Journal of Radiation Research, Vol. 66, No. 3, 2025, pp. 272–279
https://doi.org/10.1093/jrr/rraf018
Advance Access Publication: 14 April 2025

Survival outcomes and prognostic factors in bladder cancer treated with radiotherapy

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(Received 6 January 2025; revised 12 March 2025; editorial decision 18 March 2025)

ABSTRACT

This study evaluated survival outcomes and prognostic factors in patients with bladder cancer treated with radiotherapy. A retrospective analysis was conducted on 488 patients across all cancer stages who received radiotherapy at two institutions between 1 January 2000 and 31 December 2022. Overall survival (OS) was assessed based on treatment intent (radical or palliative) and cancer stage. Among these patients, 304 with Stage II–III disease who underwent radical radiotherapy were further analyzed for OS and prognostic factors using Kaplan–Meier methods and Cox regression analysis. In the radical radiotherapy group, median survival times (MSTs) were 43 months for Stage 0–I, 29 months for Stage II–III, and 17 months for Stage IV (M0). In the palliative radiotherapy group, MSTs were 16 months (95% confidence interval [CI]: 11–25) for M0 and 9 months (95% CI: 7–15) for M1. Among the 304 patients with Stage II–III disease treated with radical radiotherapy, the 3-year OS rate was 43.0%. Hydronephrosis was the only independent prognostic factor significantly associated with worse OS (hazard ratio: 1.915, $P < 0.001$). Age, sex, stage, treatment era, prophylactic pelvic radiotherapy, chemotherapy and prescribed dose had no significant impact on OS. Radiotherapy remains a viable treatment option for patients at any stage of cancer. Although hydronephrosis negatively affects survival, it should not preclude the use of radiotherapy.

Keywords: survival rate; prognosis; radiotherapy; urinary bladder neoplasms

INTRODUCTION

Bladder cancer is a common cancer worldwide and represents a significant health concern. According to GLOBOCAN estimates, 573 278 new cases of bladder cancer and 212 536 related deaths occurred in 2020 [1]. In Japan, age distribution data for patients with bladder cancer in 2020 indicated that half of the cases occurred among elderly individuals aged ≥75 years [2]. With an aging population, the incidence of bladder cancer is increasing [3].

The standard treatment for bladder cancer depends on the disease stage. Non–muscle-invasive bladder cancer (NMIBC), which accounts for ∼70% of new bladder cancer cases, is typically treated with transurethral resection of the bladder tumor (TUR-BT). High-risk cases may require radical cystectomy [4]. The role of radiotherapy in this stage is not well established but may act as an alternative to cystectomy for high-risk cases [5]. Muscle-invasive bladder cancer (MIBC) comprises ∼15% of new bladder cancer cases, with the standard treatment involving radical cystectomy combined with neoadjuvant chemotherapy [6]. Trimodal therapy (TMT), which combines TUR-BT, chemotherapy and radiotherapy, is a reasonable alternative to cystectomy for patients who are medically unfit for surgery and those seeking an alternative to radical cystectomy [7, 8]. The overall survival (OS) rate for MIBC patients undergoing radical cystectomy, neoadjuvant chemotherapy with radical cystectomy or TMT is ∼45% at 5 years [9, 10]. Metastatic bladder cancer accounts for ∼5% of newly diagnosed cases, with cisplatin-based chemotherapy serving as the primary treatment modality. Surgery or radiotherapy may be feasible in highly select metastatic cases for patients who show a major partial response in a previously unresectable primary tumor or who have a solitary site of residual disease that is resectable after chemotherapy [11]. Furthermore, radiotherapy has been well established as an effective treatment option for relieving urinary symptoms associated with locally advanced disease [12].

While surgery and chemotherapy are essential components for treating bladder cancer, the majority of bladder cancer patients are elderly, and some face challenges such as poor performance status and diminished organ function, making surgery and cisplatin-based chemotherapy impractical. Radiotherapy is a minimally invasive option for tumor control and symptom management, making it a promising treatment when surgery and/or chemotherapy is not suitable or as a palliative approach. However, the current literature offers limited comprehensive insights into radiotherapy outcomes in these groups, posing challenges for optimizing treatment strategies and improving patient care [13].

