

Prognostic Impact of Early Recurrence After Radical Cystectomy: A Multicenter Analysis Using Restricted Cubic Splines

Suguru Ito

sugu1219@yahoo.co.jp

Yamagata University Faculty of Medicine: Yamagata Daigaku Igakubu Daigakuin Igakukei Kenkyuka
<https://orcid.org/0009-0007-6256-023X>

Takafumi Narisawa

Yamagata University Faculty of Medicine: Yamagata Daigaku Igakubu Daigakuin Igakukei Kenkyuka

Hiroki Fukuhara

Yamagata University Faculty of Medicine: Yamagata Daigaku Igakubu Daigakuin Igakukei Kenkyuka

Sei Naito

Yamagata University Faculty of Medicine: Yamagata Daigaku Igakubu Daigakuin Igakukei Kenkyuka

Naoki Fujita

Hirosaki Daigaku Igakubu Fuzoku Byoin

Mizuki Kobayashi

Akita University Faculty of Medicine: Akita Daigaku Daigakuin Igakukei Kenkyuka Igakubu

Daiki Ikarashi

Iwate Medical University: Iwate Ika Daigaku

Takuma Sato

Tohoku University School of Medicine: Tohoku Daigaku Daigakuin Igakukei Kenkyuka Igakubu

Akifumi Onagi

Fukushima Medical University: Fukushima Kenritsu Ika Daigaku

Kento Morozumi

Tohoku Medical and Pharmaceutical University: Tohoku Ika Yakka Daigaku

Shingo Myouen

Miyagi Cancer Center: Miyagi Kenritsu Gan Center

Masanobu Shiga

University of Tsukuba Faculty of Medicine: Tsukuba Daigaku Igaku Iryokei

Shuya Kandori

University of Tsukuba Faculty of Medicine: Tsukuba Daigaku Igaku Iryokei

Takamitsu Inoue

Kokusai Iryo Fukushi Daigaku

Shintaro Narita

Akita University Faculty of Medicine: Akita Daigaku Daigakuin Igakukei Kenkyuka Igakubu

Wataru Obara

Iwate Medical University: Iwate Ika Daigaku

Akihiro Ito

Tohoku University Graduate School of Medicine: Tohoku Daigaku Daigakuin Igakukei Kenkyuka Igakubu

Yoshiyuki Kojima

Fukushima Medical University: Fukushima Kenritsu Ika Daigaku

Yasuhiro Kaiho

Tohoku Medical and Pharmaceutical University: Tohoku Ika Yakka Daigaku

Hisanobu Adachi

Miyagi Cancer Center: Miyagi Kenritsu Gan Center

Jun Miyazaki

Kokusai Iryo Fukushi Daigaku

Shingo Hatakeyama

Hirosaki Daigaku Igakubu Fuzoku Byoin

Norihiko Tsuchiya

Yamagata University Faculty of Medicine: Yamagata Daigaku Igakubu Daigakuin Igakukei Kenkyuka

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Abstract

Background

The prognostic impact of time to recurrence (TTR) after radical cystectomy (RC) remains incompletely understood. We evaluated the association between TTR and post-recurrence survival (PRS) in patients with muscle-invasive bladder cancer using restricted cubic spline (RCS) analysis.

Methods

We retrospectively analyzed 299 patients who developed recurrence after RC between 2005 and 2022 across 10 institutions. TTR was modeled as a continuous variable using multivariable Cox regression with RCS functions. Receiver operating characteristic analyses were additionally performed to explore cutoff values.

Results

Median TTR was 7.8 months, and 123 patients (41.1%) developed recurrence within 6 months after RC. RCS analysis demonstrated a nonlinear association between TTR and PRS (overall $p = 0.019$; nonlinear $p = 0.016$). Mortality risk increased steeply among patients recurring within the first several postoperative months. TTR was not significantly associated with mortality when modeled linearly (hazard ratio 0.99 per month, $p = 0.211$). ROC analyses identified cutoff values of approximately 6 months. Patients with recurrence within 6 months had significantly worse PRS, and early recurrence remained independently associated with worse survival in multivariable analysis (hazard ratio 1.50, $p = 0.015$). Limitations include the retrospective design and lack of external validation.

Conclusions

The prognostic impact of recurrence timing after RC was concentrated within the earliest postoperative months. Recurrence within 6 months after RC was independently associated with poor PRS and may identify patients with biologically aggressive disease.

Advancing Practice

- Time to recurrence after radical cystectomy showed a nonlinear association with post-recurrence survival.
- Excess mortality risk was concentrated within the first several postoperative months rather than changing linearly over time.

- Recurrence within 6 months after surgery identified a subgroup with particularly poor post-recurrence survival.
- Restricted cubic spline analysis may provide a more clinically informative assessment of recurrence timing than conventional categorical approaches.

