

Oncologic Surveillance After Radical Nephroureterectomy in Upper Tract Urothelial Carcinoma Patients: A Novel Risk-Based Approach

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Objective

To develop a follow up model for post RNU surveillance applying Weibull model estimates which dynamically illustrates oncologic surveillance that balances the risk of UTUC related death and the risk of non-UTUC death.

Materials and Methods

Patient Background

Patient Samples

We retrospectively identified 888 UTUC patients, and total of 714 patients diagnosed with Ta-T4 UTUC without positive lymph node or distant metastasis (Ta-4N0M0) were included.

Surgical Procedure

Laparoscopic or open RNU was performed according to the standard procedure, involving extrafascial dissection of the kidney with the entire length of the ureter and adjacent segment of the bladder cuff being removed.

Follow up Regimen

Patients were generally followed-up routinely 3 and 6 months after surgery, every 6 months during the first 5 years, and annually thereafter.

Definition of disease recurrence, UTUC related death, and non-UTUC related death

Disease-recurrence: local or distant recurrence detected by radiography.

UTUC related death: patients died with UC listed on the death certificate.

Non-UTUC related death: patients died from any cause except that related to UTUC.

Statistical Analysis

Weibull models are an alternative parametric approach to Cox's proportional hazard regression models. It allows for simultaneous estimation of the hazard rate and the relative increase or decrease of the competing risks over time.

The risk hazard function $H(t)$ can be calculated from following formula;

$$H_i(t) = \exp(X_i) \times \lambda \times \gamma \times t^{\gamma-1}$$

(λ : Weibull coefficient. γ : shape parameter, λ : scale parameter)

Risk of UTUC related death was estimated after stratifying patients by pathologic stages: pTa-1N0M0, pT2N0M0, pT3N0M0, and pT4N0M0.

Risk of non-UTUC related death was estimated after stratifying patients with chronological age: age ≤ 60 , 61-70, 71-80, and over 80).

The risk hazard calculated by Weibull models were then graphed, allowing us to identify the specific time point where the risk of non-UTUC death exceeded the UTUC death.

Table 1. Descriptive characteristics of 714 upper tract urothelial carcinoma patients treated with radical nephroureterectomy

Characteristics		Total	p value
Gender	male	537(75.2)	0.005
	female	177(24.8)	
Age	≤ 60	117(16.4)	0.327
	61-70	195(27.3)	
	71-80	272(38.1)	
	>80	130(18.2)	
Tumor location	pelvis	363(50.8)	0.984
	ureter	351(49.2)	
Pathological T stage	T ≤ 1	279(39.1)	0.005
	T2	121(16.9)	
	T3	273(38.2)	
	T4	41(5.7)	
Local or distant recurrence	yes	157(22.0)	<0.001
	no	557(78.0)	
Cancer related death	yes	190(26.6)	<0.001
	no	524(73.4)	
Overall death	yes	328(45.9)	<0.001
	no	386(54.1)	

UC; urothelial carcinoma, LVI; Lymphovascular invasion

Result

Figure 1: The over time risk change of disease recurrence and non-UTUC related death