This retrospective cohort study evaluated the survival outcomes of patients with bladder cancer at any stage who received radiotherapy to the bladder. Additionally, it identified factors influencing survival outcomes in patients undergoing radical radiotherapy for MIBC.

MATERIALS AND METHODS

Ethics approval

This study was conducted in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. All procedures complied with the relevant laws and institutional guidelines and were approved by the Institutional Review Boards of Iwate Medical University Hospital and Iwate Prefectural Central Hospital on 28 December 2023 (MH2023-086).

Patients and radiotherapy protocol

Patients who underwent external beam radiotherapy for primary bladder cancer, with radical or palliative intent, at two hospitals between 1 January 2000 and 31 December 2022 were included in this study.

At both institutions, the standard approach for radical treatment was surgery following neoadjuvant chemotherapy, and TMT was not routinely recommended. Most patients who received radiotherapy as a radical treatment were deemed unsuitable for surgery and/or chemotherapy, or were found to be ineligible for surgery after evaluation following neoadjuvant chemotherapy, leading to a decision for radiotherapy. For radical radiotherapy, conventional fractionation with doses of 60–66 Gy was administered; however, there were differences between the two facilities, as well as changes in protocols over time. At Iwate Medical University Hospital, from 2000 to 2011, prophylactic pelvic irradiation of 40–46 Gy in 20–23 fractions were administered, followed by an additional 20 Gy in 10 fractions to the whole bladder. From 2012 onwards, prophylactic pelvic irradiation was performed only in cases where lymph node metastasis was clinically positive or suspected. Additionally, the treatment approach varied depending on whether partial bladder irradiation was feasible. When partial bladder irradiation was possible, 46 Gy in 23 fractions was delivered to the whole bladder, followed by an additional 20 Gy in 10 fractions to the partial bladder. Conversely, when partial bladder irradiation was not feasible, such as in cases with multiple bladder lesions or in patients unable to adequately fill their bladder due to incontinence, whole bladder irradiation of 60 Gy in 30 fractions was administered [14]. At Iwate Prefectural Central Hospital, from 2000 to 2013, prophylactic pelvic irradiation of 40 Gy in 20 fractions was administered, followed by an additional 22.0–26.4 Gy in 10–12 fractions (2.2 Gy per fraction) to the whole bladder. From 2013 onwards, the treatment protocol was modified so that 39.6 Gy in 22 fractions of prophylactic pelvic irradiation was followed by 26 Gy in 13 fractions of whole bladder irradiation. At both facilities, the upper boundary of the prophylactic pelvic irradiation field was set at the fifth lumbar (L5) or first sacral (S1) vertebra.

For palliative radiotherapy, no facility had a clearly defined protocol. In general, low-dose hypofractionation (8–30 Gy) was used for patients with a large volume of distant metastases or poor performance status, while a curative dose ($\geq$60 Gy) was used for those with a small volume of distant metastases and good performance status. For cases that did not fall into either category, a moderate dose (30–60 Gy) was administered at the discretion of the attending physician.

The image-guided radiotherapy system was introduced around 2010 and has since been routinely used for correcting isocenter displacement in both facilities.

Following radiotherapy, patients were advised to attend follow-up visits at their respective clinics. However, some were referred to other hospitals for follow-up due to poor performance status, transportation difficulties or both.

Data collection

Data on patient characteristics, treatment methods and survival outcomes were collected from medical records. Bladder cancer staging followed the seventh edition of the Union for International Cancer Control TNM (UICC TNM) classification. Hydronephrosis was assessed using simulation computed tomography for radiotherapy. Information on the last clinic visit and date of death was obtained from the two hospitals and other referring hospitals.