Patient Summary

We studied patients whose bladder cancer recurred after bladder removal surgery. Patients who developed recurrence within 6 months had poorer survival after recurrence than those recurring later. Early recurrence may indicate biologically aggressive disease.

Introduction

Bladder cancer is the ninth most commonly diagnosed malignancy worldwide, and approximately 25–30% of patients present with muscle-invasive disease (MIBC) [1]. Radical cystectomy (RC) with pelvic lymph node dissection remains the standard treatment for localized MIBC, often combined with perioperative systemic therapy [2, 3]. Despite these approaches, recurrence after RC remains common and is the major cause of cancer-related mortality [4, 5]. Most recurrences develop within the first 2 years after surgery [5, 6].

Several studies have suggested that shorter time to recurrence (TTR) after RC is associated with worse post-recurrence survival (PRS) [6–10]. Stewart-Merrill et al. reported particularly poor survival among patients recurring within 6 months after RC [7], while other groups incorporated recurrence timing into post-recurrence risk models [8, 9]. These findings suggest that early recurrence may reflect aggressive disease biology.

Most previous studies, however, categorized TTR using arbitrary intervals such as 6 or 12 months. This approach may oversimplify the relationship between recurrence timing and prognosis, particularly if the effect of TTR is nonlinear across time.

In the present study, we evaluated the association between TTR and PRS in patients with recurrence after RC using restricted cubic spline (RCS) analysis in a multicenter Japanese cohort.

Patients and Methods

Study population and variables

This retrospective multicenter study utilized the Michinoku Urological Cancer database, including patients who underwent RC for bladder cancer across 10 institutions in eastern Japan between 2005 and 2022. Patients who developed recurrence after RC for MIBC were included. Patients with pure non-urothelial carcinoma, metastatic disease at surgery, or missing essential survival data were excluded. Of 313 patients with recurrence, 299 with complete data were included in multivariable analyses (Fig. 1).

TTR was defined as the interval from RC to radiologically or pathologically confirmed recurrence. PRS was defined as the interval from recurrence to death from any cause or last follow-up. Survival analyses were anchored at the date of recurrence to minimize immortal time bias.

Clinicopathological variables included age, sex, body mass index (BMI), Eastern Cooperative Oncology Group performance status (ECOG PS), serum albumin, estimated glomerular filtration rate (eGFR), hydronephrosis, pathological stage, lymphovascular invasion, lymph node status, histology, perioperative treatment, treatment era, and recurrence pattern. Treatment era was categorized into three periods reflecting major therapeutic changes in advanced urothelial carcinoma management, including the introduction of pembrolizumab and enfortumab vedotin.

The study was approved by the institutional review boards of all participating institutions and conducted in accordance with the Declaration of Helsinki. The requirement for informed consent was waived because of the retrospective study design.

Statistical analysis

Continuous variables were summarized as median and interquartile range (IQR), and categorical variables as counts and percentages. Comparisons between groups were performed using the Mann–Whitney U test or Fisher’s exact test.

The association between TTR and PRS was evaluated using Cox proportional hazards models. TTR was modeled as a continuous variable using RCS functions with four knots placed at Harrell’s recommended percentiles [11]. Multivariable analyses were adjusted for clinicopathological variables. Model fit was compared between linear and spline models using likelihood ratio tests.

For exploratory analyses, patients were categorized according to TTR (≤ 6 months vs > 6 months). Receiver operating characteristic analyses were performed using fixed-time ROC methods for 1- and 2-year mortality after recurrence.

All analyses were conducted using R software version 4.5.1 (R Foundation for Statistical Computing, Vienna, Austria). A two-sided p value < 0.05 was considered statistically significant.

Results

Patient characteristics

Among 299 patients included in the analyses, median age was 70 years (IQR 64–75), and 72% were male (Table 1). Median TTR was 7.8 months (IQR 4.0–15.7), and median follow-up after recurrence was 24.1 months (IQR 12.2–47.2). Pathological lymph node positivity was observed in 40% of patients, while lymphatic and venous invasion were present in 53% and 52%, respectively.

