CLINICAL RESEARCH

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Hemostatic Efficacy and Clinical Outcomes of Radiotherapy in Older Adult Patients With Advanced Bladder Cancer and Hematuria Unsuitable for Standard Treatment

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEF 1 Judi Xu*
ABCDEF 1 Ying Huang*
ABCDEF 1 Guoying Ni
ABCD 1 Yan Huang
BCD 1 Qian Huang
BCF 1 Hongxiang Liang
BCF 1 Yufeng Ni
BC 1 Haijing Xie
CF 1 Zhuangzhuang Yue
AG 1 Zhiyong Yang
ABCEFG 1,2 Hedai Liu

1 Department of Oncology, Chongming Hospital Affiliated with Shanghai University of Medicine and Health Sciences, Shanghai, PR China
2 Dingxi Cancer Institute of Traditional Chinese and Western Medicine, Dingxi, Gansu, PR China

* Judi Xu and Ying Huang contributed equally to this work

Corresponding Authors: Zhiyong Yang, e-mail: yzy056006@163.com; Hedai Liu, e-mail: liuhedai@aliyun.com

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Background: Older adult patients with advanced bladder cancer and frailty or comorbidities are often unsuitable for surgery or systemic therapy and may present with persistent gross hematuria and severe urinary symptoms. This study evaluated the hemostatic efficacy and clinical value of radiotherapy in this population.

Material/Methods: This retrospective study included 49 older adult patients with advanced bladder cancer and hemorrhagic hematuria, with a mean age of 78.3 ± 6.4 years. All patients had pathologically confirmed urothelial carcinoma of the bladder and persistent hematuria and were unsuitable for surgery or chemotherapy. After thorough communication and written informed consent, radiotherapy was administered. Outcomes included hemostatic efficacy, overall survival, and adverse events.

Results: Bleeding decreased after 5 fractions of radiotherapy with a cumulative dose of 10 Gy. After 10 fractions and 20 Gy, urinary irritation symptoms improved or resolved, and bladder irrigation was discontinued. After 15 fractions and 30 Gy, gross hematuria disappeared in all patients, with a hemostatic response rate of 100%. After 4 weeks and 40 Gy, patients were re-evaluated; 40 continued dose escalation, including 13 who discontinued at 52 to 56 Gy and 27 who completed 62 to 72 Gy. At follow-up, 24 patients had died and 25 remained alive. Median overall survival was 14 months. Exploratory univariate analysis showed different overall survival between radical-dose and palliative-dose radiotherapy.

Conclusions: Radiotherapy was associated with effective hematuria control, urinary symptom relief, and acceptable clinical value in older adult patients with advanced bladder cancer. Larger controlled studies are needed to validate these findings.

Keywords: bladder neoplasms • hematuria • oncology • prognosis • radiotherapy

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Introduction

Bladder cancer is a common malignancy arising from the bladder urothelium and represents one of the major cancers of the urinary system [1]. According to GLOBOCAN 2022 [2,3], bladder cancer accounted for approximately 614 298 new cases and 220 596 deaths worldwide in 2022, with a marked predominance in men. China, the United States, and Italy had the highest numbers of new bladder cancer cases worldwide; among them, China ranked first, with 92 883 new cases and 41 367 deaths in 2022. The male predominance was also evident in China, where 73 218 new cases occurred in men and 19 665 in women. Recent China-specific disease burden analyses further showed that bladder cancer remains a substantial public health burden [4]. The burden is particularly relevant in older populations, as age is one of the strongest risk factors for bladder cancer, and population aging is expected to further increase the number of older adult patients requiring individualized treatment strategies [5].

Hematuria is the most common and typical initial symptom of bladder cancer. A pooled analysis reported bladder cancer in 17% of patients with visible hematuria and 3.3% of patients with non-visible hematuria [6]. Hematuria is present in approximately 80% to 90% of patients with bladder cancer [7]. In advanced disease, hematuria may become persistent or severe and can lead to clot retention, urinary obstruction, and the need for bladder irrigation. In the present study, hematuria refers to gross hematuria unless otherwise specified. Gross hematuria can cause marked urinary irritation symptoms, and in some patients, blood clots can obstruct the urethra, resulting in urinary retention that requires bladder irrigation, interventional tumor-vessel embolization, or surgical hemostasis.

The management of bladder cancer depends on tumor invasiveness. Non–muscle-invasive bladder cancer is primarily treated with transurethral resection of bladder tumor, followed by intravesical therapy, including Bacillus Calmette-Guérin vaccination and chemotherapeutic agents [8,9]. Muscle-invasive bladder cancer is typically managed with partial or radical cystectomy, often supplemented by adjuvant radiotherapy or systemic therapy [10]. Radiotherapy has historically been considered an adjunct rather than a first-line intervention for curable bladder cancer but has increasingly demonstrated efficacy comparable to surgery, particularly in patients who are ineligible for operative management [11,12].

Although multidisciplinary treatment and individualized precision therapy have improved bladder cancer care, real-world treatment decisions are influenced not only by tumor stage but also by frailty, performance status, comorbidities, cognitive function, treatment tolerance, and social or family support. Current guidelines emphasize that treatment selection in older or frail patients with invasive bladder cancer should be based on tumor characteristics and frailty assessment, and that comorbidities should be evaluated using validated tools [10,13]. Similarly, geriatric oncology guidelines recommend comprehensive assessment of physical function, cognition, emotional status, comorbidities, polypharmacy, nutrition, and social support when planning systemic cancer therapy in older adults [14,15]. Therefore, older adult patients with bladder cancer who are unable to receive standard therapy remain an under-recognized and clinically vulnerable population. Many are unable or unwilling to undergo surgery because of cardiac, cerebral, pulmonary, or other comorbidities, while systemic treatments such as chemotherapy may be infeasible because of poor tolerance or limited expected benefit. Older adult patients with recurrent disease after prior treatment may also become less willing to seek further care, leading to progression to advanced disease for which standard treatment is no longer feasible. Such patients may enter a hospice-oriented stage of care and present with persistent hematuria and refractory urinary symptoms. They often experience substantial physical and psychological distress, including fear of bleeding, painful urination, and limitations in activities of daily living. To our knowledge, this patient population has received limited clinical attention, and few studies have specifically focused on older adult patients with advanced bladder cancer and active bleeding after standard treatment options have been exhausted or deemed infeasible.