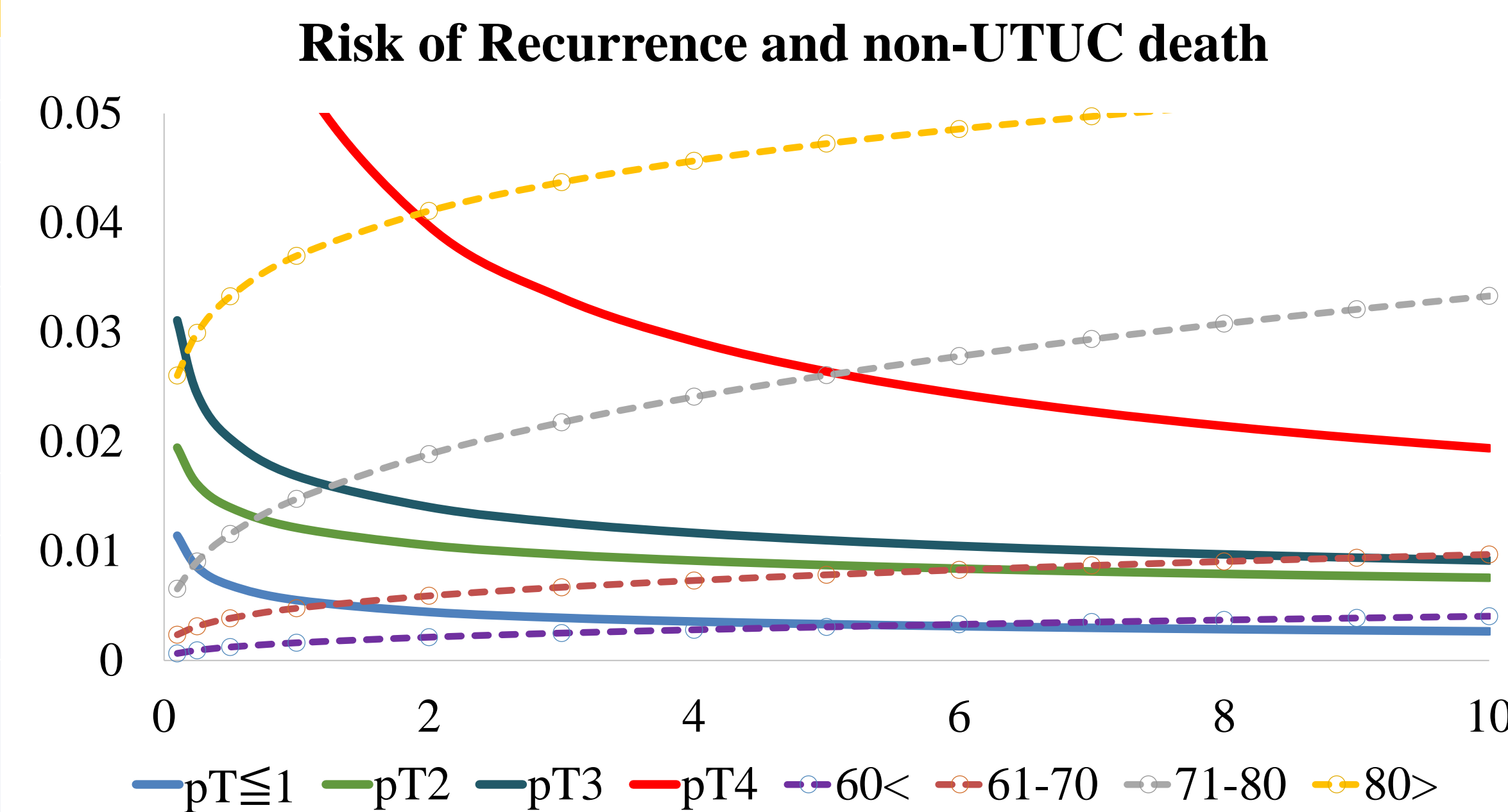


Table 2: Age-specific and stage-status-specific time points when the non-UTUC related death exceeds the risk of disease recurrence

Pathological Stage	Time Points in Years, by Age Group			
	age ≤ 60	age61-70	age71-80	age>80
pTa/CIS/1N0M0	5	1	0.5	-
pT2N0M0	>10	6	1	-
pT3N0M0	>10	10	1.5	0.5
pT4N0M0	>10	>10	5	2

Figure 2: The over time risk change of UTUC related death and non-UTUC related death