Table 1
Baseline patient characteristics

Characteristics	All patients (N = 299)
Age (years)	
Median [IQR]	70 [64, 75]
Sex	
Male, N (%)	215 (72)
Female, N (%)	84 (28)
ECOG PS	
0, N (%)	266 (89)
1, N (%)	24 (8)
≥ 2, N (%)	9 (3)
BMI (kg/m ²)	
Median [IQR], kg/m ²	22.8 [20.5, 24.8]
eGFR (mL/min/1.73m ²)	
Median [IQR], mL/min/1.73m ²	60.2 [47.8, 75.4]
Albumin (g/dL)	
Median [IQR], g/dL	3.9 [3.6, 4.2]
Hydroureteronephrosis	
N (%)	106 (36)
Clinical T stage	
cT2, N (%)	112 (38)
cT3, N (%)	142 (47)
cT4, N (%)	45 (15)
Clinical N stage	
Data are presented as median [interquartile range] or N (%).	
Treatment era was categorized into three periods reflecting major therapeutic changes in the management of advanced urothelial carcinoma: Era 1 (until March 2018); Era 2 (April 2018 to August 2021; after the introduction of robot-assisted radical cystectomy and pembrolizumab); and Era 3 (September 2021 onward; after the introduction of enfortumab vedotin).	

Characteristics		All patients (N = 299)
	cN0, N (%)	222 (74)
	cN1, N (%)	46 (15)
	cN2, N (%)	23 (8)
	cN3, N (%)	8 (3)
Pathological T stage		
	pT0, N (%)	3 (1)
	pT1, N (%)	3 (1)
	pT2, N (%)	15 (5)
	pT3, N (%)	38 (13)
	pT4, N (%)	11 (4)
	pTis, N (%)	2 (1)
	ypT0, N (%)	22 (7)
	ypTa, N (%)	3 (1)
	ypT1, N (%)	10 (3)
	ypT2, N (%)	47 (16)
	ypT3, N (%)	95 (32)
	ypT4, N (%)	43 (14)
	ypTis, N (%)	7 (2)
Pathological N stage		
	pN0, N (%)	178 (60)
	pN1, N (%)	64 (21)
	pN2, N (%)	44 (15)
	pN3, N (%)	13 (4)
Data are presented as median [interquartile range] or N (%).		
Treatment era was categorized into three periods reflecting major therapeutic changes in the management of advanced urothelial carcinoma: Era 1 (until March 2018); Era 2 (April 2018 to August 2021; after the introduction of robot-assisted radical cystectomy and pembrolizumab); and Era 3 (September 2021 onward; after the introduction of enfortumab vedotin).		

Characteristics		All patients (N = 299)
Lymphatic invasion		
	ly0, N (%)	142 (47)
	ly1, N (%)	157 (53)
Venous invasion		
	v0, N (%)	145 (48)
	v1, N (%)	154 (52)
Histological Type		
	Pure UC, N (%)	247 (83)
	UC with DD, N (%)	45 (15)
	Other, N (%)	7 (2)
Neoadjuvant		
	None, N (%)	72 (24)
	Yes, N (%)	227 (76)
Adjuvant		
	None, N (%)	240 (80)
	Yes, N (%)	59 (20)
Follow-up period		
	median [IQR], months	24.1 [12.2, 47.2]
Clinical outcome at final		
	Survival after recurrence, N (%)	114 (38)
	Cancer specific death, N (%)	175 (59)
	Other-cause mortality, N (%)	10 (3)
Time to recurrence		
Data are presented as median [interquartile range] or N (%).		
Treatment era was categorized into three periods reflecting major therapeutic changes in the management of advanced urothelial carcinoma: Era 1 (until March 2018); Era 2 (April 2018 to August 2021; after the introduction of robot-assisted radical cystectomy and pembrolizumab); and Era 3 (September 2021 onward; after the introduction of enfortumab vedotin).		

Characteristics	All patients (N = 299)
median [IQR], months	7.8 [4.0, 15.7]
Treatment era	
Era 1 (pre-ICI), N (%)	185 (62)
Era 2 (ICI era), N (%)	73 (24)
Era 3 (EV era), N (%)	41 (14)
Data are presented as median [interquartile range] or N (%).	
Treatment era was categorized into three periods reflecting major therapeutic changes in the management of advanced urothelial carcinoma: Era 1 (until March 2018); Era 2 (April 2018 to August 2021; after the introduction of robot-assisted radical cystectomy and pembrolizumab); and Era 3 (September 2021 onward; after the introduction of enfortumab vedotin).	

Abbreviations: BMI, body mass index; ECOG PS, Eastern Cooperative Oncology Group performance status; eGFR, estimated glomerular filtration rate; UC, urothelial carcinoma; DD, divergent differentiation; IQR, interquartile range.

Association between continuous TTR and PRS

Among the 299 patients, 123 (41.1%) experienced recurrence within 6 months after RC (Fig. 2A). RCS analysis demonstrated a nonlinear association between TTR and PRS (overall $p = 0.019$; nonlinear $p = 0.016$) (Fig. 2B). Mortality risk increased steeply among patients recurring within the first several postoperative months and gradually plateaued thereafter.