METHODS

Patients were divided into two groups based on bladder cancer stage and treatment intent. One group was designated as the radical radiotherapy group, defined as patients without distant metastases who received radiotherapy with a dose of $\geq$60 Gy. This group was further divided into three subgroups: NMIBC (Stage 0–I), MIBC (Stage II–III) and bladder cancer with infiltration of the pelvic wall or regional lymph node metastasis (Stage IV [M0]). The other group was designated the palliative radiotherapy group, defined as patients with distant metastases or those who received radiotherapy with a dose of $<$60 Gy. This group was further divided into two subgroups: patients without distant metastases treated with $<$60 Gy (M0) and patients with distant metastases (M1). OS was evaluated across these subgroups. Subsequently, a subgroup analysis was conducted, focusing on patients with Stage II–III who received radical radiotherapy. Patients were stratified based on age, sex, cancer stage, treatment era, prophylactic pelvic irradiation, presence of hydronephrosis, combined chemotherapy and prescribed dose, and differences in OS were assessed.

The primary endpoint was OS, defined as the duration from the initiation of radiotherapy to death from any cause.

Statistics

Median survival time (MST) was calculated using the Kaplan–Meier method, and differences between survival curves were assessed using

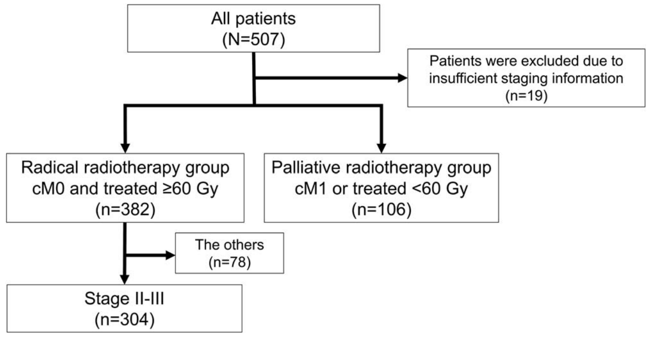

Fig. 1. Study flowchart.

the log-rank test. Multivariate analyses were conducted using Cox proportional hazards regression. Statistical significance was defined as $P < 0.05$. All statistical analyses were performed with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). Specifically, it is a modified version of R commander designed to add statistical functions frequently used in biostatistics [15].

RESULTS

In this study, 507 patients were enrolled; however, 19 patients were excluded due to insufficient information regarding staging. As a result, 488 patients were included in the analysis, with 382 classified as the radical radiotherapy group and 106 the palliative radiotherapy group. The Stage II–III subgroup of the radical radiotherapy group consisted of 304 patients (Fig. 1).

Survival outcomes in the radical and palliative radiotherapy groups

The characteristics of the 488 patients included in the analysis are summarized in Table 1. Most of the patients were elderly males with advanced disease.

The number of patients in the three subgroups of the radical radiotherapy group was as follows: Stage 0–I ($n = 30$), Stage II–III ($n = 304$) and Stage IV [M0] ($n = 48$). Of the 48 patients with Stage IV (M0), 43 (90%) had regional lymph node metastases. The MSTs in the radical radiotherapy group were 43 months (95% confidence interval [CI]: 14–78) for Stage 0–I, 29 months (95% CI: 23–34) for Stage II–III and 17 months (95% CI: 12–41) for Stage IV (M0). Log-rank tests were conducted to compare OS among the subgroups (Fig. 2a), but none of the comparisons showed a statistically significant difference: Stage 0–I vs Stage II–III ($P = 0.956$), Stage 0–I vs Stage IV [M0] ($P = 0.360$) and Stage II–III vs Stage IV [M0] ($P = 0.264$). Among censored cases, the median follow-up duration was 19 months (95% CI: 13–25 months). During this period, a total of 206 patients died.

