients over 75 years old had significantly worse 10-year OS rates compared to patients under 64 years old (34.2%, 95% CI: 27.7–42.4 vs. 67.3%, 95% CI: 58.8–77.1, $p < 0.001$).

We next analyzed OS rates for UrC (Fig. 2C and D), finding far worse OS in patients over 75 years old (versus 64 or younger) with pT1 (47.2%, 95% CI: 37.4–59.6 vs. 72.4%, 95% CI: 57.8–90.7, $p = 0.028$) and pT2-3 staging (22.2%, 95% CI: 17.1–28.8 vs. 55.7%, 95% CI: 45.2–68.7, $p < 0.001$).

In terms of the OS stratified by age group (< 75 years and ≥ 75 years), tumor location (RPC and UrC), and treatment (surgery with or without chemotherapy) as shown in Fig. S1, there were no significant differences in the OS with or without chemotherapy in each group.

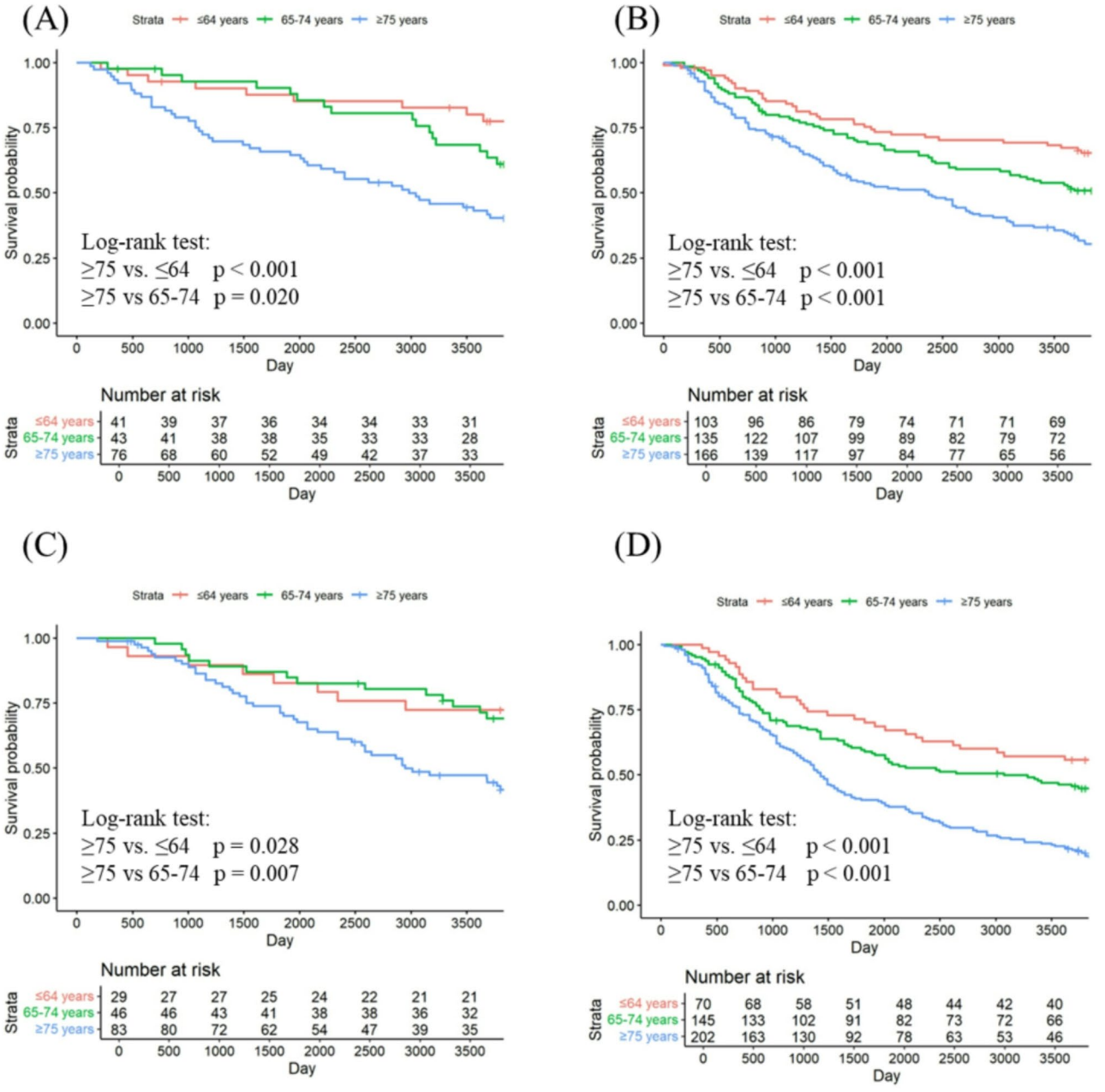

Fig. 2 Kaplan-Meier analyses of the OS of patients with pT1 **(A)** or pT2-3 **(B)** RPC, and pT1 **(C)** or pT2-3 **(D)** UrC, stratified by age groups