In contrast, TTR was not significantly associated with mortality when modeled linearly (hazard ratio [HR] 0.99 per month, 95% confidence interval [CI] 0.98–1.00; $p = 0.211$; Supplementary Table 1). The spline model showed better fit than the linear model (likelihood ratio test $p = 0.019$; Supplementary Table 2).

Higher albumin level, treatment during the enfortumab vedotin era, and recurrence confined to lymph nodes were independently associated with improved PRS in multivariable spline analysis (Supplementary Table 5).

Six-month cutoff analysis

Fixed-time ROC analyses identified cutoff values of 5.5 months for 1-year mortality and 5.8 months for 2-year mortality (Supplementary Fig. 1). Based on these findings and spline curve morphology, 6 months was selected for exploratory analyses.

Patients with recurrence within 6 months had significantly worse PRS than those recurring later (log-rank $p = 0.029$) (Fig. 3). Median PRS was 12.9 months in the ≤ 6 months group and 19.5 months in the > 6

months group. In multivariable analysis, recurrence within 6 months remained independently associated with worse survival (HR 1.50, 95% CI 1.08–2.08; $p = 0.015$) (Table 2).

Table 2
Multivariable Cox model for post-recurrence survival including TTR group (≤ 6 vs > 6 months)

Variable	Adjusted HR	95% CI	P value
TTR ≤ 6 months (vs > 6 months)	1.50	1.08–2.08	0.015
Age (per year)	1.00	0.99–1.03	0.385
BMI (per kg/m ²)	0.97	0.93–1.02	0.199
Sex (male vs female)	1.14	0.79–1.62	0.478
ECOG PS 1 (vs 0)	1.06	0.59–1.90	0.845
ECOG PS 2 (vs 0)	0.57	0.19–1.66	0.304
Albumin (per g/dL)	0.58	0.41–0.81	0.001
eGFR (per mL/min/1.73 m ²)	0.99	0.99–1.00	0.108
Hydronephrosis (yes vs no)	0.56	0.38–0.82	0.003
Histology: Pure UC vs UC with DD or Other	0.96	0.64–1.45	0.859
Neoadjuvant chemotherapy	0.95	0.63–1.41	0.787
Adjuvant therapy	1.16	0.78–1.74	0.459
Advanced pathological stage ($\geq$ pT3 or ypT2–4)	0.93	0.61–1.44	0.760
Lymphatic invasion (positive vs negative)	1.21	0.82–1.76	0.329
Venous invasion (positive vs negative)	1.13	0.77–1.65	0.539
Lymph node positive	1.12	0.79–1.59	0.514
Treatment era 2 vs 1	0.79	0.53–1.17	0.234
Treatment era 3 vs 1	0.47	0.25–0.87	0.016
Recurrence confined to lymph nodes	0.53	0.37–0.77	< 0.001
Adjusted hazard ratios were estimated using multivariable Cox proportional hazards models.			
Abbreviations: TTR, time to recurrence; BMI, body mass index; ECOG PS, Eastern Cooperative Oncology Group performance status; eGFR, estimated glomerular filtration rate; UC, urothelial carcinoma; DD, divergent differentiation; HR, hazard ratio; CI, confidence interval.			

The early recurrence group showed higher rates of lymph node positivity and venous invasion, whereas recurrence site distribution did not significantly differ between groups (Supplementary Tables 3 and 4).

Discussion

In this multicenter cohort of patients with recurrence after RC for MIBC, we found that the association between TTR and PRS was nonlinear. Mortality risk was highest among patients recurring within the first several postoperative months and gradually plateaued thereafter. By contrast, linear modeling did not demonstrate a significant association between TTR and survival.

Previous studies have shown worse outcomes in patients with shorter TTR after RC [6–10]. Stewart-Merrill et al. reported particularly poor survival among patients recurring within 6 months after surgery [7]. Our findings are consistent with these observations while additionally suggesting that the prognostic impact of recurrence timing is concentrated within an early postoperative period rather than changing linearly over time.

Very early recurrence after RC likely reflects occult metastatic disease already present at the time of surgery. In the present cohort, early recurrence was associated with higher rates of lymph node positivity and venous invasion, both established adverse pathological features [12, 13]. However, these pathological factors were not independently associated with PRS in multivariable analyses, suggesting that TTR may partly capture aggressive disease biology not fully reflected by conventional clinicopathological variables.

Using ROC analyses and spline curve morphology, we selected 6 months as a clinically relevant cutoff for exploratory analyses. Patients recurring within 6 months had significantly worse PRS, and early recurrence remained independently associated with mortality after multivariable adjustment. Although the discriminatory performance of TTR alone was modest, recurrence timing may still provide useful prognostic information when interpreted together with other clinicopathological factors.