The number of patients in the two subgroups of the palliative radiotherapy group was as follows: M0 ($n = 51$) and M1 ($n = 55$). A higher proportion of patients in this group had a poor performance status. The MSTs in the palliative radiotherapy group were 16 months (95% CI: 11–25) for M0 and 9 months (95% CI: 7–15) for M1. Log-rank tests were conducted to compare OS between the subgroups (Fig. 2b), but none of the comparisons showed a statistically significant difference: M0 vs M1 ($P = 0.118$). Among censored cases, the median follow-up duration was 6 months (95% CI: 4–8 months). During this period, a total of 62 patients died.

Survival outcomes and prognostic factors in patients undergoing radical radiotherapy for Stage II–III

Table 2 summarizes the characteristics of the 304 patients with a median age of 78 years. In 42 patients, the irradiation field was either unavailable or adapted because they underwent radical radiotherapy for Stage II–III, coexisting ureteral cancer. Chemotherapy was administered before radiotherapy in 63 patients (21%) and concurrently with radiotherapy in 47 patients (15%). The commonly used concurrent regimens were gemcitabine plus cisplatin ($n = 15$), tegafur/uracil ($n = 9$), gemcitabine plus carboplatin ($n = 6$) and cisplatin ($n = 5$).

The median length of follow-up for censored cases was 21 (95% CI: 12–31) months. The 3-year OS rates after radiotherapy were 43.0% (95% CI: 36.4–49.4%). The OS of patients was reduced than that of patients who were $\geq$80 years old (MST: 26 vs 30 months, respectively; $P = 0.902$), female (MST: 27 vs 28 months, respectively; $P = 0.989$), had Stage III disease (MST: 28 vs 31 months, respectively; $P = 0.811$), underwent treatment in the 2000s [2000–2009] (MST: 19 vs 36 months, respectively; $P = 0.123$), received prophylactic pelvic irradiation (MST: 24 vs 37 months, respectively; $P = 0.065$), received chemotherapy before radiotherapy (MST: 23 vs 30 months, respectively; $P = 0.910$), had not received concurrent chemoradiotherapy (MST: 27 vs 37 months, respectively; $P = 0.223$) or received a radiation dose of 60 to <65 Gy (MST: 27 vs 28 months, respectively; $P = 0.426$). However, none of these differences were statistically significant. Patients with bladder cancer accompanied by hydronephrosis had a shorter MST of 16 (95% CI: 12–26) months than those without hydronephrosis (38 [95% CI: 30–48] months), also with a significant difference in OS ($P < 0.001$; Fig. 3). The coexistence of hydronephrosis was the only independent factor identified to be correlated with OS [hazard ratio, 1.915; $P < 0.001$] (Table 3).

DISCUSSION

This study analyzed a cohort of patients with bladder cancer who underwent radiotherapy at two institutions over 20 years and examined their survival outcomes.

Table 1. Patient characteristics of 488 patients in the radical (n = 382) and palliative (n = 106) radiotherapy groups

	Radical radiotherapy group, n (%)				Palliative radiotherapy group, n (%)		
	Stage 0–I	Stage II–III	Stage IV (M0)	Total	M0	M1	Total
Characteristics	n = 30	n = 304	n = 48	n = 382	n = 51	n = 55	n = 106
Age (years), median (range)	85 (73–91)	78 (42–95)	73 (58–84)	78 (42–95)	86 (59–101)	72 (39–88)	79 (39–101)
Sex (male)	21 (70)	221 (73)	34 (71)	276 (72)	32 (63)	40 (73)	72 (68)
Performance status							
0–1	26 (87)	252 (83)	43 (90)	321 (84)	31 (61)	33 (60)	64 (60)
2–4	4 (13)	46 (15)	5 (10)	55 (14)	20 (39)	21 (38)	41 (39)
Unknown	0	6 (2)	0	6 (2)	0	1 (2)	1 (1)
Regional node metastasis							
N0	30 (100)	304 (100)	5 (10)	339 (89)	51 (100)	18 (33)	69 (65)
N1–3	0	0	43 (90)	43 (11)	0	37 (67)	37 (35)
Prescribed dose							
≤30 Gy	0	0	0	0	14 (27)	11 (20)	25 (24)
30–60 Gy	0	0	0	0	37 (73)	15 (27)	52 (49)
≤60 Gy	30 (100)	304 (100)	48 (100)	382 (100)	0	29 (53)	29 (27)
Histological diagnosis							
Urothelial cancer	23 (77)	272 (89)	40 (83)	335 (88)	35 (69)	38 (69)	73 (69)
Squamous cell cancer (and mixed urothelial cancer)	1 (3)	14 (5)	4 (8)	19 (5)	3 (6)	5 (9)	8 (8)
Adenocarcinoma (and mixed urothelial cancer)	1 (3)	6 (2)	1 (2)	8 (2)	2 (4)	2 (4)	4 (4)
Other	1 (3)	3 (1)	1 (2)	5 (1)	2 (4)	1 (2)	3 (3)
Unknown or not performed	4 (13)	9 (3)	2 (4)	15 (4)	9 (18)	9 (16)	18 (17)