To address this clinical gap, we retrospectively analyzed 49 older adult patients with advanced bladder cancer and hematuria who were unsuitable for standard treatment and received radiotherapy for hemostasis at Chongming Hospital Affiliated with Shanghai University of Medicine and Health Sciences between January 2017 and January 2025. This study aimed to evaluate the hemostatic effect of radiotherapy, symptom relief, local tumor control, and survival outcomes in older adult patients with advanced bladder cancer and hematuria, thereby providing clinical reference for hospice-oriented care and earlier treatment decision-making in similar patients.

Material and Methods

Clinical Data

The inclusion criteria were as follows: (1) age ≥18 years; although the eligibility criterion was age ≥18 years, this analysis focused on older adult patients, and all included patients were 71 years or older; (2) pathologically confirmed transitional cell carcinoma/urothelial carcinoma of the bladder with visible bladder lesions on imaging; (3) persistent bladder cancer-related bleeding requiring hemostatic intervention; (4) stable vital signs; (5) no feasible treatment options for surgery, embolization, or chemotherapy; and (6) adequate understanding and cooperation from the patient and family, with signed informed consent.

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The exclusion criteria were as follows: (1) unstable vital signs; (2) limited willingness of the patient or family to receive treatment; (3) Eastern Cooperative Oncology Group (ECOG) performance status (PS) score of 4; (4) severe cardiac, cerebral, pulmonary, or renal disease; and (5) hematuria caused by urinary tract tumors other than bladder cancer.

A total of 49 older adult patients diagnosed with advanced bladder cancer and hematuria were included. The cohort consisted of 42 men and 7 women, with a mean age of 78.3 ± 6.4 years and a median age of 82 years. All patients presented with persistent gross hematuria, characterized by bright-red urine with blood clots. Other clinical manifestations included urinary tract obstruction and tumor-related pain in 47 patients, bladder irritation symptoms, including urgency, frequency, and dysuria, in 39 patients, and cancer-related pain in 8 patients. Fourteen patients had urinary obstruction requiring continuous bladder irrigation, and 8 patients had blood loss anemia requiring transfusion of 2 to 8 units.

TNM staging showed stage II disease in 3 patients, stage III disease in 33 patients, and stage IV disease in 13 patients. ECOG PS scores were 1 in 14 patients, 2 in 20 patients, and 3 in 15 patients. Numerical rating scale (NRS) pain scores were 0 to 3 in 29 patients, 4 to 6 in 12 patients, and 7 to 10 in 8 patients. Nine patients were treatment-naive, and 40 had received prior treatment. Among the previously treated patients, all had undergone transurethral resection of bladder tumor and intravesical chemotherapy; 13 had received intravenous chemotherapy, 1 had received intravenous chemotherapy and followed with antibody-drug conjugate therapy, and 6 had received chemotherapy combined with programmed death-1 inhibitor therapy. Twenty-eight patients had a history of cystoscopic electrocoagulation for hemostasis, and 11 had undergone interventional embolization for bleeding control. None of the patients had received partial or radical cystectomy, and none had a history of radiotherapy. Baseline characteristics are summarized in **Table 1**.

Ethics Approval and Consent to Participate

This study was approved by the Research Ethics Committee of Chongming Hospital Affiliated with Shanghai University of Medicine and Health Sciences (No. 2019YA29). Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Consent for Publication

Informed written consent was obtained from all patients included in this study. All the authors approved the publication of this paper.

Clinical Treatment

All patients were unable to tolerate surgery because of advanced age, advanced tumor stage, poor performance status, and/or severe comorbidities. They were also considered unlikely to tolerate bladder tumor arterial embolization and were unsuitable for chemotherapy, or chemotherapy alone was unlikely to achieve the expected hemostatic effect. Therefore, after thorough communication with the patients and their families, and after obtaining their understanding, cooperation, and written informed consent for radiotherapy, palliative radiotherapy was administered to control bleeding and relieve pain and related symptoms.

Before radiotherapy, tumor localization was performed using a 16-slice large-bore spiral computed tomography (CT) scanner. Patients were instructed to empty the bladder before simulation and each radiotherapy session to minimize bladder volume. The gross tumor volume was delineated based on CT simulation images, together with cystoscopic and imaging findings to define the tumor extent. Clinical target volume 1 (CTV1) included the whole bladder, prostate, and regional lymph nodes. CTV2 included the whole bladder and the tumor region visible on CT images. CTV3 included the gross tumor volume to ensure local boost irradiation. Planning target volume 1 (PTV1) corresponded to the small pelvic field, PTV2 to the whole-bladder field, and PTV3 to the planned target volume for local tumor boost irradiation. Treatment planning and evaluation were performed using the Monaco radiotherapy treatment planning system. Radiotherapy was delivered using a 4-dimensional image-guided Infinity linear accelerator (Infinity, Elekta, Sweden).

Radiotherapy was delivered using 6-MV X-rays and intensity-modulated radiotherapy. The prescribed doses were 51 Gy in 30 fractions at 1.7 Gy per fraction to 96% of PTV1, 54 Gy in 30 fractions at 1.8 Gy per fraction to 96% of PTV2, and 64.5 Gy in 30 fractions at 2.15 Gy per fraction to 96% of PTV3. Treatment was administered once daily, 5 days per week. Four patients with bone metastases also received radiotherapy to metastatic bone lesions during the same treatment course.