Higher albumin level was independently associated with improved PRS, consistent with previous reports demonstrating the prognostic value of nutritional and inflammatory markers in urothelial carcinoma [14]. Treatment during the enfortumab vedotin era was also associated with improved survival, reflecting recent advances in systemic therapy for advanced urothelial carcinoma [15–18].

Recurrence confined to lymph nodes was associated with improved survival. Previous studies have similarly shown better outcomes in patients without visceral metastases [9]. In the present cohort, recurrence site distribution was comparable between early and late recurrence groups, suggesting that recurrence timing and metastatic pattern may represent different aspects of tumor biology.

Several limitations should be acknowledged. First, this was a retrospective study and unmeasured confounding cannot be excluded. Second, surveillance protocols differed across institutions. Third, the 6 months cutoff was exploratory and requires external validation. Finally, the study population mainly consisted of Japanese patients, which may limit generalizability.

Conclusions

The prognostic impact of recurrence timing after RC was concentrated within the earliest postoperative months rather than changing linearly over time. Recurrence within 6 months after RC was independently associated with poor PRS and may identify patients with biologically aggressive disease.

Declarations

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Conflict of Interest

The authors declare that they have no competing interests.

Data availability

The data underlying this article cannot be shared publicly because of institutional privacy regulations. De-identified data may be available from the corresponding author upon reasonable request and with permission of the participating institutions.

Ethics approval

This study was approved by the institutional review boards of all participating institutions and was conducted in accordance with the ethical principles of the Declaration of Helsinki and its later amendments.

Consent to participate

The requirement for informed consent was waived by the institutional review boards because of the retrospective nature of this study.

References

1. Mari A, Campi R, Tellini R et al (2018) Patterns and predictors of recurrence after open radical cystectomy for bladder cancer: a comprehensive review of the literature. *World J Urol* 36:157–170
2. Grossman HB, Natale RB, Tangen CM et al (2003) Neoadjuvant chemotherapy plus cystectomy compared with cystectomy alone for locally advanced bladder cancer. *N Engl J Med* 349:859–866

3. Bajorin DF, Witjes JA, Gschwend JE et al (2021) Adjuvant nivolumab versus placebo in muscle-invasive urothelial carcinoma. *N Engl J Med* 384:2102–2114
4. Hautmann RE, de Petriconi RC, Pfeiffer C, Volkmer BG (2012) Radical cystectomy for urothelial carcinoma of the bladder without neoadjuvant or adjuvant therapy: long-term results in 1100 patients. *Eur Urol* 61:1039–1047
5. Kaufmann E, Black PC, Catto JWF et al (2023) Oncological surveillance after radical cystectomy: a narrative review of the enhanced recovery after surgery cystectomy committee. *JU Open Plus* 1:e00051
6. Dason S, Cha EK, Falavolti C et al (2020) Late recurrences following radical cystectomy have distinct prognostic and management considerations. *J Urol* 204:460–465
7. Stewart-Merrill SB, Boorjian SA, Thompson RH et al (2016) Interval to recurrence following radical cystectomy impacts survival. *Urol Oncol* 34:431e1–431e7
8. Nakagawa T, Hara T, Kawahara T et al (2013) Prognostic risk stratification of patients with urothelial carcinoma of the bladder with recurrence after radical cystectomy. *J Urol* 189:1275–1281
9. Nakagawa T, Taguchi S, Uemura Y et al (2017) Nomogram for predicting survival of postcystectomy recurrent urothelial carcinoma of the bladder. *Urol Oncol* 35:457e15–457e21
10. Mitra AP, Alemozaffar M, Harris BN et al (2014) Outcomes after urothelial recurrence in bladder cancer patients undergoing radical cystectomy. *Urology* 84:1420–1426
11. Harrell FE Jr (2015) *Regression Modeling Strategies: With Applications to Linear Models, Logistic Regression, and Survival Analysis*, 2nd edn. Springer, Cham
12. Mari A, Kimura S, Foerster B et al (2018) A systematic review and meta-analysis of lymphovascular invasion in patients treated with radical cystectomy for bladder cancer. *Urol Oncol* 36:293–305
13. Karl A, Carroll PR, Gschwend JE et al (2009) The impact of lymphadenectomy and lymph node metastasis on the outcomes of radical cystectomy for bladder cancer. *Eur Urol* 55:826–835
14. Pinato DJ, Shiner RJ, Seckl MJ et al (2014) Prognostic performance of inflammation-based prognostic indices in metastatic renal cell carcinoma and metastatic urothelial carcinoma. *Br J Cancer* 110:1055–1060
15. Bellmunt J, de Wit R, Vaughn DJ et al (2017) Pembrolizumab as second-line therapy for advanced urothelial carcinoma. *N Engl J Med* 376:1015–1026
16. Powles T, Park SH, Voog E et al (2020) Avelumab maintenance therapy for advanced or metastatic urothelial carcinoma. *N Engl J Med* 383:1218–1230
17. Powles T, Valderrama BP, Gupta S et al (2024) Enfortumab vedotin plus pembrolizumab in previously untreated advanced urothelial carcinoma. *N Engl J Med* 390:875–888
18. Powles T, Catto JWF, Galsky MD et al (2024) Perioperative durvalumab with neoadjuvant chemotherapy in operable bladder cancer. *N Engl J Med* 391:1773–1786