Most patients who received radical radiotherapy were at Stage II–III, where radiotherapy was provided as an alternative to surgery. However, a subset of patients with NMIBC or Stage IV without distant metastases also received radical radiotherapy, despite its less established role with limited evidence in these settings.

The standard treatment for NMIBC consists of TUR-BT and radical cystectomy for high-risk cases. In this study's cohort, radiotherapy was performed as an alternative treatment for patients who were ineligible for radical cystectomy. Additionally, some elderly patients with significant comorbidities, for whom even TUR-BT was not feasible, also received radiotherapy. As a result, the median age of NMIBC patients who received radiotherapy was 85 years, indicating a particularly elderly cohort. Although NMIBC typically has a more favorable prognosis than MIBC, no significant difference in survival outcomes was observed between NMIBC and Stage II–III patients in this study. This may be explained by the frailty and advanced age of the NMIBC cohort, as well as the small sample size.

The standard treatment for Stage IV bladder cancer is chemotherapy. According to the UICC TNM 7th edition, patients with pelvic wall invasion (T4b) or regional lymph node metastases (N1–3) are classified as Stage IV, even in the absence of distant metastases. Consequently, some patients with Stage IV bladder cancer without distant metastases may still be candidates for curative treatment. In this study, 90% of Stage IV (M0) patients were classified as Stage IV due to regional lymph node metastases. These patients received ≥60 Gy radiotherapy to the pelvis, either in combination with chemotherapy or as radiotherapy alone when chemotherapy was not feasible.

Regional lymph node metastasis is well known as a poor prognostic factor in bladder cancer. For example, Stein *et al.* [9] conducted a cohort study involving 1054 bladder cancer patients who underwent radical cystectomy and reported that patients with lymph node metastases had a 5-year recurrence-free survival rate of 35%, which was significantly lower than that of patients without nodal involvement. Furthermore, data from the American Cancer Society (2013–2019) indicated 5-year survival rates of 71% for localized disease and 39% for regional disease [16]. However, in this study, Stage IV (M0) patients did not show a significant difference in OS compared to Stage II–III patients. This finding contrasts with previous research. Several factors may explain the divergent findings of this study: First, variability in the diagnostic accuracy of lymph node metastases between institutions may have influenced the results [17, 18]. Second, patients with regional lymph node metastases who responded well to chemotherapy may have been selectively treated with radiotherapy, potentially contributing to the improved OS in this subgroup. Third, the relatively small sample size of metastatic cases may have affected the statistical power of the analysis.

Additionally, the UICC TNM 8th edition, published in 2016, has reclassified regional lymph node metastases as Stage III rather than Stage IV. Moreover, recent studies have reported the feasibility of bladder-preserving therapy in patients with lymph node involvement