Multivariable analysis for the OS of UTUC patients

Multivariable Cox regression analysis for the OS of UTUC patients showed that the hazard ratio (HR) in the 65–74 and ≥ 75 years groups was significantly worse than patients in the ≤ 64 years group (65–74 years HR 1.53, 95% CI: 1.18–1.97 and ≥ 75 years HR 2.82, 95% CI: 2.22–3.58) (Fig.S2). In addition, pT2-3 stage (HR 1.81, 95% CI: 1.49–2.19) and UrC (HR 1.28, 95% CI: 1.09–1.49) were also poor prognostic factors. In contrast, being female was the only significant favorable prognostic factor (HR 0.88, 95% CI: 0.72–0.97).

The NS rates of UTUC patients stratified by location of cancer and age groups

Figure S3 shows Kaplan-Meier analyses of the NS of patients stratified by tumor location, pT stage, and age groups, and the results of the NS in patients with RPC and UrC are summarized in Table 2 for 10 years, and in Tables S1-2 for 3 and 5 years. After adjustment for cancer survival, the difference between NS and OS diverged as age increased overall. In contrast to the 10-year OS rates, the 10-year NS rates of elderly patients over 75 years old with RPC was comparable to other younger age groups with no significant differences for pT1 and pT2-3 stages

Table 2 The 10-year survival rates of RPC and urc patients, stratified by age groups

		RPC 10-year Survival Rates (95% CI)		UrC 10-year Survival Rates (95% CI)	
Variables		**Overall Survival**	**Net Survival**	**Overall Survival**	**Net Survival**
All	≤ 64 years	71.0 (63.9–78.9)	77.6 (69.9–86.2)	60.6 (51.7–71.0)	66.6 (56.9–78.1)
	65–74 years	55.5 (48.6–63.4)	72.3 (63.3–82.7)	52.3 (45.7–60.0)	66.3 (57.7–76.2)
	≥ 75 years	37.1 (31.4–43.8)	83.4 (69.3–100.0)	29.3 (24.4–35.2)	58.5 (47.5–72.0)
pT1N0M0	≤ 64 years	80.1 (68.6–93.5)	87.0 (74.4-101.6)	72.4 (57.8–90.7)	77.1 (61.8–96.1)
	65–74 years	65.9 (52.9–82.1)	85.6 (68.4–107.0)	71.3 (59.3–85.8)	91.1 (74.8–111.0)
	≥ 75 years	43.1 (33.3–55.9)	93.3 (70.4-123.7)	47.2 (37.4–59.6)	87.7 (68.1-113.1)
pT2-3N0M0	≤ 64 years	67.3 (58.8–77.1)	73.7 (64.5–84.3)	55.7 (45.2–68.7)	61.7 (50.1–76.0)
	65–74 years	52.3 (44.5–61.5)	68.2 (58.0-80.1)	46.3 (38.8–55.2)	57.9 (48.5–69.2)
	≥ 75 years	34.2 (27.7–42.4)	77.4 (60.9–98.3)	22.2 (17.1–28.8)	42.6 (31.5–57.7)

(93.3%, 95% CI: 70.4-123.7 and 77.4%, 95%CI: 60.9–98.3, respectively). Similar trends were also demonstrated in patients with pT1 UrC (87.7%, 95% CI: 68.1-113.1). On the other hand, the 10-year NS rates of elderly patients over 75 years old with pT2-3 UrC (42.6%, 95% CI: 31.5–57.7) were significantly worse compared to patients under 64 years old (61.7%, 95% CI: 50.1–76.0, $p = 0.004$) and those aged 65–74 years (57.9%, 95% CI: 48.5–69.2, $p = 0.025$).

Prognostic analysis in the advanced elderly

Focusing on the advanced elderly (≥ 80 years old) group (Table S3), there were larger differences between OS and NS in pT1 (RPC: 30.6% vs. 97.8%, UrC: 41.4% vs. 90.8%) and pT2-3 RPC (27.6% vs. 87.0%) than other age groups. On the other hand, the difference between OS and NS in pT2-3 UrC was relatively small (13.5% vs. 33.0%) and significantly different from pT1 UrC ($p < 0.001$).

Discussion

Treatments for elderly patients, such as surgery and chemotherapy, should be performed with caution, taking into account their performance status and comorbidities. Frailty syndrome, especially in elderly cancer patients, is a chief concern as it is a state of vulnerability in which homeostasis fails [18], making recovery arduous. The prevalence in elderly patients was reported at 42% [6], making thorough consideration necessary when choosing treatment options for the elderly based on efficacy reports from younger patients.