Figures

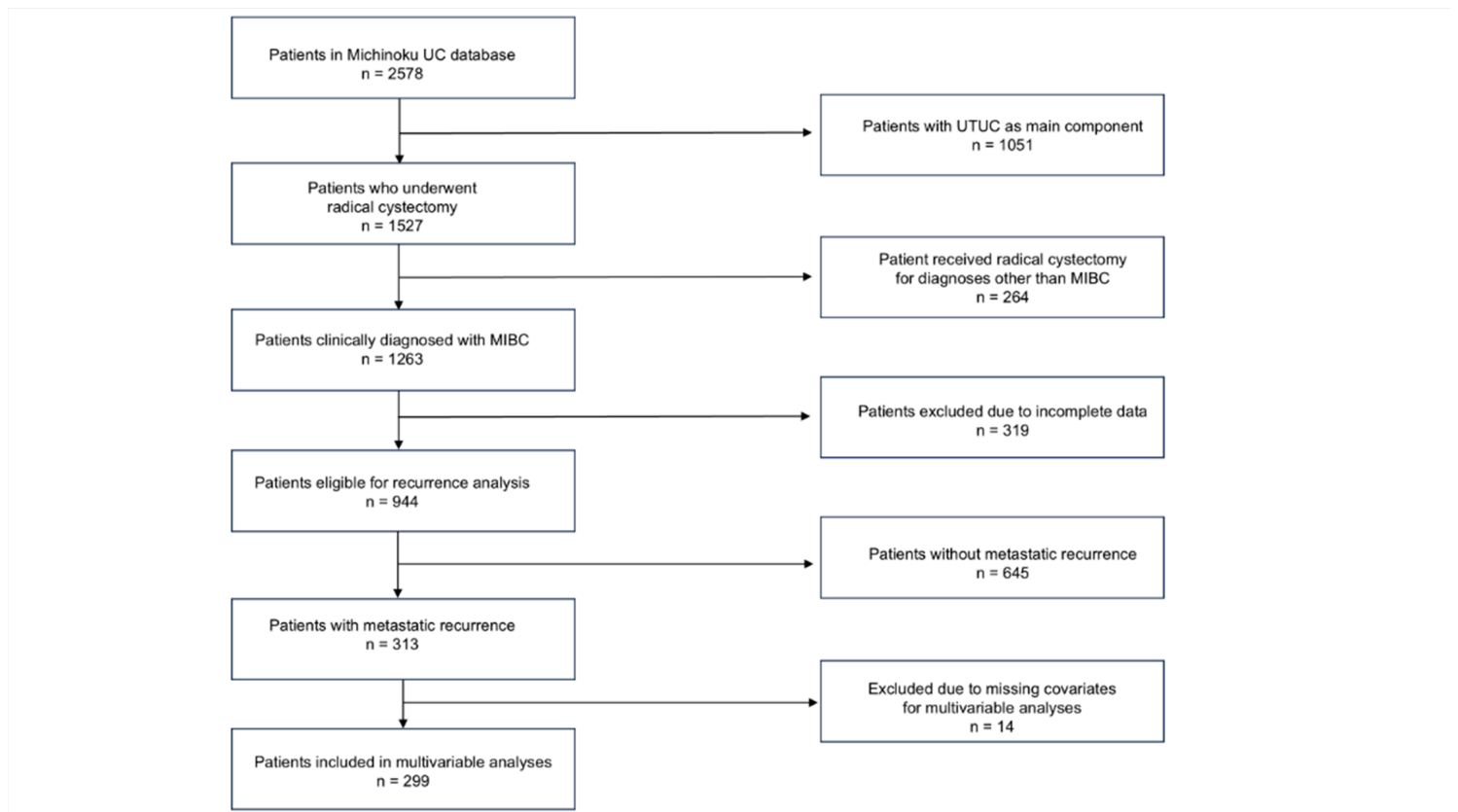


Figure 1

Flow diagram of patient selection

Flow diagram the selection of patients from the Michinoku Society of Urologic Oncology database. A total of 2578 patients were initially identified, of whom 944 patients with clinically diagnosed muscle-invasive bladder cancer (MIBC) who underwent radical cystectomy were included in the final analysis. Among them, 313 patients developed metastatic recurrence after surgery, and 299 with complete data were included in multivariable analyses.