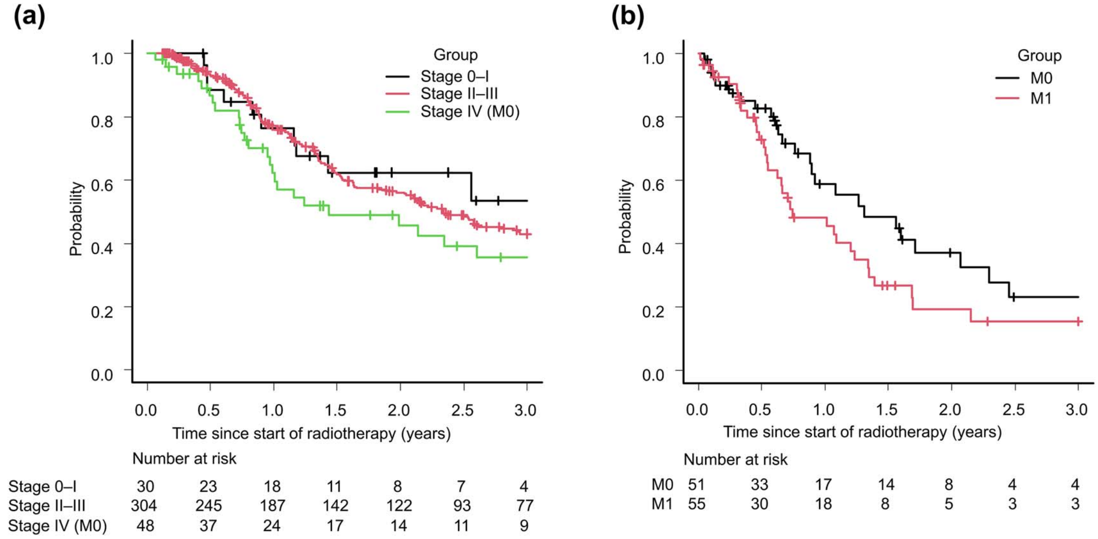

Fig. 2. Kaplan–Meier survival curves for the radical radiotherapy group and the palliative radiotherapy group. (a) Radical radiotherapy group: comparison by cancer stage. Patients with non–muscle-invasive bladder cancer (Stage 0–I) had a median survival time (MST) of 43 months. Patients with muscle-invasive bladder cancer (Stage II–III) and those with locally advanced disease or regional lymph node metastasis without distant metastasis (Stage IV [M0]) had MSTs of 29 and 17 months, respectively. There was no significant difference in survival time among these groups. (b) Palliative radiotherapy group: Comparison of patients with and without distant metastasis. Patients without distant metastases (M0) had an MST of 16 months, while those with distant metastases (M1) had an MST of 9 months. There was no significant difference in survival time between these groups.

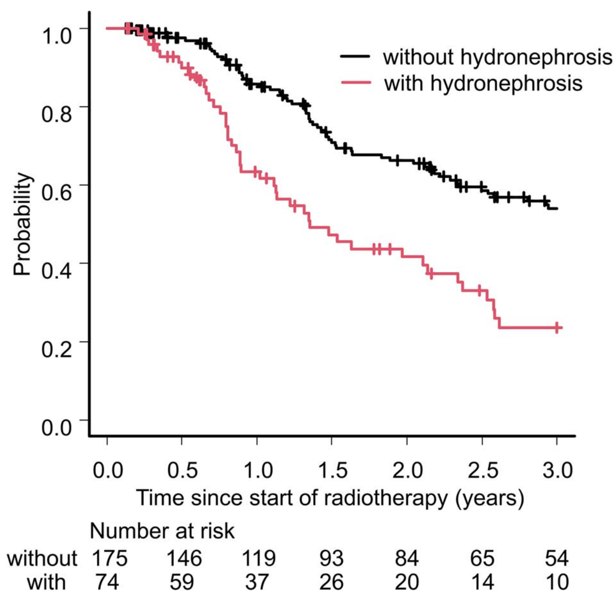

Fig. 3. Kaplan–Meier survival curves for radical radiotherapy: comparison of patients with and without hydronephrosis. Patients with hydronephrosis had a significantly shorter median survival time of 16 months (95% CI: 12–26) compared to 38 months (95% CI: 30–48) for those without hydronephrosis ($P < 0.001$).

[19]. These changes suggest a shift in treatment strategies for such cases.