During radiotherapy, changes in urine color, urinary irritation symptoms, blood clot-related urinary obstruction, and the need for bladder irrigation were monitored. After 4 weeks of radiotherapy, when the cumulative dose reached 40 Gy and the intended palliative hemostatic effect had been achieved, patients were comprehensively re-evaluated based on performance status and tumor shrinkage, and the willingness of the patients and their families to continue treatment was reassessed. After this evaluation and discussion, 9 patients discontinued radiotherapy because of withdrawal of informed consent or physician-assessed unsuitability for further treatment. In the remaining 40 patients, the radiotherapy plan was

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Table 1. Baseline characteristics of patients in the 2 treatment groups.

Characteristic	Palliative-dose RT group (n = 22)	Radical-dose RT group (n = 27)	Total (n = 49)
Age, median (IQR), years	80 (71-92)	76 (71-101)	82 (71-101)
Sex			
Male	19 (86.4%)	23 (85.2%)	42 (85.7%)
Female	3 (13.6%)	4 (14.8%)	7 (14.3%)
ECOG PS			
1	5 (22.7%)	9 (33.3%)	14 (28.6%)
2	8 (36.4%)	12 (44.4%)	20 (40.8%)
3	9 (40.9%)	6 (22.2%)	15 (30.6%)
TNM stage			
II	2 (9.1%)	1 (3.7%)	3 (6.1%)
III	11 (50.0%)	22 (81.5%)	33 (67.3%)
IV	9 (40.9%)	4 (14.8%)	13 (26.5%)
NRS pain score			
0	2 (9.1%)	0 (0.0%)	2 (4.1%)
1-3	7 (31.8%)	20 (74.1%)	27 (55.1%)
4-6	8 (36.4%)	4 (14.8%)	12 (24.5%)
7-10	5 (22.7%)	3 (11.1%)	8 (16.3%)
Treatment history			
Initial treatment	5 (22.7%)	4 (14.8%)	9 (18.4%)
Retreatment/prior treatment	17 (77.3%)	23 (85.2%)	40 (81.6%)
Bladder irrigation	9 (40.9%)	5 (18.5%)	14 (28.6%)
History of electrocoagulation	16 (72.7%)	12 (44.4%)	28 (57.1%)
Tumor-vessel embolization	5 (22.7%)	6 (22.2%)	11 (22.4%)

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance score; NRS, numerical rating scale; TNM, tumor, node, metastasis.

escalated from a palliative-dose regimen to a radical-dose regimen. Fourteen patients received once-weekly concurrent chemotherapy to enhance the effect of radiotherapy, using gemcitabine plus cisplatin or paclitaxel plus cisplatin. Among them, 3 patients received 1 cycle, 9 received 2 cycles, and 2 received 3 cycles. All patients received radiotherapy during hospitalization. Complete blood count, urinalysis, liver function, and renal function were monitored weekly during radiotherapy. After completion of radiotherapy, patients entered follow-up treatment and real-world management.

Clinical Observation and Assessment Methods

The primary endpoint was the disappearance of gross hematuria, assessed by clinical examination and patient-reported symptoms. Secondary endpoints included overall survival, defined as the time from the initiation of radiotherapy to death from any cause or the last follow-up in January 2025. Adverse events were recorded according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0, with particular attention to radiotherapy-related toxicities.

Statistical Analysis

Statistical analyses were performed using R version 4.2.3. Survival analyses were conducted using the survival package, and Kaplan-Meier curves were generated using the survminer package. Cox proportional hazards models were used to adjust for potential confounders, including age, performance status, disease stage, and concomitant treatment, and to estimate hazard ratios (HRs) with 95% confidence intervals (CIs). Subgroup survival comparisons based on clinical characteristics were performed using the log-rank test. A 2-sided *P* value <0.05 was considered statistically significant.