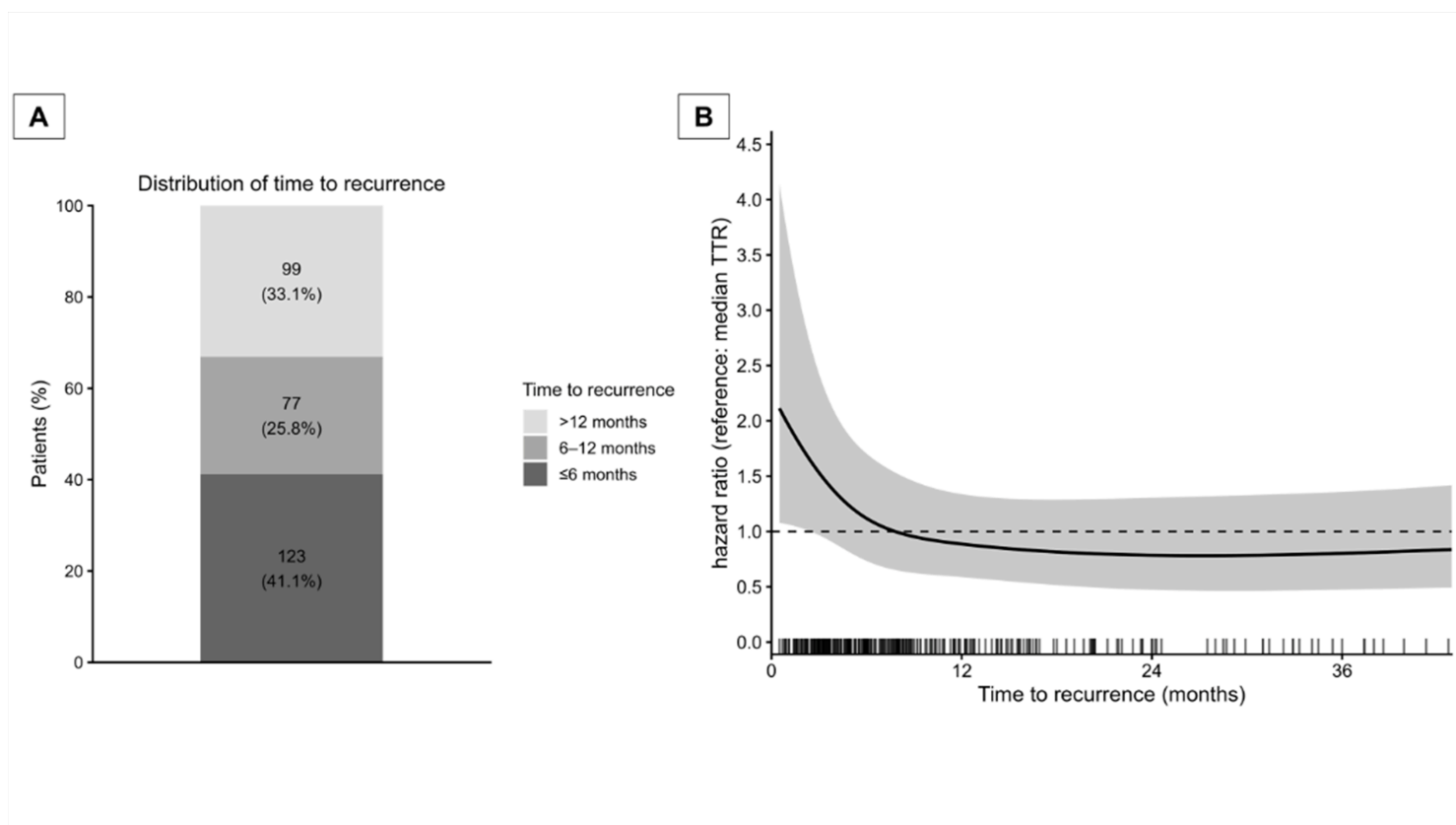


Figure 2

Distribution of recurrence timing and restricted cubic spline analysis of time to recurrence and post-recurrence survival

(A) Distribution of TTR among the 299 analyzed patients, categorized as ≤6 months, 6–12 months, and >12 months. Percentages are shown within each segment.