The cohort of patients who received palliative radiotherapy was classified into two groups: those who had no distant metastases but were unsuitable for definitive-dose radiotherapy and those with distant metastases. In the palliative radiotherapy group, 39% of patients had a performance status of 2–4, indicating that overall they were in poorer condition compared to the group that underwent radical radiotherapy.

At the two institutions included in this study, approximately half of the M1 patients received radiotherapy at doses of $\geq$60 Gy. With conventional palliative radiotherapy, such as 30 Gy in 10 fractions, 69% of patients reportedly experience recurrent bleeding at the 6-month follow-up, suggesting that recurrence is common [20]. Higher-dose treatment was likely administered to patients expected to survive for $>$6 months, aiming for long-term local control.

Although OS did not significantly differ between M0 and M1 patients, the survival curve for the M0 group was better, with an MST of 16 months. Given the previously mentioned recurrence rates following palliative radiotherapy, conventional palliative regimens may be insufficient for long-term control in M0 patients. Even if radical treatment is not feasible, a certain degree of local control may still be necessary. For example, a study evaluating weekly 36 Gy radiotherapy using standard or adaptive planning for cT2-4aN0M0 patients reported a 2-year OS rate of 46.2% [21]. These findings suggest that for frail patients with bladder cancer without distant metastases, alternative

Table 2. Patient characteristics of the 304 patients undergoing radical radiotherapy for the Stage II–III subgroup

	Total, *n* (%)
Characteristics	*n* = 304
Age	
<80 years	171 (56)
≥80 years	133 (44)
Sex	
Male	221 (73)
Female	83 (27)
Stage	
II	95 (31)
III	209 (69)
Treatment era	
2000–2009	126 (41)
2010–2020	154 (51)
2021–2022	24 (8)
Prophylactic pelvic irradiation	
Yes	148 (49)
No	114 (38)
Other[a]	42 (13)
Hydronephrosis	
Yes	74 (24)
No	175 (58)
Unknown	55 (18)
Chemotherapy prior to radiotherapy	
Yes	63 (21)
No	241 (79)
Concurrent chemoradiotherapy	
Yes	47 (15)
No	257 (85)
Prescribed dose	
60 to <65 Gy	111 (37)
65 to 70 Gy	193 (63)

[a]Includes cases of simultaneous irradiation for ureteral cancer and cases of unknown field.

radiotherapy regimens may offer better disease control compared to conventional palliative radiotherapy.

Next, we analyzed prognostic factors in patients with non-metastatic MIBC who underwent radical radiotherapy. Most patients in this study were ineligible for surgery and/or chemotherapy and represented a more vulnerable population compared to those eligible for TMT as an alternative to surgery. Consequently, only 15% of patients underwent concurrent chemoradiotherapy, while the majority received radiotherapy alone. The 3-year OS rate in this study was 43.0%, which is lower than the ∼50% survival rate estimated from the Kaplan–Meier curve reported in the BC2001 randomized controlled trial comparing radiotherapy with or without chemotherapy [22] and the 46% survival rate reported in the BCON trial evaluating radiotherapy for locally advanced bladder cancer with or without carbogen-nicotinamide [23], both of which were reported for the radiotherapy-alone group. This discrepancy may be attributed to the higher median age of patients in this study (78 years) and the inclusion of patients with compromised organ function who did not meet the eligibility criteria for randomized controlled trials. Thus, the results of this study should be compared with those from cohorts consisting of patients eligible for some form of treatment but not for standard therapies. For instance, based on a multi-institutional questionnaire survey conducted in Japan, the 3-year OS rate for patients with bladder cancer (cTis-4N0-2) treated with radiation therapy alone was estimated to be 40% from the Kaplan–Meier curve [24]. Moreover, a retrospective study of cT1-4bN0-1M1 patients with bladder cancer treated with radiotherapy showed a 3-year OS rate of 34.3% [25].