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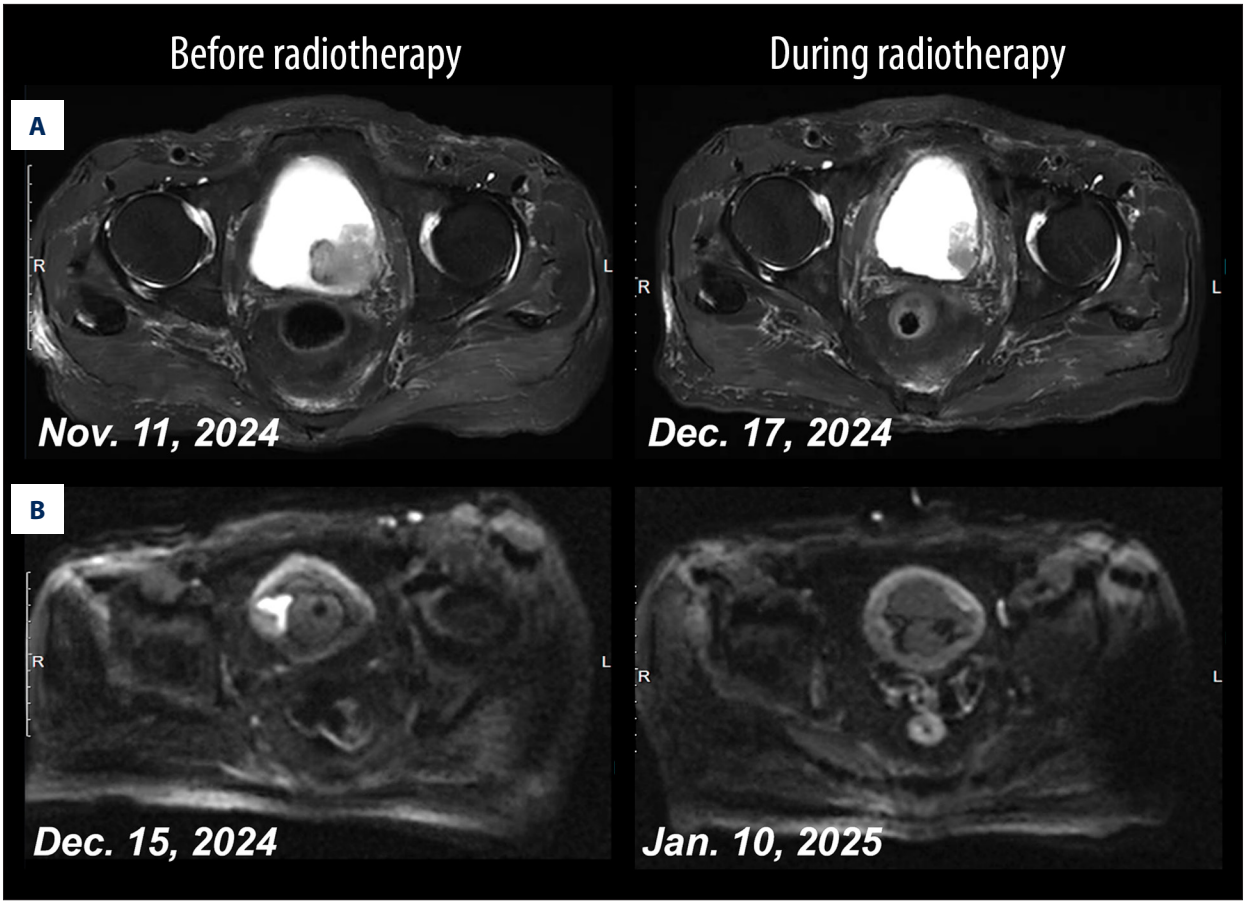

Figure 1. The magnetic resonance images of 2 patients (**A,** patient A: male, 90 years old; **B,** patient B: male, 101 years old) before and during radiotherapy.

Results

Treatment Outcomes

Among the 49 patients, 9 received 36 to 40 Gy, 13 received 52 to 56 Gy, and 27 received 62 to 72 Gy of radiotherapy. After 1 week of radiotherapy, corresponding to 5 fractions and a cumulative dose of 10 Gy, bleeding gradually decreased, urine color became lighter, blood clots were reduced, and the need for bladder irrigation gradually decreased. After 2 weeks of radiotherapy, corresponding to 10 fractions and a cumulative dose of 20 Gy, urine became clear, urinary irritation symptoms, including urgency, frequency, and dysuria, improved or resolved, and bladder irrigation was discontinued. After 3 weeks of radiotherapy, corresponding to 15 fractions and a cumulative dose of 30 Gy, gross hematuria disappeared, and urinary irritation symptoms improved or resolved. Radiotherapy was continued for 4 weeks until a palliative dose of 40 Gy was reached, at which point the hemostatic goal was achieved and urinary symptoms had resolved.

After reassessment, 40 patients were considered eligible for dose escalation, among whom 14 also received once-weekly concurrent chemotherapy. Thirteen patients discontinued radiotherapy at 52 to 56 Gy because of declining ECOG PS or withdrawal of informed consent, whereas 27 patients completed radical-dose radiotherapy of 62 to 72 Gy.

The median follow-up duration was 20 months. At the time of follow-up, 24 patients had died and 25 remained alive. Among those who died, 15 died from tumor progression and 9 died from non-neoplastic diseases. Survival after radiotherapy was as follows: 34 patients were alive at 6 months, 25 at 12 months, 17 at 18 months, 13 at 24 months, and 13 beyond 36 months, corresponding to survival rates of 69.4%, 51.0%, 34.7%, 26.5%, and 26.5%, respectively. The median overall survival was 14 months. The shortest survival time was 2 months, and the longest exceeded 53 months (>4 years). CT images before and during radiotherapy from 2 representative patients, one 90-year-old man and one 101-year-old man, are shown in **Figure 1**.

Cox proportional hazards modeling was performed to adjust for potential confounders, including age, ECOG PS, disease stage, and concomitant treatment, and to estimate HRs with

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Table 2. Cox proportional hazards analysis of factors associated with overall survival.

No.	Variable	HR	SE	z statistic	*P* value	95% CI lower	95% CI upper
1	Female sex	0.631	0.648	-0.710	0.478	0.177	2.247
2	TNM stage	1.532	0.457	0.934	0.351	0.626	3.753
3	Age	0.998	0.043	-0.043	0.966	0.917	1.086
4	Retreatment/prior treatment	2.033	0.661	1.073	0.283	0.556	7.433
5	Bladder irrigation	0.849	0.593	-0.277	0.782	0.266	2.712
6	Palliative-dose RT	1.231	0.518	0.401	0.689	0.446	3.400
7	ECOG PS	0.858	0.338	-0.452	0.651	0.442	1.665
8	Moderate NRS pain score	1.444	0.549	0.670	0.503	0.493	4.235
9	Severe NRS pain score	2.740	0.908	1.111	0.267	0.463	16.226
10	Embolization history	1.805	0.628	0.940	0.347	0.527	6.185
11	Concurrent chemotherapy	0.835	0.291	-0.620	0.535	0.472	1.478

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance score; NRS, numerical rating scale; TNM, tumor, node, metastasis; RT, radiotherapy.

95% CIs. None of the evaluated variables showed a statistically significant association with overall survival. The results are summarized in **Table 2**.