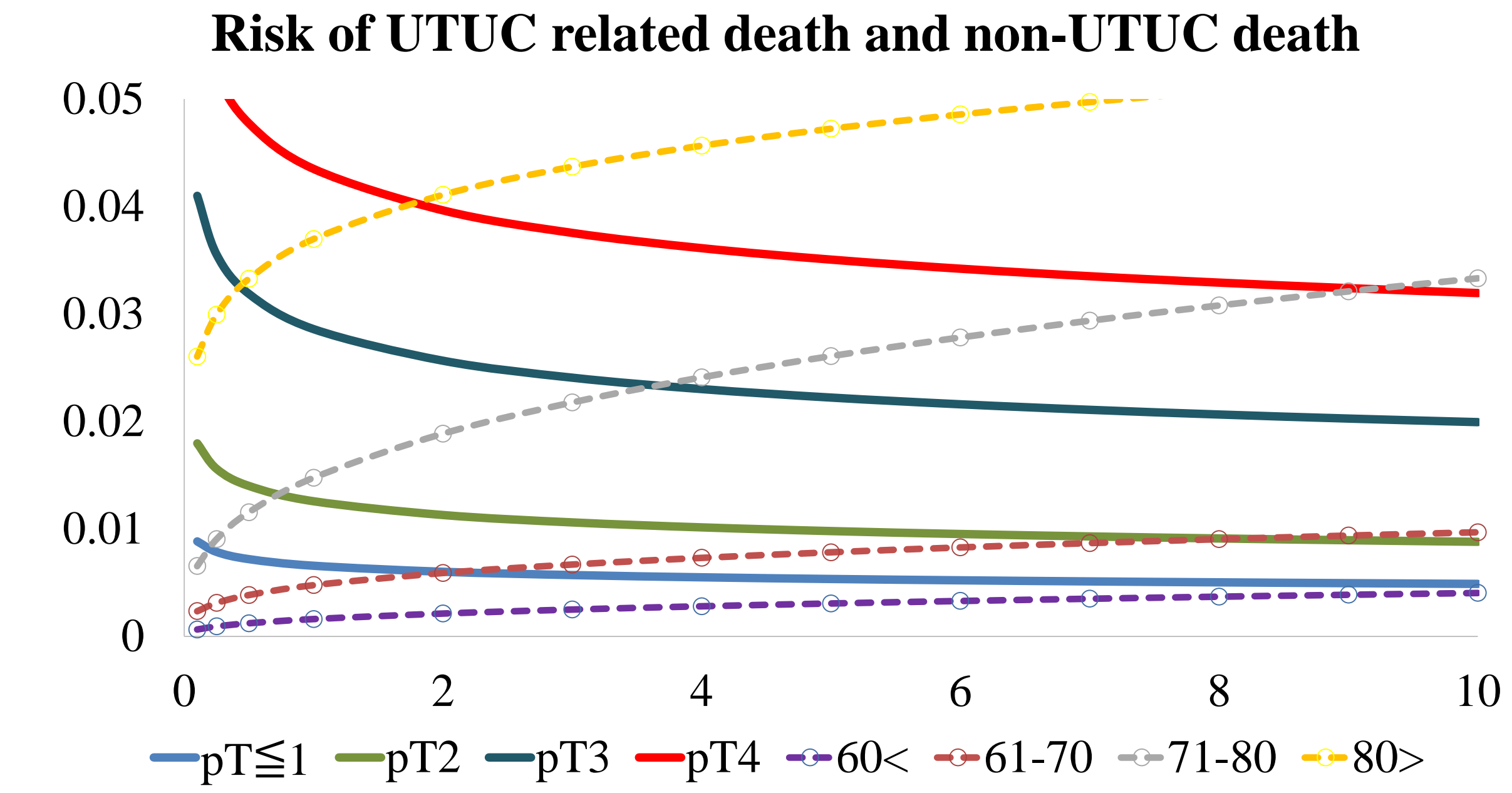


Table 3: Age-specific and stage-status-specific time points when the risk of non-UTUC death exceeds the risk of UTUC related death

Pathological Stage	Time Points in Years, by Age Group			
	age ≤ 60	age61-70	age71-80	age>80
pTa/CIS/1N0M0	>10	3	0.5	-
pT2N0M0	>10	8	1	-
pT3N0M0	>10	>10	4	0.5
pT4N0M0	>10	>10	9	2

Summary of Key Findings

- The interaction between Weibull model estimates for the risk of disease recurrence and UTUC related death stratified by stage and the risk of non-RCC death stratified by age are presented in Figure 1 and 2. **As the pathological stage become advanced, the hazard risk tended to become high at the starting point, but diminished over time. In contrast, high age tended to have higher risk of developing non-UTUC death, and it increased with changing time.**
- At the time point when the risk of non-UTUC deaths exceeded the risk of UTUC death can be assessed as the recommended surveillance duration for UTUC patients, which are shown in Table 2 and 3. **The specific time points shown in the table can be regarded as the recommended surveillance duration for UTUC patients after RNU.** For example, for younger than 60 years old group, the risk of non-UTUC death mostly needs for more than 10 years to exceed the risk of recurrence or UTUC related death regardless of their pathological stage. In contrast, for older than 80s, the risk of non-UTUC death would exceed the risk of cancer death within 2 years or less, which suggests that dense follow up schedule would not be necessary for the elderly stage.

Conclusion

We present a novel methodology which simulated the patient's course of death with UTUC and the natural interplay with the patient's age status.