Among patients in the radical radiotherapy group, the only prognostic factor identified was hydronephrosis. Hydronephrosis has been previously reported as a poor prognostic factor in patients with bladder cancer following radical cystectomy [26, 27] and in patients with MIBC undergoing radical radiotherapy [28, 29]. Interestingly, no significant differences in survival were observed based on age. While elderly patients with bladder cancer generally have poor survival outcomes following surgery, this trend was not evident in this study. The minimally invasive nature of radiotherapy may have contributed to improved survival rates among elderly patients. In the context of an aging population, future studies comparing surgery and radiotherapy, particularly focusing on elderly patients, are warranted. Although not statistically significant, a slight trend toward lower survival rates was observed in patients who received prophylactic pelvic irradiation compared to those who did not. The incidence of lymph node metastasis in MIBC is generally reported to be ∼23% [30]. While some studies suggest that pelvic lymph node irradiation is unnecessary in chemoradiotherapy [31], it is noteworthy that the results of this study were achieved with radiotherapy alone. Confounding factors, such as the presence of hydronephrosis, must be considered. However, in elderly patients, prophylactic pelvic irradiation may have negatively impacted survival by increasing the treatment burden and weakening immunity [32].

One limitation of this study is the lack of a systematic assessment of surgical tolerance in the radical radiotherapy group. Many patients were deemed unsuitable for surgery and/or chemotherapy based on the clinical judgment of their physicians before undergoing a formal evaluation of surgical tolerance. As a result, this cohort potentially includes cases in which patients had sufficient surgical tolerance but were treated with external beam radiotherapy. Future studies should establish standardized criteria for assessing surgical tolerance to clarify this issue. Another limitation is that the median follow-up period from the initiation of radiotherapy to the last follow-up was relatively short, preventing comprehensive survival data collection. Additionally, some patients were followed up at other institutions after radiation therapy, making it difficult to obtain sufficient data on treatment-related toxicity. This limitation may affect the accuracy of the study results. However, despite these limitations, this study included a large sample size, which may have partially mitigated these issues.

In conclusion, radiotherapy remains a viable treatment option for patients at any stage of cancer. Moreover, while hydronephrosis negatively affects survival, it should not prohibit the use of radiotherapy. Future research is needed to validate the findings of this study and to explore strategies for improving treatment outcomes. Overall, this study provides valuable insights into the OS of bladder cancer patients, particularly those who are not eligible for surgery and/or chemotherapy.

Table 3. Cox regression analysis for overall survival

Variable	Univariate				Multivariate			
	Hazard ratio	95% confidence interval		*P*-value	Hazard ratio	95% confidence interval		*P*-value
		Lower	Upper			Lower	Upper	
Age								
<80 vs ≥80 years	1.02	0.749	1.387	0.902				
Sex								
Male vs female	1.002	0.705	1.425	0.989				
Stage								
II vs III	1.042	0.745	1.458	0.811				
Treatment era								
2000–2009 vs 2010–2019	0.779	0.568	1.068	0.121				
Prophylactic pelvic irradiation								
Yes vs no	0.717	0.504	1.022	0.065	0.73	0.501	1.063	0.101
Hydronephrosis								
Yes vs no	1.946	1.349	2.807	<0.001	1.915	1.305	2.812	<0.001
Chemotherapy prior to radiotherapy								
Yes vs no	0.978	0.67	1.428	0.91				
Concurrent chemoradiotherapy								
Yes vs no	1.298	0.852	1.976	0.223	1.216	0.741	1.995	0.439
Prescribed dose								
60 to <65 Gy vs 65 to 70 Gy	0.878	0.638	1.21	0.426				

CLINICAL TRIAL REGISTRATION

None.

ACKNOWLEDGEMENTS

The authors acknowledge the patients who participated in this study. This study was supported by the Iwate Prefecture Community Medical Research Project and the JASTRO Interdisciplinary Conference Presentation Grant.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

FUNDING

This research received no funding.

PRESENTATION AT A CONFERENCE

The 36th Annual Meeting of the Japanese Society for Radiation Oncology (JASTRO).

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