The exploratory univariate subgroup analyses are shown in **Figure 2**. Survival differed significantly only between patients who received radical-dose radiotherapy and those who received palliative-dose radiotherapy ($P = 0.046$; **Figure 2A**). No significant associations with overall survival were observed for sex ($P = 0.68$; **Figure 2B**), TNM stage ($P = 0.46$; **Figure 2C**), ECOG PS ($P = 0.43$; **Figure 2D**), NRS pain score ($P = 0.093$; **Figure 2E**), treatment-naive versus previously treated status ($P = 0.48$; **Figure 2F**), requirement for bladder irrigation due to hematuria ($P = 0.55$; **Figure 2G**), prior bladder tumor embolization ($P = 0.74$; **Figure 2H**), or concurrent chemotherapy ($P = 0.93$; **Figure 2I**).

Toxicities and Adverse Events

The primary treatment objective in this study was palliative hemostasis. After 15 or more fractions of radiotherapy, treatment was temporarily interrupted if patients developed clinically evident symptoms, such as fatigue, anorexia, urinary irritation, or rectal irritation, that were considered potential radiotherapy-associated adverse events. During treatment interruption, supportive and symptomatic management was provided, including antibiotics, nutritional support, and traditional Chinese medicine preparations when clinically appropriate. Radiotherapy was resumed after symptom relief or permanently discontinued according to the patient's ECOG PS and treatment tolerance. Except for Grade 3 neutropenia in 4 patients, all other adverse events, including proctitis, cystitis, fatigue, decreased platelet count, renal dysfunction, and hematuria, were Grade 2 or lower. No severe radiotherapy-related adverse events were observed in this cohort. Notably, the 101-year-old patient completed radical-dose radiotherapy to 68 Gy. Adverse events are summarized in **Table 3**.

Discussion

Epidemiology and Clinical Challenges

The World Health Organization defines older adults as individuals aged 60 years or above, with those aged 60 to 74 years classified as young-old, those aged 75 to 89 years as old-old, and those aged 90 years or above as long-lived older adults [16]. In many medical studies, elderly, or older adult, patients are commonly defined as those aged 65 years or older [17]. Age is one of the strongest risk factors for cancer, and cancer incidence increases with advancing age. Bladder cancer is one of the most common malignancies of the urinary system and follows this age-related pattern, with a higher incidence in men [2,3]. In the present cohort, the median age was 82 years, with a range of 71 to 101 years, and the male-to-female ratio was 42: 7.

Some older adult patients with cancer are unable to receive standard treatment because of aging-related functional decline and multiple comorbidities. As a result, they may take

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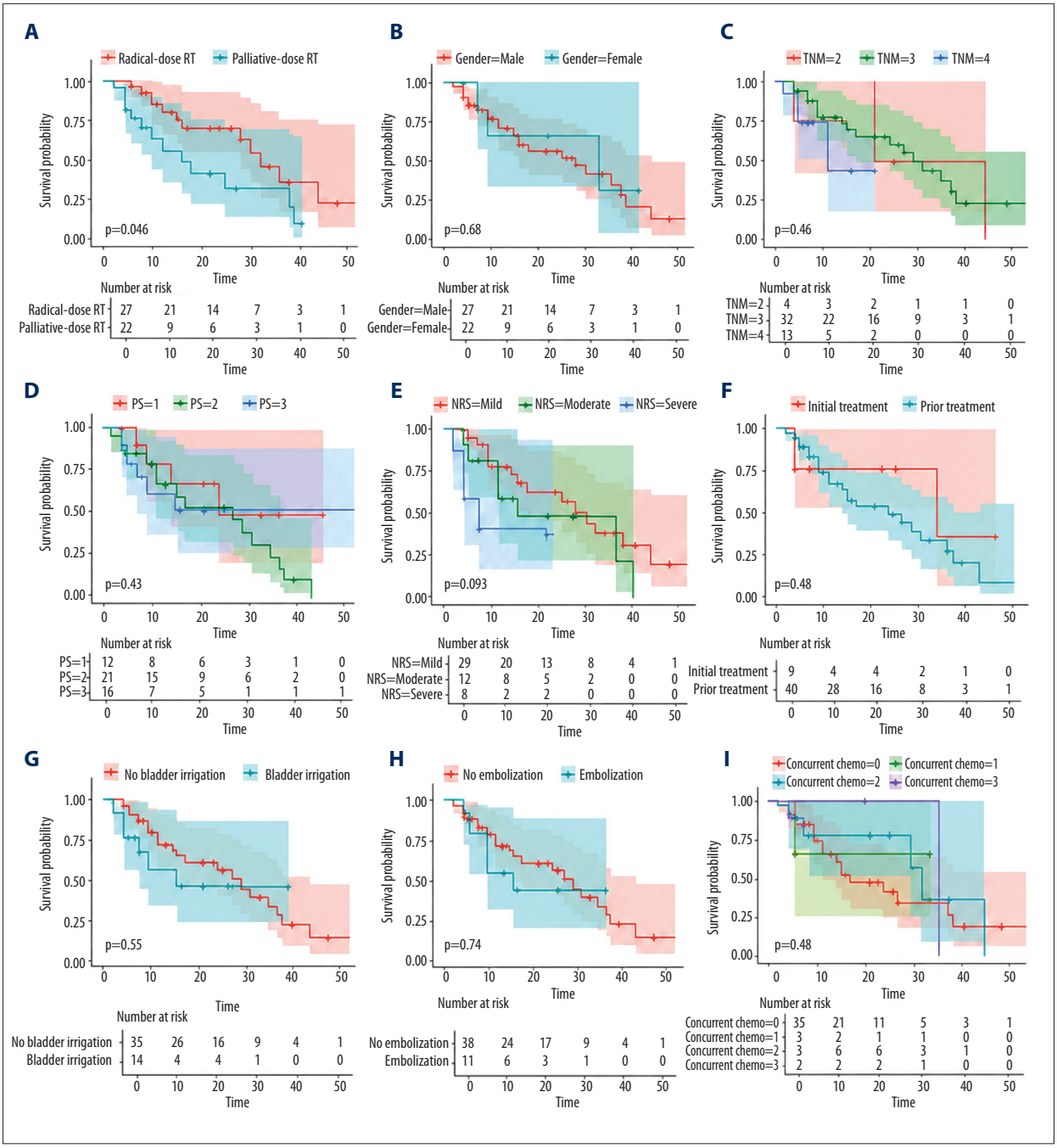