In terms of elderly UTUC patients, Shariat et al. [9] analyzed the prognosis of elderly UTUC patients who underwent RNU and showed that patients over 80 years old had poorer CSS (HR 1.63) compared to patients under 50 years old. In addition, Seisen et al. [19] reported that age was identified as a prognostic factor that predicts the CSS in patients with non-metastatic UTUC. In this study, the NS rates of patients over 75 years old with the pT1-3 RPC and pT1 UrC groups had prognoses comparable to those of younger patients under 64 years old, which differed from the results of the OS. These results indicated that deaths from causes other than cancer were more frequent in elderly patients, highlighting the importance of delineating causes of death in groups susceptible to age- and co-morbidity-related conditions. In contrast, patients with pT2-3 UrC had a significant difference between the two groups in the NS rates as well as the OS rates. These trends were similar in the advanced elderly patient group (≥ 80 years of age). A possible reason was due to the generally poor prognosis of UrC compared to RPC [13]. In addition, as mentioned above, it has been reported that the prognosis of older UTUC patients is worse than younger patients and the cause is considered to be changes in the biological potential of tumor cells and declines in host defense mechanisms [9]. In contrast, in a recent Japanese study, Ishikawa et al. [20], investigated the prognosis of UTUC patients that underwent RNU from 2012 to 2021 (stratified by age) and revealed a 3-year CSS of 80.3–85.7% and a consistent therapeutic benefit of RNU across age groups. The lower proportion of elderly patients receiving chemotherapy may have an impact on prognoses, which could be the result of carefully considering side effect risks in those of advanced age. On the other hand, no significant differences were found in the analysis by treatment in the present study. We speculate that disadvantages, such as poor renal function, in the elderly might have affected the chemotherapy regimen, dose setting, treatment period, and/or prognoses [21] but, unfortunately, the lack of detailed information on chemotherapy makes it difficult to discuss this point.

Given the results of our study, the prognosis after surgery in elderly patients with resectable UTUC, especially pT1-3 stage RPC and pT1 UrC, may be comparable to younger patients. However, mortality from non-cancer causes and the incidence of adverse events should not be underestimated. In addition, Schaffar et al. showed that the difference of NS between the two groups increased

with time from diagnosis in a comparison between relative survival setting (the method used in this study) and cause-specific setting [14]. Furthermore, Tanaka et al. reported that the elderly group and the long observation period affected the difference of the NS between two different life Table [22]. Therefore, the analysis of the NS for long-term survival rates in the elderly should be carefully evaluated.

Since prognostic information is of importance to patients and their families in the SDM process [23, 24], the differences we observed between long-term OS and NS in elderly UTUC patients may help patients in their treatment choices. Also important is screening for frailty syndrome and stratifying offered treatment choices based on case-by-case assessments. When treating elderly patients, it is important to carefully explain the prognosis and safety of suitable treatments to facilitate SDM.

This study has several limitations. First, since the HBCR data did not include information on causes of death, we estimated cancer-related deaths by analyzing the NS. Second, the HBCR data did not include detailed treatment information, such as chemotherapy regimens or surgical procedures. Because of these limitations, it was difficult to evaluate the correlation of differences in chemotherapy and prognoses, especially in the elderly and young. Finally, the HBCR did not include information on performance status and comorbidity, which should be considered in a prognostic analysis, especially in elderly patients. However, the HBCR database did enable this initial analysis to support SDM for geriatric oncology cases in treatment selection considering prognoses.

Conclusion

This showed that the 10-year OS rates of elderly groups in resectable pT1-3 UTUC patients were worse than those of younger patients overall, but the 10-year NS rates were comparable between elderly and younger patients except for pT2-3 UrC patients. In these elderly patients, although causes of death other than cancer cannot be ignored, surgery with consideration for comorbidities may lead to improved survival. These findings could be helpful in the discussion of treatment strategies between elderly patients and urologists.

Abbreviations

UTUC	Upper tract urothelial carcinoma
UC	Urothelial carcinoma
RNU	Radical nephroureterectomy
SDM	Shared decision-making
HBCR	Hospital-based cancer registry
DCCHs	Designated cancer care hospitals
OS	Overall survival
CSS	Cancer specific survival
NS	Net survival
RPC	Renal pelvis cancer
UrC	Ureteral cancer
CI	Confidence interval
HR	Hazard ratio

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12885-025-13852-3.

Supplementary Material 1

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Author contributions

Writing - Original Draft Preparation: SS. Writing - Review & Editing: YN, BJM. Formal Analysis: SS. Methodology: SS, YN, SN, MS. Data Curation: KK. Visualization: HS, RT, BI, AY, KH. Investigation and Project Administration: AO. Conceptualization: YN, KT, AI, TK, AH. Supervision: YN, SK, HNe, HNi.

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Data availability

The datasets generated and analyzed during the current study are not publicly available because the data were provided by third parties.

Declarations

Ethics approval and consent to participate

The protocol of this study was approved by the Institutional Review Board of the University of Tsukuba Hospital (R03-228), and informed consent was obtained from participants by opt-out. This study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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