(B) Restricted cubic spline analysis showing the nonlinear association between TTR and PRS. HRs were adjusted for age, BMI, sex, ECOG performance status, albumin, eGFR, hydrourteronephrosis, histology, neoadjuvant chemotherapy, adjuvant therapy, pathological T stage ($\geq pT3$ or $\geq ypT2$), lymphatic invasion, venous invasion, lymph node positivity, treatment era, and recurrence pattern. The HR was normalized to 1.0 at the median TTR (7.8 months). The solid line indicates the adjusted HR and the shaded area indicates the 95% confidence interval. The dashed horizontal line corresponds to HR = 1. Vertical tick marks indicate observed TTR values. The curve was truncated at the 95th percentile of TTR (42.9 months).

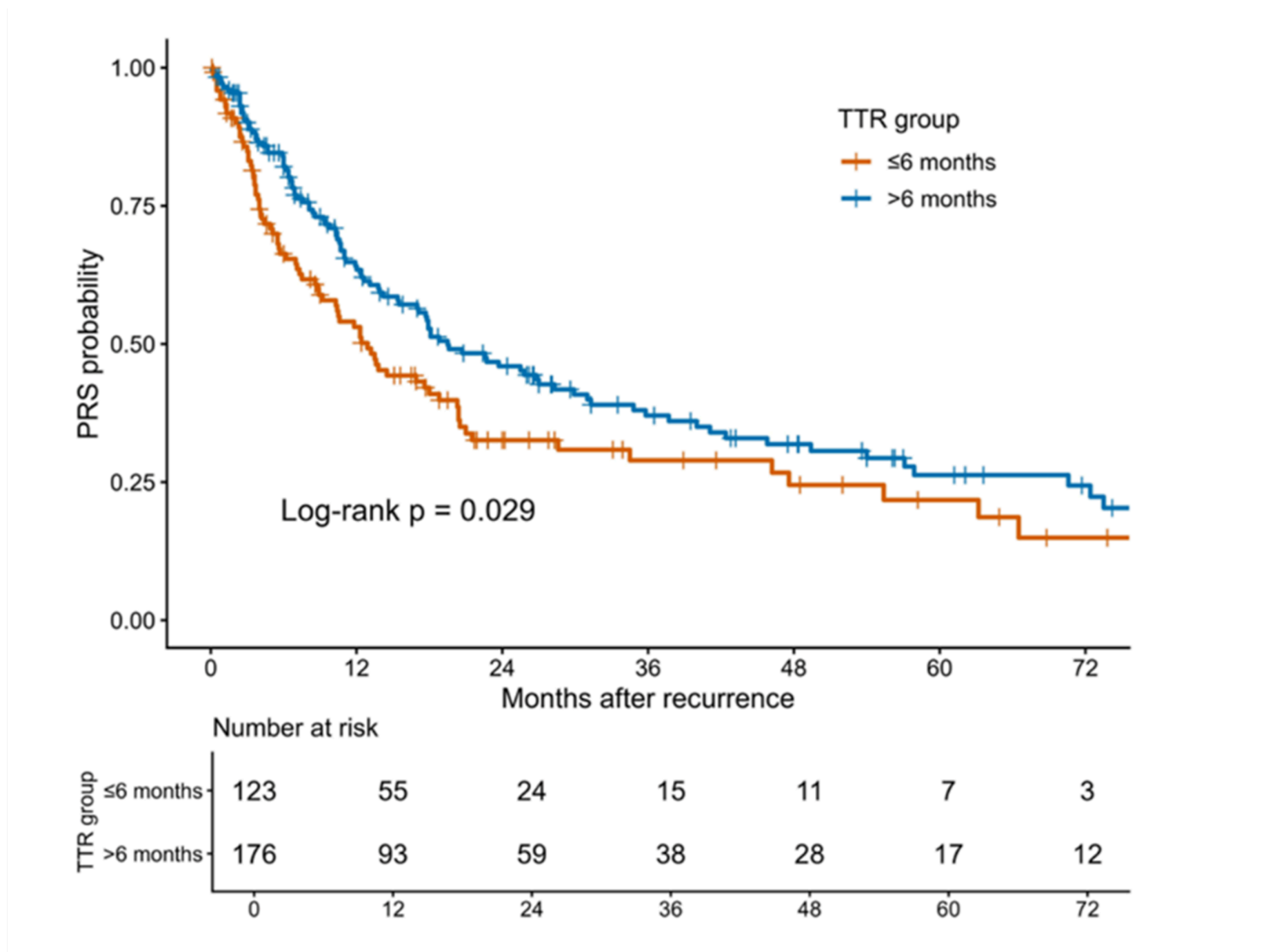


Figure 3

Kaplan–Meier curves of post-recurrence survival according to time to recurrence

Kaplan–Meier curves of PRS according to TTR group. Numbers at risk are shown below the x-axis. Median PRS was 12.9 months in the ≤6 months group and 19.5 months in the >6 months group.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SupplementaryTables.docx](#)