Figure 2. Exploratory univariate subgroup analyses of overall survival after radiotherapy. Kaplan-Meier survival curves comparing overall survival according to (**A**) radiotherapy dose category; (**B**) sex; (**C**) tumor, node, metastasis (TNM) stage; (**D**) Eastern Cooperative Oncology Group (ECOG) performance status; (**E**) numerical rating scale (NRS) pain score; (**F**) treatment history; (**G**) requirement for bladder irrigation due to hematuria; (**H**) prior bladder tumor embolization; and (**I**) concurrent chemotherapy.

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Table 3. Radiotherapy (RT)-related toxicities and adverse events according to Common Terminology Criteria for Adverse Events, version 5.0.

Adverse event during radiotherapy	Palliative-dose RT group (n = 22)	Radical-dose RT group (n = 27)
Cystitis		
Grade 1	4 (18.2%)	3 (11.1%)
Grade ≥2	0 (0.0%)	0 (0.0%)
Proctitis		
Grade 1	2 (9.1%)	4 (14.8%)
Grade ≥2	0 (0.0%)	0 (0.0%)
Hematuria		
Gross hematuria	0 (0.0%)	0 (0.0%)
Microscopic hematuria	19 (86.4%)	15 (55.6%)
Fatigue		
Grade 1	8 (36.4%)	11 (40.7%)
Grade 2	6 (27.3%)	4 (14.8%)
Grade ≥3	0 (0.0%)	0 (0.0%)
Neutropenia		
Grade 1	3 (13.6%)	5 (18.5%)
Grade 2	3 (13.6%)	3 (11.1%)
Grade ≥3	2 (9.1%)	2 (7.4%)
Grade ≥4	0 (0.0%)	0 (0.0%)
Thrombocytopenia		
Grade 1	2 (9.1%)	5 (18.5%)
Grade 2	0 (0.0%)	1 (3.7%)
Grade ≥3	0 (0.0%)	0 (0.0%)
Renal dysfunction		
Grade 1	1 (4.5%)	3 (11.1%)
Grade ≥2	0 (0.0%)	0 (0.0%)

a passive approach to treatment and delay seeking care until severe symptoms develop. The patients in this cohort were older adult patients with advanced bladder cancer who were unable to undergo surgery or chemotherapy, had discontinued or declined standard anticancer treatment, and were essentially managed in a hospice-oriented setting. They sought treatment because of persistent gross hematuria, which caused substantial psychological distress for both the patients and their families. In 14 patients, blood clots obstructed the urinary tract, causing urinary retention and requiring bladder irrigation. Because of concerns about radiation and limited understanding of radiotherapy, patients are often first presented to urology or interventional vascular departments rather than radiation oncology. Most patients were referred to oncology through multidisciplinary consultation or hospice-care pathways. Therefore, case accumulation was challenging, and only 49 patients were included over an 8-year period. Continued case collection and larger multicenter studies are warranted to further validate these findings.

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Surgical and Pharmacologic Management

The management of bladder cancer relies on multidisciplinary strategies integrating surgery, radiotherapy, and pharmacologic therapy to improve disease control. For potentially curable bladder cancer, surgery remains the cornerstone of treatment. Non–muscle-invasive bladder cancer is usually treated with transurethral resection of bladder tumor, whereas muscle-invasive bladder cancer is primarily managed with radical cystectomy. Adjuvant and systemic treatment options include intravesical chemotherapy, systemic chemotherapy, targeted therapy, and immunotherapy [9,10,12,13]. However, recurrence and progression remain important clinical challenges in bladder cancer management. After transurethral resection of bladder tumor, non–muscle-invasive bladder cancer has a high risk of recurrence, with reported recurrence rates ranging from approximately 50% to 80%, depending on tumor risk category, follow-up duration, and use of adjuvant intravesical therapy. Progression to muscle-invasive disease occurs in a smaller but clinically important subset of patients, particularly among those with high-risk or recurrent disease. Disease progression, distant metastasis, and disease-specific mortality may occur during long-term follow-up; therefore, selected patients with high-risk non–muscle-invasive bladder cancer may require more aggressive treatment strategies, including partial or radical cystectomy [8,10,12,13,18].

For muscle-invasive bladder cancer, radical cystectomy with pelvic lymph node dissection remains the standard surgical approach for surgically eligible patients. However, this procedure is highly invasive and is associated with substantial perioperative morbidity, particularly in older adult or frail patients. Large surgical series have reported 5-year overall survival of approximately 50% to 70% after radical cystectomy, depending on tumor stage, nodal status, and perioperative treatment [19,20]. Recurrence-free survival also varies substantially across risk groups, with poorer outcomes in patients with non–organ-confined or node-positive disease. In selected cases, perioperative systemic therapy and/or postoperative local radiotherapy may be required to reduce the risk of recurrence or metastasis. Nevertheless, because of high complication risks, frailty, comorbidities, and potential impairment of quality of life, invasive surgery and systemic therapies are often unsuitable or contraindicated in older adult patients.

Role of Radiotherapy

Radiotherapy can preserve bladder function, control local tumor growth, resolve hematuria, and relieve urinary symptoms, thereby offering potential advantages for improving quality of life. Radical radiotherapy has emerged as an alternative treatment option for patients with muscle-invasive bladder cancer who are unable or unwilling to undergo surgery. Duncan et al reported outcomes in 963 patients treated with radical radiotherapy, among whom T1, T2, T3, and T4 tumors accounted for 20%, 32%, 40%, and 8%, respectively. After bladder radiotherapy of 55 Gy in 20 fractions, 65% of patients achieved a complete response, and cystoscopic examination confirmed disappearance of lesions in 46%. The 5- and 10-year survival rates were 30% and 18%, respectively, and the corresponding local recurrence rates were 47% and 53% [21]. Zhang et al reviewed the latest research progress and clinical applications of radiotherapy in muscle-invasive bladder cancer, highlighting that radiotherapy plays an important role in bladder preservation and may provide a feasible alternative for patients who are unsuitable for or unwilling to undergo radical cystectomy [22].

Several studies suggest that radical radiotherapy can achieve outcomes comparable to surgery while better preserving bladder function and quality of life. Kotwal et al analyzed 169 patients, including 72 treated with radical cystectomy and 97 treated with radical radiotherapy. Although patients in the radiotherapy group were, on average, 7 years older than those in the surgical group, the 5-year overall survival was similar between the 2 groups, at 34.6% and 41.3%, respectively [11]. These findings suggest that radical surgery and radical radiotherapy may provide comparable survival outcomes, including in older patient populations.

Radiotherapy is also effective for controlling hematuria and improving symptoms. Liu et al applied 3-dimensional conformal radiotherapy in 23 patients with bladder cancer, using 3 to 8 Gy per fraction every other day, with a total tumor dose of 48 to 66 Gy. After treatment for 3 months, tumors had completely disappeared in 17 patients and decreased by more than 50% in 6 patients. Hematuria completely resolved, with a hematuria control response rate of 100%. No severe complications occurred during treatment, and mild bladder irritation symptoms in some patients were relieved with symptomatic management [23]. Therefore, for older adult patients who cannot tolerate or refuse cystectomy, or for those in whom chemotherapy alone is ineffective or intolerable, radiotherapy represents a feasible and practical treatment approach.

The relatively noninvasive nature of radiotherapy and its limited absolute contraindications represent important advantages compared with surgery and systemic pharmacologic therapy. Radiotherapy is widely used in cancer treatment, and a substantial proportion of patients with cancer receive radiotherapy during the course of their disease [24]. For older adult patients with bladder cancer and hematuria, especially those in whom bleeding causes urethral obstruction and requires continuous bladder irrigation, the patients and family members are generally willing to accept treatment if bleeding can be controlled. Because the hematuria is caused by bladder cancer, tumor-directed treatment is necessary to control bleeding at its source. When surgery is infeasible and pharmacologic therapy

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is contraindicated, radiotherapy may be the only feasible and effective local treatment option for patients with stable vital signs. After thorough communication with patients and their families and after obtaining signed informed consent, conventional fractionated radiotherapy was administered.

Clinical Treatment and Survival Outcomes

During radiotherapy, urine color, urinary irritation symptoms, blood clot-related urinary obstruction, and the need for bladder irrigation were monitored. After 1 week of radiotherapy, urine color became lighter, blood clots decreased, and bladder irrigation was gradually reduced. After 2 weeks, gross hematuria disappeared, urine color normalized, urinary irritation symptoms improved or resolved, and bladder irrigation was discontinued. After 3 weeks, gross hematuria remained absent. Radiotherapy was continued for 4 weeks until a palliative dose of 40 Gy was reached, at which point the hemostatic goal was achieved.

Treatment response was then comprehensively reassessed based on ECOG PS and imaging-based tumor shrinkage. For patients considered suitable for further dose escalation, the willingness of the patients and their families to continue treatment was discussed again. After reassessment and communication, 9 patients discontinued radiotherapy because of withdrawal of informed consent or physician-assessed unsuitability for further treatment, whereas 40 patients continued radiotherapy. In this cohort, initial palliative radiotherapy of approximately 30 Gy achieved rapid hemostasis and allowed selected patients to undergo further escalation to radical-dose radiotherapy. This strategy suggests a potential role of radiotherapy in both symptom relief and longer-term local disease control, particularly in patients with limited treatment options.

The therapeutic effects and adverse reactions of radiotherapy usually become progressively evident with an increasing cumulative dose [25]. The patients in this cohort were older adult patients with advanced bladder cancer and bleeding who were unsuitable for standard treatment and were essentially receiving hospice-oriented care. Treatment expectations were therefore limited, and the primary therapeutic goal was hemostasis. After bleeding was controlled, compliance among patients and/or family members improved, providing an opportunity to adjust the treatment plan from palliative radiotherapy to radical-dose radiotherapy according to disease stage and ECOG PS.

In real-world oncology practice, multimodal treatment is common. Among the 40 patients who underwent dose escalation, 14 received weekly concurrent chemotherapy with gemcitabine plus cisplatin or paclitaxel plus cisplatin to enhance the radiotherapeutic effect; 3 patients received 1 dose, 9 received 2 doses, and 2 received 3 doses. During the initial 4 weeks, radiotherapy alone was administered to facilitate treatment completion and achieve rapid hemostasis, without concurrent chemotherapy. The favorable hemostatic effect increased confidence among the physicians and patients, and no radiotherapy-related adverse events were observed during this period. Among the 40 patients who underwent dose escalation, 13 discontinued radiotherapy at 52 to 56 Gy because of declining EGOC PS associated with aging, anorexia, and fatigue, withdrawal of informed consent, or physician decision. These 13 patients included 2 who received 1 dose and 4 who received 2 doses of concurrent chemotherapy. The remaining 27 patients completed 62 to 72 Gy of radiotherapy; among them, 1 received 1 dose, 5 received 2 doses, and 2 received 3 doses of concurrent chemotherapy.

A radiotherapy dose of 60 Gy or higher is generally considered radical-dose radiotherapy [10,26]. In this retrospective study, patients receiving 60 Gy or higher were classified into the radical-dose radiotherapy group. The term “radical” in this study refers to the radiotherapy dose rather than definitive tumor cure. Overall, 27 patients received radical-dose radiotherapy and 22 received palliative-dose radiotherapy.

After adjustment for potential confounders using Cox proportional hazards modeling, overall survival was not significantly associated with radiotherapy dose category, sex, TNM stage, ECOG PS, NRS pain score, treatment-naive versus previously treated status, bladder irrigation for hematuria, bladder tumor embolization, or concurrent chemotherapy. Nevertheless, the median overall survival reached 14 months, and exploratory subgroup analysis showed a difference in survival between the radical-dose and palliative-dose radiotherapy groups ($P = 0.046$), suggesting a potential clinical benefit of dose escalation in selected patients. This finding should be interpreted cautiously because of the small sample size, advanced age and poor physical condition of the patients, limited treatment expectations, variable compliance, and lack of detailed recording and stratified analysis of post-radiotherapy treatments. Therefore, although the observed difference between radical-dose and palliative-dose radiotherapy suggests that dose escalation may be associated with improved survival outcomes in selected patients, causality cannot be established in the absence of a randomized control group and fully adjusted analysis.

Adverse Events

The patients in this cohort were older adult patients with bladder cancer and bleeding who were unsuitable for standard treatment. They were generally older, physically frail, and had limited treatment tolerance. Therefore, safety was the primary consideration, and all patients received radiotherapy during hospitalization. Radiotherapy was temporarily interrupted when early signs of adverse reactions were observed, and active supportive and symptomatic management was provided. Treatment was resumed after symptom resolution.

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For patients with advanced age and frailty, radiotherapy was sometimes delivered intermittently according to performance status, even in the absence of obvious adverse reactions, following the principle of continuing treatment when feasible and withholding treatment when necessary. Treatment interruptions ranged from 1 to 4 weeks, and the final radiation dose was adjusted according to the duration of interruption [27,28]. Ultimately, 1 patient received a total dose of 72 Gy. According to the Common Terminology Criteria for Adverse Events, version 5.0, except for Grade 3 neutropenia in 4 patients, all other adverse events were Grade 2 or lower. No severe radiotherapy-related adverse events occurred in this cohort.

Limitations

After completion of either palliative-dose or radical-dose radiotherapy, patients entered real-world follow-up treatment and management. Depending on their general condition, some patients subsequently received systemic therapies, including antiangiogenic agents, programmed death-1/programmed death-ligand 1 inhibitors, or chemotherapy, which may have contributed to overall survival. Although this approach was consistent with routine clinical practice, it increased the complexity of survival analysis. The lack of detailed recording and stratified analysis of post-radiotherapy systemic treatments is therefore an important limitation. Nevertheless, the hemostatic effect was directly associated with radiotherapy, and control of bleeding provided the clinical basis for subsequent treatment.

Because of ethical constraints, an untreated control group could not be established. Persistent bladder cancer–related hematuria can lead to clinically serious consequences, including ongoing blood loss, urinary tract obstruction caused by blood clots, urinary retention, and postrenal renal failure. In patients with active bleeding, withholding potentially effective hemostatic treatment would be ethically difficult. Therefore, although the absence of a control group limits causal interpretation, a radiotherapy versus no-radiotherapy design would not have been appropriate in this clinical context. In addition, natural-history data for persistent bladder cancer–related hematuria are limited. In practice, the palliative-dose and radical-dose radiotherapy groups provided an exploratory comparison, but this comparison remains subject to selection bias and confounding.

This study has several limitations, including its retrospective single-center design, small sample size, absence of a negative control group, heterogeneity of previous treatments, and lack of detailed stratification of post-radiotherapy systemic therapies in the real-world setting. Despite these limitations, the study provides clinically relevant observations for the management of older adult patients with advanced bladder cancer and hematuria and highlights the potential role of radiotherapy in symptom control in this population.

Conclusions

Bleeding imposes a substantial physical and psychological burden on patients. In this cohort, patients sought treatment because of persistent bladder cancer-related hematuria. For patients who were unable to undergo surgery and were unsuitable for chemotherapy, palliative radiotherapy achieved hemostasis in all cases according to the predefined clinical assessment, relieved urinary symptoms and fear of bleeding, and may have improved quality of life. In selected patients, after bleeding control and improvement in general condition, reassessment allowed escalation from initial palliative radiotherapy to radical-dose radiotherapy and subsequent systemic treatment, which may have contributed to longer overall survival. These findings suggest that radiotherapy can reliably control hematuria, relieve symptoms, and provide meaningful clinical benefit in older adult patients with advanced bladder cancer who are unsuitable for surgery or chemotherapy. Radiotherapy may therefore represent a safe, feasible, and practical option for local tumor control and symptom palliation, while helping preserve patient dignity during care. The limitations of this study include the advanced age and frailty of the cohort, the late-line or hospice-oriented disease stage, the small sample size, limited stratification, and the fact that some patients declined further radiotherapy after bleeding was controlled. Further studies with larger cohorts and more refined stratified analyses are needed to optimize treatment protocols, improve clinical outcomes, and provide more precise evidence for this patient population and potentially for older adult patients at earlier disease stages.

Availability of Data and Material

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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Disclosure

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Declaration of Figures' Authenticity

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